NOVEL BULKY FLUORINATED LIGANDS FOR HOMOGENEOUS CATALYSIS

Jamie J. R. Frew

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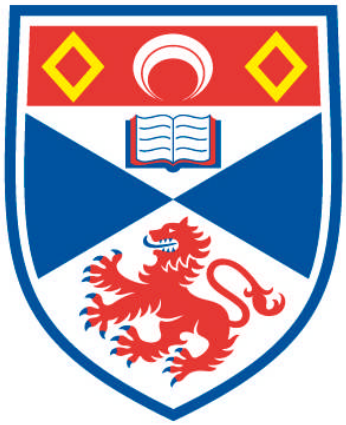
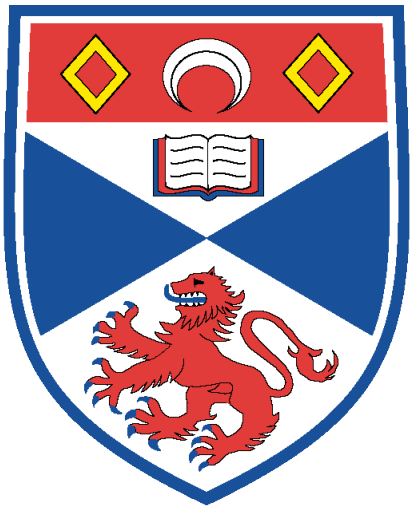


2008

Novel Bulky Fluorinated Ligands for Homogeneous Catalysis.



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A thesis presented by Jamie J. R. Frew in application for the degree of Doctor of Philosophy.

February 2008

Acknowledgments

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Abstract

A series of novel monodentate and bidentate phosphine ligands substituted with bulky *tert*-butyl and fluorinated aryl groups have been synthesised. Borane protection has proved to be an excellent method for easy synthesis and purification of bidentate ligands in some cases. However, several of the bulky fluorinated ligands do not form stable borane complexes leading to complications in the synthesis and purification of these compounds. By reaction with transition metal platinum and palladium precursors, it was possible to form dichloride complexes from the synthesised ligands, which were characterised by X-ray crystallography. The complexes were found to be effective catalysts for the hydroxycarbonylation of vinyl arenes (yields of up to 95 % with 3 mol% catalyst). An unsymmetrical bidentate complex (**3.18**) in combination with *para*-toluenesulfonic acid and LiCl promoters has given exceptional (for a diphosphine ligand) regioselectivity for the branched acid (98.7 % branched) in the hydroxycarbonylation of styrene. The role of the promoters has been found to be crucial in deciding the activity and selectivity in this reaction.

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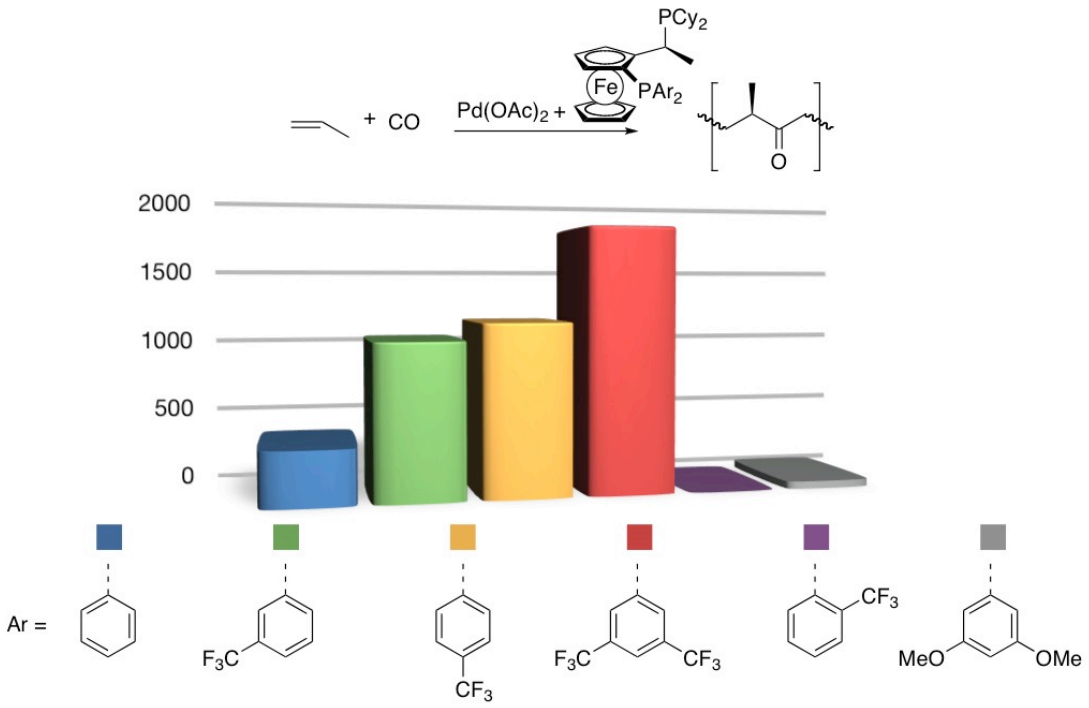
Abbreviations.

Å	Angstrom.
$	United States dollars
°	Degrees
Ar	Aromatic group
Ar^f	Fluorine containing aryl group
B	Branched isomer
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
cat.	Catalyst
COD	1,4-Cyclooctadiene
Conc.	Concentrated
d	Doublet
δ	Chemical shift
dba	(1*E*,4*E*)-1,5-diphenylpenta-1,4-dien-3-one
DMF	N,N-dimethylformide
DPPE	1,2-Bis-(Diphenylphosphino)ethene
DPPF	1,1'-Bis-(Diphenylphosphino)ferrocene
DPPP	1,3-Bis-(Diphenylphosphino)propane
dtbpx	α,αbis(di-*tert*-butylphosphino)xylene
Et	Ethyl
Hr	Hour
Hz	Hertz
L	Linear isomer
μ	Bridging
m	multiplet
Me	Methyl
Mgs	Milligrams
MHz	Megahertz
ml	Millilitre
mM	Millimolar
Ms	Methane Sulfonyl
NBD	2,5-Norbornadiene
NMR	Nuclear magnetic resonance
p	pentet
Ph	Phenyl
ppm	Parts per million
q	Quartet
R	Organic group
rac	Racemic
σ	Sigma
s	sextet
σ	Sigma bond
σ*	Sigma antibonding orbital
t	Triplet
T.O.F.	Turn over frequency
t-Bu	Tertiary Butyl

Abbreviations.

Tert	Tertiary
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TsOH	*Para*-toluenesulphonic acid
βn	Natural Bite Angle
θ	Tolman cone angle

1. Introduction: Fluorinated Ligands in Homogeneously Catalysed Reactions.



1.1. Background.

The use of homogeneous catalysis represents one of the most efficient and important methods for carrying out chemical transformations. There are many processes in industry (with more being developed every year) that utilise organo-transition metal catalysts. The development of selective chemical processes generally requires modifying ligands on the transition metal centre. Although P, N, O, S, Se, C and Te ligands are all known, by far the most important class in catalysis are the phosphorus based ligands. These ligands have a unique ability to stabilise metals in several oxidation states and geometries and, more importantly, they can be tuned to radically change the reactivity of a catalyst. Simple changes to the structure of a phosphorus ligand can completely alter the product distribution, activity, regiochemistry or enantioselectivity of a transition metal catalysed reaction. Indeed, there are many processes that do not work at all unless the correct choice of ligand is made.

In an attempt to rationalise what features can be tuned within phosphorus ligands, chemists have classified according to their co-ordinate modes (e.g. monodentate, bidentate, tridentate, tetradentate and hemilabile) and stereoelectronic properties. The stereo electronic properties are quantified in the following ways:

1.1.1. Cone angle (θ).

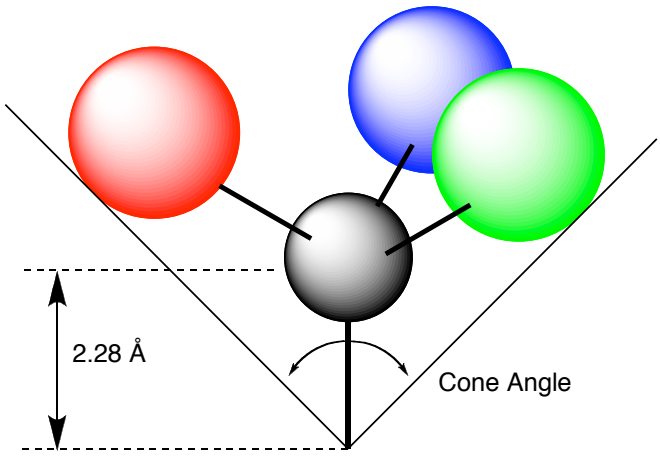


Figure 1 - 1. Graphic representation of Tolman's cone angle concept.

A steric effect is a change in the properties of a molecule as a result of a change to the structure. An example of this is replacing an *ortho*-$CH_3C_6H_4$ with *para*-$CH_3C_6H_4$. The cone

angle (θ), introduced by Tolman,[1] is a quantative measure of the steric effect of the substituents surrounding phosphorus. θ for symmetrical ligands is the apex angle of a cone centred 2.28 Å from the centre of the P atom that just touches the outer Van der Waals radii of the outermost atoms of the substituents (Figure 1 – 1). Steric effects can be as important if not more important than electronic effects in deciding the properties of phosphorus ligands. Therefore, there is considerable interest in developing sterically demanding phosphines as these make up one of the most important ligand classes in homogeneous catalysis.[2-7]

1.1.2. Electronic measurements.

The change in the properties of a molecule when changing a substituent from *para*-MeO-C_6H_4 to *para*-Cl-C_6H_4 is a good example of an almost purely electronic effect (it should be noted that changes in electronic properties can induce steric changes and vice versa). The quantative measurement of electronic effect of ligands is made by observing differences in CO stretching frequencies in metal complexes such as $Ni(CO)_3L$ where L is a phosphine ligand.[1] The CO stretching frequency is sharp and readily measurable, because of this it provides a measure of the effect phosphorus substituents have on the metal centre.

1.1.3. Bite angle.

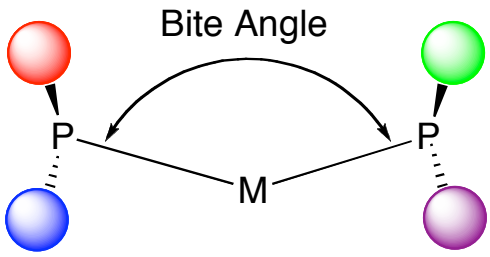


Figure 1 - 2. Graphic representation of the bite angle measurements.

The natural bite angle (βn) is one of the most important parameters for bidentate ligands and, is defined as the preferred chelation angle of a bidentate ligand, determined only by the ligand backbone constraints, and not by metal valence angles.[8] It has been discovered that there is a strong correlation between the natural bite angle of chelating diphosphines and regioselectivity in Rh hydroformylation.[9-13] This may be the result of the tendency of diphosphines with bite angles of near 120˚ to form diequatorial complexes, and the mechanistic implications of this during the catalytic cycle.

1.1.4. Ligand metal interactions.

According to the Dewar-Chatt-Duncanson derived model, the σ bond between the metal p or d orbitals and the phosphorus lone pair is supplemented by back donation of the electron density from the filled d-orbitals of the metal into either the empty d-orbitals or a σ*orbital of phosphorus (Figure 1 – 3). It is currently thought that the latter is more likely due to the relatively high energy of a phosphorus d-orbital.[14-19]

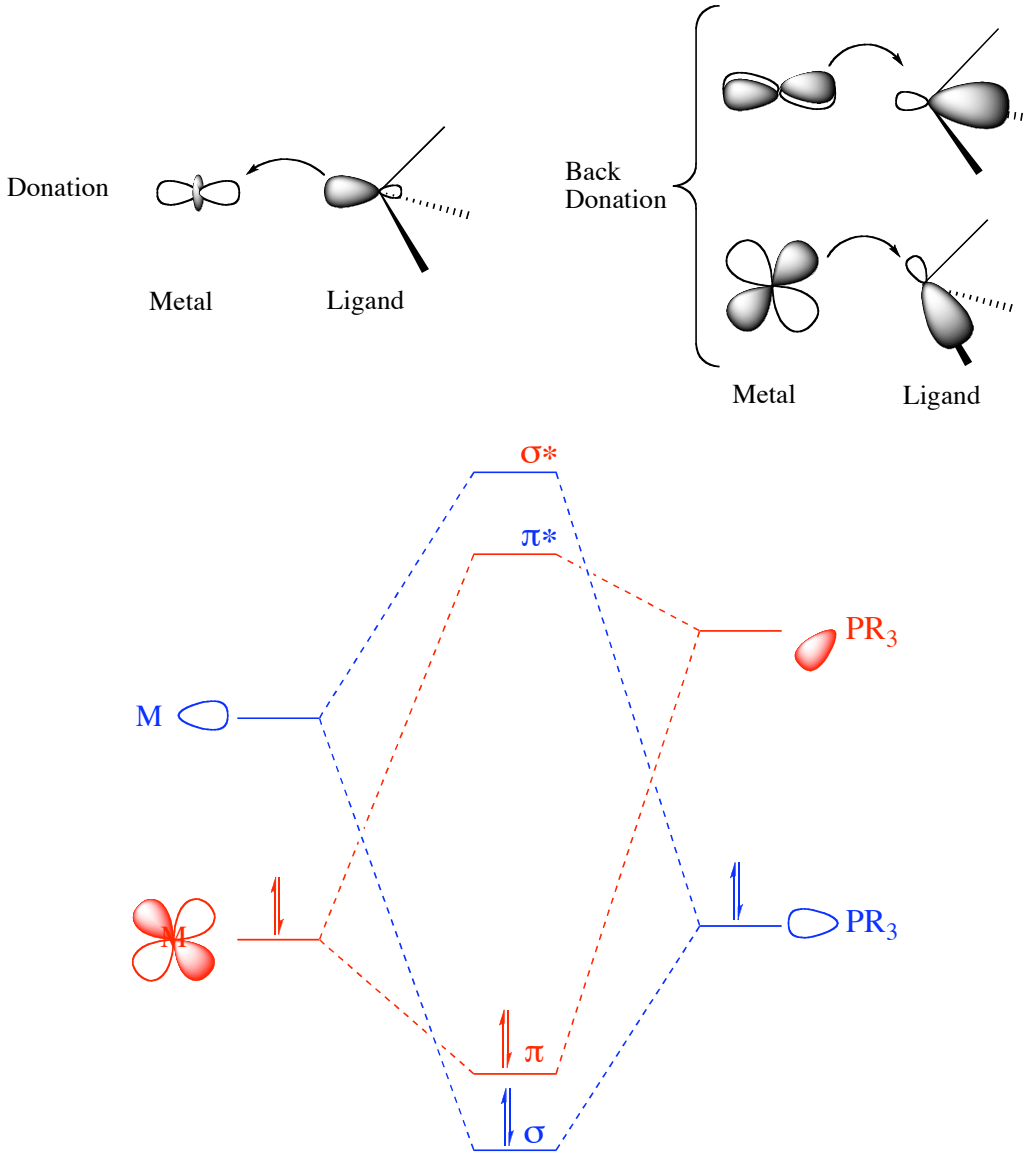


Figure 1 - 3. Schematic representations of ligand metal interactions for π acceptor phosphines.

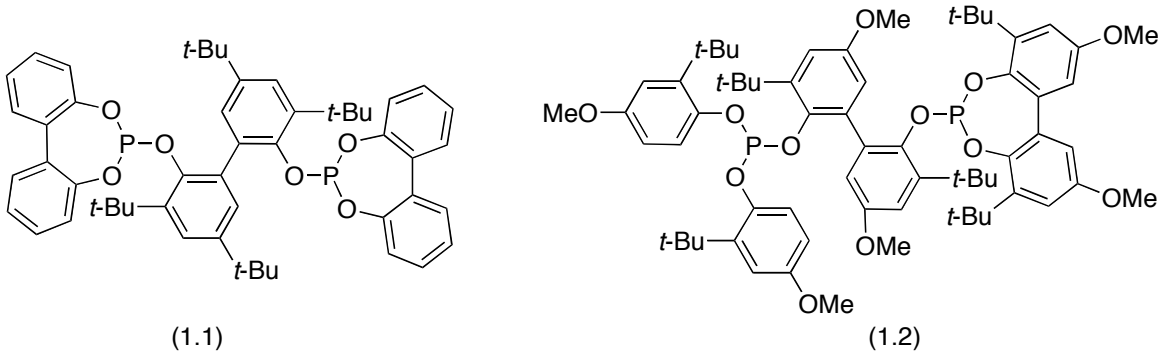
$$PMe_3 < PPh_3 < P(OPh)_3 < P(NR_2)_3 < CO \approx PF_3$$

Better π acceptors →

Figure 1 - 4. Relative π accepting ability of some common ligands

It is thought that in phosphorus ligands, electron poor groups lower the energy of the π accepting orbitals increasing the π acceptor character of the ligand (Figure1 – 4). The greater the π acceptor character of phosphorus the less the metal will tend to donate electron density to other π accepting ligands, especially those in the *trans* position to the phosphorus ligand. This can lead to significantly modified catalytic behaviour and, for this reason, attempts have been made to exploit the changes in the electronic characteristics of transition metal complexes caused by the presence of electron poor ligands in a number of homogeneously catalysed reactions.

1.1.5. P-O bond containing ligands in homogeneous catalysis



(1.1) (1.2)

Figure 1 - 5. Examples of phosphites developed by Union Carbide.

Rhodium complexes derived from phosphites **1.1** and **1.2**, which are members of a family of diphosphites developed by Union Carbide, are highly active in hydroformylation and have achieved high selectivity for linear products under milder reaction conditions than those traditionally used.[20-22] The presence of electron withdrawing oxygen atoms is thought to be crucially important to the function of this ligand, due to the enhanced π acceptor character this gives the ligand. This π acceptor character makes CO binding slower with respect to the β elimination of hydrogen, the result of this is isomerisation, making this type of catalyst very good at producing linear products from mixtures of internal and terminal alkenes. This is an important goal in industry and synthetic organic chemistry, as isomeric mixtures of alkene feedstocks are significantly cheaper than pure single isomer feedstocks.[6, 23-26] Whilst these phosphite ligands do exhibit desirable catalytic activity, mention should be made of the fact that the P-O bond is intolerant of water, acidic conditions and strong nucleophiles. This limits the potential applications for phosphites in homogeneous catalysis. Thus although hydrolysis of the Union Carbide ligands is partially prevented by their cyclic structure, steric bulk and

lipophilicity of the neighbouring substituents, they have not seen widespread use despite many years of research. Therefore, there is considerable interest in developing alternative ligands, which have a similar π acceptor character but are more stable under catalytic conditions.[27-29]

1.2. Fluorinated ligands in homogeneously catalysed reactions.

Fluorinated ligands have received much attention in recent years due to their wide range of potential applications. The electron withdrawing character of fluorine and larger size compared to hydrogen (van der Waals radius of 1.47 Å compared with 1.20 Å) have a profound influence on phosphorus ligands and their transition metal complexes.[30-37] Fluorinated phosphine ligands have the advantage of being more robust than phosphites as the P-C bond is relatively inert and, due to the very high strength of the bond, examples of C-F bond activation are rare.[38-41] In addition, fluorinated phosphines are often less prone to oxidation than more electron rich phosphines.[42, 43]

1.2.1. Reductive elimination.

By reducing the charge on the metal centre, electron poor ligands facilitate reductive elimination. It has been shown that the highly fluorinated Pt complex **1.3** undergoes reductive elimination under milder conditions than the corresponding perfluoroaryl ligand complex (**1.4**), whilst the corresponding DPPE complex (**1.5**) is thermally stable (Figure 1 – 6).[34, 44]

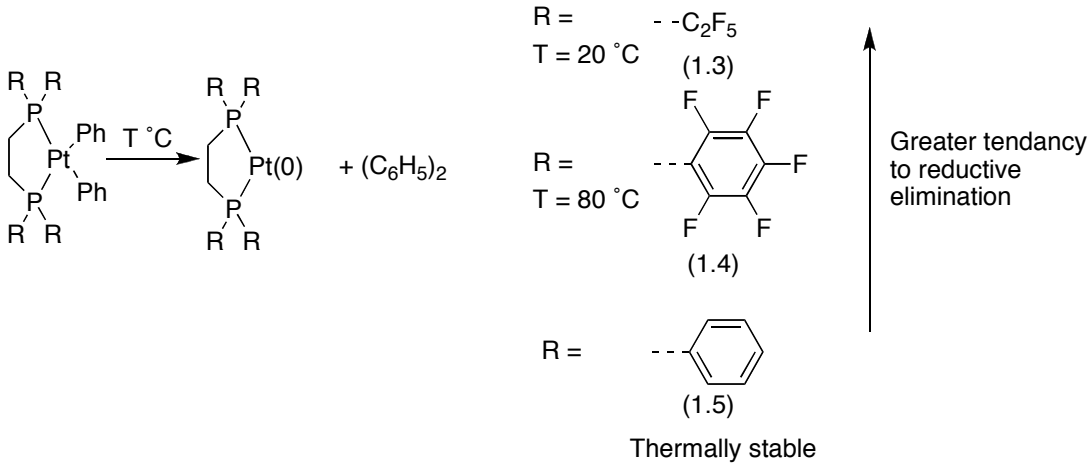


Figure 1 - 6. Trends in the reductive elimination of biphenyl from ethylene bridged platinum diphosphine complexes.

1.2.2. Oxidative addition.

Electron rich ligands are known to be more active in oxidative addition as the higher electron density induced makes the metal centre more nucleophilic toward incoming reactants.[45] Amatore and co-workers have found that there is a strong linear correlation between the rate of oxidative addition of phenyl iodide to a series of palladium triarylphosphine complexes and the Hammett values of the substituents in the *para* of the positions of the aryl rings (Figure 1 - 7).[46]

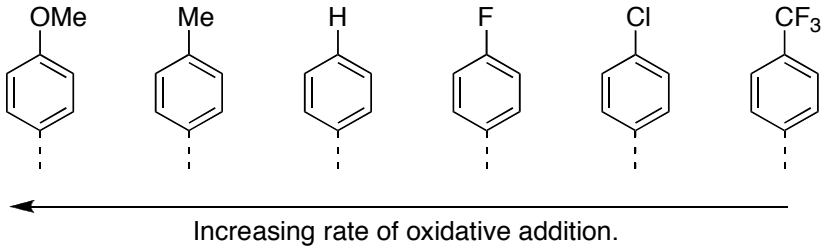
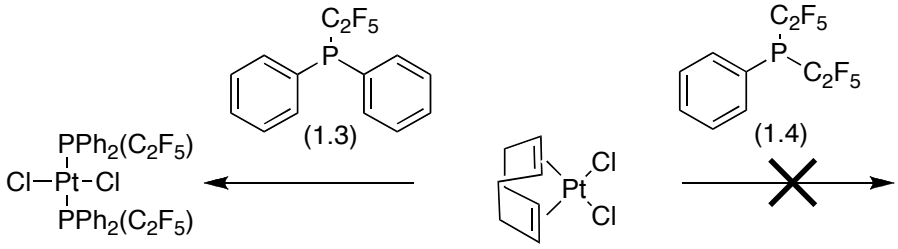


Figure 1 - 7. Trends in the rate of oxidative addition to palladium triaryl phosphine complexes.

1.2.3. Coordination chemistry.

1.2.3.1. Fluoroalkyl substituted ligands.

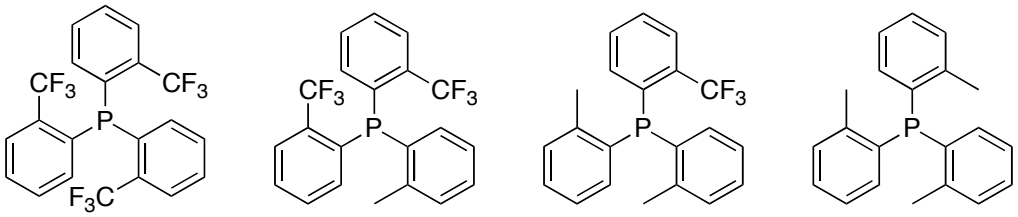
In general, it has been found that highly electron withdrawing fluoroalkyl ligands coordinate poorly with transition metals. This is mainly due to lower σ donation ability incurred by the presence of fluoroalkyl substituents on phosphines.[34, 35] The effect of increasing fluoroalkyl content is illustrated in work by Roddick and co-workers which shows that ligand **1.3** is capable of displacing the labile cyclooctadiene ligand from the platinum dichloride complex whereas the more highly fluorinated analogue **1.4** cannot (Scheme 1 – 1).[41]



Scheme 1 - 1. Coordination behaviour for phosphines with varying fluoroalkyl content.

1.2.3.2. Fluorine or trifluoromethyl substitution in *ortho* positions.

When F or trifluoromethyl substitution takes place in the *ortho* position, the large size of fluorine means that significant changes to the cone angle also take place. The steric congestion around the phosphorus centre combined with the lower basicity of fluorinated phosphines, can cause non-typical binding behaviour or complete failure to bind. Kemmit and co-workers have described the synthesis of a series of tris(pentafluorophenyl)phosphine transition metal complexes. In contrast to triphenylphosphine, which readily forms complexes at room temperature, *ortho*-fluorinated phosphines required refluxing for several hours in order to form complexes, and when formed these are often more coordinatively unsaturated. In addition these ligands were easily displaced by triphenylphosphine and triphenylphosphite, and also by cyclo-octa-1,5-diene, a weakly coordinating ligand.[36, 37, 47] The effect of trifluoromethyl substitution in *ortho* positions is illustrated by the coordination behaviour of the phosphines below (Figure 1 – 8).



	(1.5)	(1.6)	(1.7)	(1.8)
θ =	**205°**	**203°**		**194°**
K =	**0**	**0.06**	**0.6**	**Stable adduct**

Figure 1 - 8. Cone angles and binding constants, in the presence of $[Fe(CO)_4(PhCH=CH_2)]$, for a range of *ortho* substituted monophosphines.

It is evident, that as the number of *ortho* CF_3 groups decreases, the cone angle decreases and the ligands show increased tendency to form complexes (shown by the value of the binding constant K) in the presence of $[Fe(CO)_4(PhCH=CH_2])$. This combined with the fact that $(3\text{-}CF_3C_6F_3)_3P$ and $(4\text{-}CF_3C_6F_3)_3P$ (which one would expect to be electronically similar) form stable complexes readily, shows that trifluoromethyl substitution in *ortho* positions can produce significant differences in coordination behaviour.[48] The difference in coordination and catalytic chemistry of bulky *ortho*-substituted ligands is emphasised by the results obtained by Pringle and Clarke.[28] The bulky electron poor ligands $(C_6F_5)_3P$ and $(ortho\text{-}CF_3\text{-}C_6H_4)_3P$ either did not react with the well known precursor $[PtCl_2(SMe)_2]$ or gave a mixture of

several products after extended refluxing. In contrast (3,5-CF_3-C_6H_3)$_3$P gave [*trans*-L_2PtCl_2] quantatively at room temperature. Similar types of observations were made for the reactions with other well-known precursors. (C_6F_5)$_3$P and (*ortho*-CF_3-C_6H_4)$_3$P (**1.5**) also failed to react with [Rh(COD)$_2$]OTf whereas (3,5-CF_3-C_6H_3)$_3$P reacts instantly. In se*para*te work, Suomalainen and co-workers have reported that (*ortho*-CF_3-C_6H_4)$_3$P gives an unusual dinuclear complex [$Rh_2(CO)_3(\mu\text{-}Cl)_2${P(*ortho*-$CF_3$)Ph)$_3$]$_2$ in reaction with [$Rh_2(CO)_4(\mu\text{-}Cl)_2$] as opposed to the more common complexes of the type [*trans*-Rh(PAr_3)$_2$(CO)Cl] one may expect.[49] One feature of these sterically congested phosphine ligands is that they have a tendency to form *trans* complexes as opposed to *cis* complexes, which are typically formed by triphenyl phosphine analogues. Hope and co-workers have found that *ortho* perfloroalkyl substituted triphenylphosphine analogues PPh_2(2-$C_6H_4CF_3$) and PPh_2(2-$C_6H_4C_6F_{13}$) exclusively formed *trans* complexes in reaction with platinum and rhodium precursors, as opposed to the *cis* isomers that are formed by the *para* analogues.[50, 51] The differences in electronic character are considered negligible in these reactions, therefore the preference for the formation of the *trans* isomers for these phosphines is thought to be due to repulsive forces between the bulky *ortho* groups.

1.3. Catalysis.

1.3.1.1. Hydroformylation with monodentate ligands.

Due to the apparent electronic similarity of fluorinated phosphines and phosphites it was hoped that it would be possible to develop phosphines which display similarly desirable catalytic activity in the hydroformylation reaction, without the drawbacks associated with the labile P-O bond. However, it has been found that (C_6F_5)$_3$P and (*ortho*-CF_3-C_6H_4)$_3$P give virtually inactive catalysts for Rh catalysed hydroformylation, whereas (3,5-CF_3-C_6H_3)$_3$P and the less bulky ligand (3,4,5-$C_6F_3H_2$)$_3$P give catalysts that are more active than commercially applied triphenylphosphine (Table 1 – 1).[28] Even so, the activity in these reactions is an order of magnitude lower than that seen in reactions catalysed with active phosphites.[52]

Ligand	Linear/branched ratio	Turnover frequency
$(C_6F_5)_3P$	0.6	<10
$(2\text{-}CF_3\text{-}C_6H_4)_3P$ (**1.6**)	0.6	<10
$(3,5\text{-}CF_3\text{-}C_6H_3)_3P$	3.0	400
$(3,4,5\text{-}C_6F_3H_2)P$	2.5	400
$(C_6H_6)_3P$	2.9	350

Table 1 - 1. 1-Hexene hydroformylation activity for a range of monodentate phosphines as observed by Clarke and Pringle.

This trend is repeated in the work of other investigators: moderately fluorinated ligands tend to catalyse the hydroformylation reaction at a rate higher than PPh_3, however increasing fluorine substitution, especially in the sterically demanding *ortho* position, does not lead to further increases in catalytic activity. Instead, this leads to catalytic results which are similar to those seen in the absence of ligand, probably due to poor coordination. [53, 54] An exception to this is Suomalainen and co-workers' finding that when a single aryl ring is substituted with CF_3 in the *ortho* or *para* position the hydroformylation of 1-hexene is completely blocked. This unexpected finding contrasts with the enhanced activity which Fujita and co-workers observed for $Ph_2(C_6F_5)P$ in the hydroformylation of the same substrate.[53] There is no clear explanation for this difference in activity, though changes in ligand polarity have been invoked.

1.3.1.2. Hydroformylation with bidentate fluorinated ligands.

In the hydroformylation of styrene and related compounds, Chan and co-workers have reported that a rhodium catalyst based on **1.9** has shown far higher selectivity towards the branched aldehyde than DPPE (Figure 1 – 9). In all cases the fluorinated catalyst gave conversions of 100 %, with selectivity for the branched aldehyde in excess of 10:1 for all substrates. The regiocontrol seen in these reactions is surprising as highly fluorinated ligands often coordinate poorly. However a 5 mol% catalyst concentration was used, and the reaction was run for 24 hours, so the turn over frequency is perhaps lower than 1 hr^{-1}.

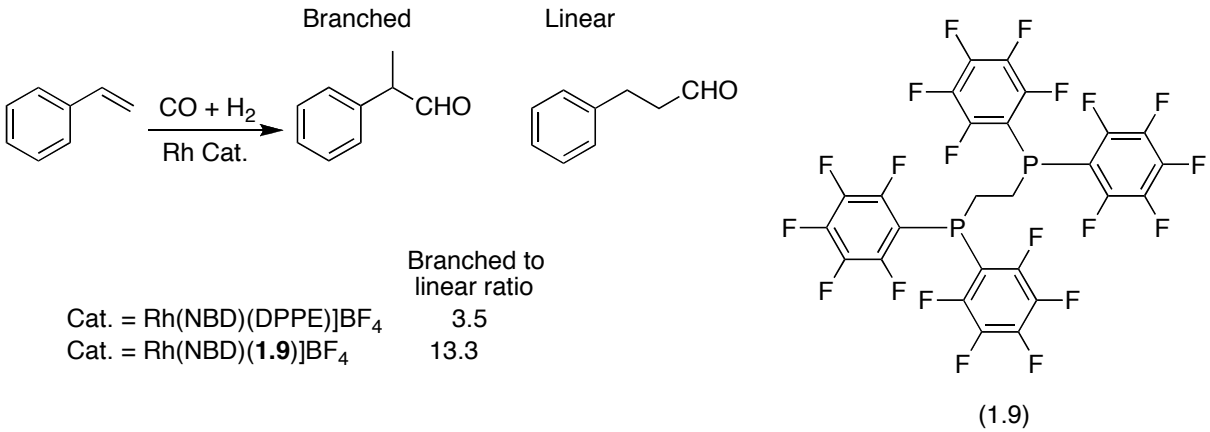
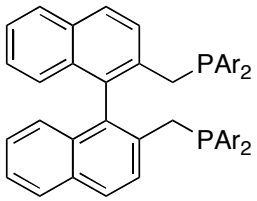


Figure 1 - 9. Selectivity observed in the hydroformylation of styrene.

In the rhodium catalysed hydroformylation of 1-hexene using ligand **1.9** in a variety of conventional solvents, and at a considerably lower catalyst concentration, Fujita and co-workers have found catalytic activity similar to, or slightly less than, that seen in the absence of modifying ligand.[53] These results are more consistent with the poor coordination expected of this poor σ donor which is also fairly bulky ($\theta = 151°$).[55] Fink and co-workers have reported that a ruthenium cluster formed by the reaction of **1.9** with $Ru_3(CO)_{12}$ is more active in the hydroformylation of ethene and propene than clusters formed using corresponding cyclohexyl substituted phosphines and the parent carbonyl complex. Whilst the activity of this catalyst is reasonable, the selectivity in these reactions was at best moderate.[56]

Klein and co-workers have reported the synthesis of a series of fluorinated NAPHOS derived ligands (Figure 1 – 10) which form Rh complexes that hydroformylate 1-alkenes in good yields with higher activity and good selectivity for the *n*-aldehyde compared with the parent ligand.[57] The catalysts have been found to be highly stable under these conditions. The most striking feature of these fluorinated catalyst systems is their phosphite-like ability to isomerise the 2-alkenes before efficient hydroformylation, resulting in *n*:*i* ratios of over 10:1 in most cases. IPHOS (**1.11**) in particular achieves almost as high regioselectivity and rate for 2 alkenes as it does for 1-alkenes, in contrast with the results achieved with the 3,5-methyl derivative (**1.12**.) (Table 1 – 2).



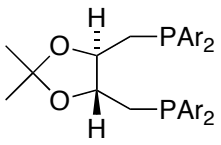
(1.10) Ar = Ph (NAPHOS)
(1.11) Ar = 3,5-$CF_3C_6H_3$, (IPHOS)
(1.12) Ar = 3,5-MeC_6H_3

Figure 1 - 10. NAPHOS derivatives tested in the hydroformylation of internal and terminal alkenes.

Ligand	Substrate	Yield (%)	B/L ratio	TOF [Hr^{-1}]
1.11	1-Pentene	82	96:4	512
1.11	2-Pentene	68	91:9	425
1.12	1-Pentene	76	81:19	475
1.12	2-Pentene	11	78:22	69

Table 1 - 2. Comparison of Rh catalysed hydroformylation activity using fluorinated and non-fluorinated NAPHOS derivatives for internal and terminal alkenes.

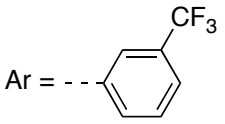
In the rhodium catalysed asymmetric hydroformylation of vinyl acetate a fluorinated DIOP derivative (**1.14**) has been found to be capable of a similar degree of chiral induction as the unsubstituted parent, yet over twice as active.[58] This effect is thought to be largely the result of electronic differences, as the substitution with CF_3 groups at the *meta* position produces little change to the steric environment at the site of catalysis.



Ar = C_6H_5

DIOP (1.13)

0.52 mol/L/h
ee = 33 %



m-CF_3 DIOP (1.14)

1.37 mol/L/h
ee = 30 %

Figure 1 - 11. Ligands used in the asymmetric hydroformylation of vinyl acetate with examples of activity.

Casey and co-workers have tested a series of symmetrical fluorinated diphosphine ligands with a range of bite angles in rhodium catalysed hydroformylation of 1-hexene in an attempt to correlate the catalytic activity with the mode of coordination (diequatorial (ee) or equatorial-apical (ea)) that electron poor phosphines adopt.[59] The results showed that the turnover rate is greater for the fluorinated phosphines and that there is a higher selectivity for

the linear aldehyde when both electron poor phosphines are both in the equatorial position (Figure 1 -12).

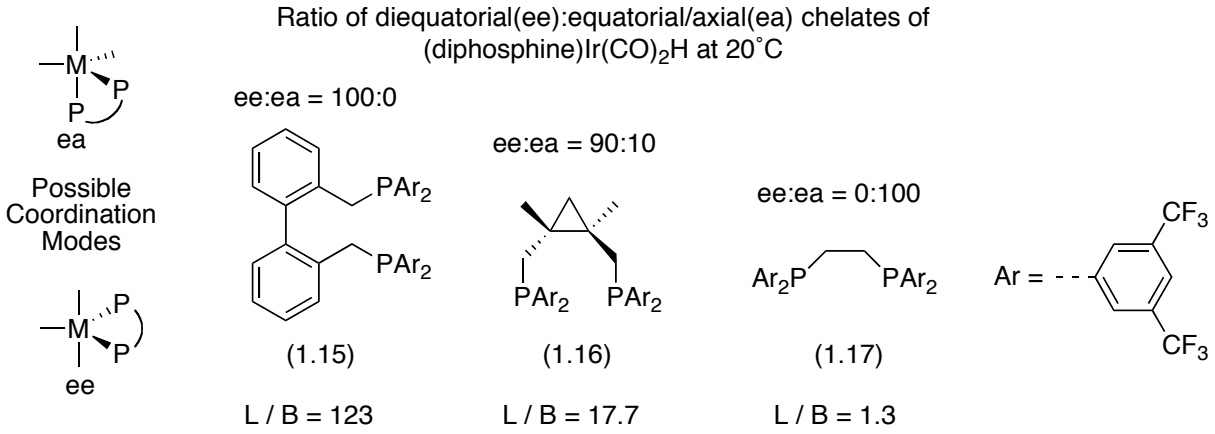


Figure 1 - 12. Coordination modes of ligands in Iridium complexes and the selectivity ratios achieved in the Rh catalysed hydroformylation of 1-hexene.

Further investigations using electronically dissymmetric DIPHOS derivatives (Figure 1 – 13) have shown that the diphosphine will tend to coordinate with the electron poor phosphine moiety in the equatorial position, and the more electron rich phosphorus in the apical position. Dissymmetric diphosphine ligands gave a higher selectivity for the linear aldehyde in the hydroformylation of 1-hexene than either symmetric analogues (Table 1 – 3).

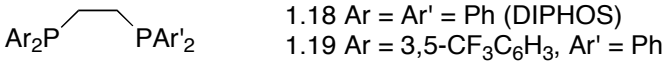


Figure 1 - 13. Dissymmetric DIPHOS analogues.

Ar'	Linear/Branched	Turnover Rate (hr^{-1})
1.18	2.6	3.5
1.17	1.3	4.3
1.19	4.2	2.5

Table 1 - 3. Rate and selectivity for the Rhodium catalysed hydroformylation of 1-hexene.

Van Leeuwen and co-workers have also investigated electronic effects in 1-octene hydroformylation, using analogues of the wide bite angle ligand Thixantphos (**1.21**) and found a strong correlation between the phosphine basicity and the rate of reaction (Figure 1 – 14).

The highest linear selectivity and turnover frequency were achieved using the fluorinated phosphine **1.22**.

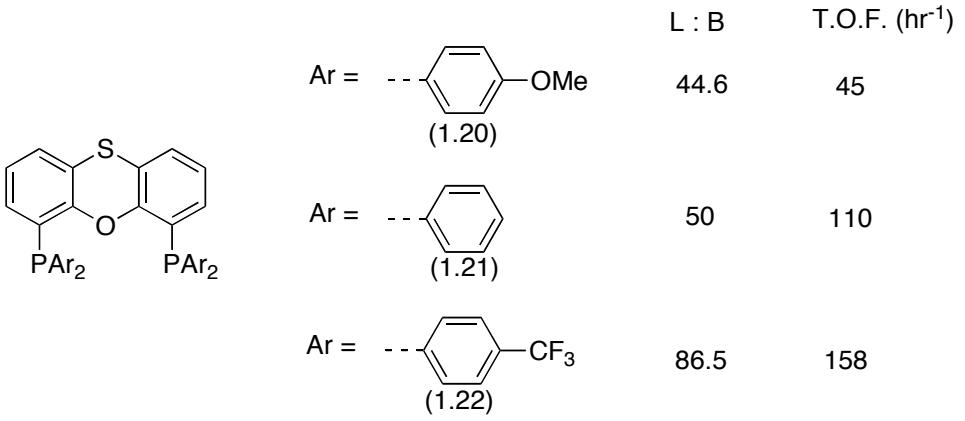
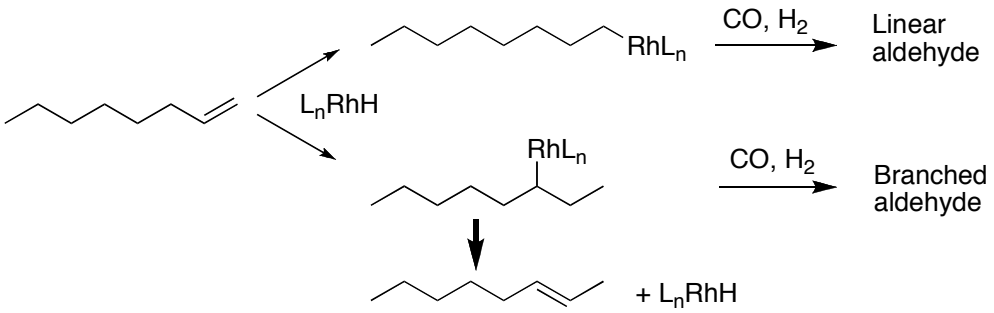


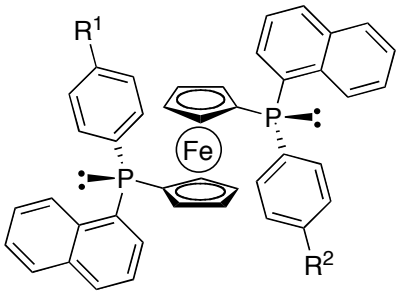
Figure 1 - 14. Activity and selectivity of Xantphos analogues in the Rh catalysed hydroformylation of 1-octene.

The increased l:b ratio was attributed to the higher electrophilicity of the rhodium centre, which leads to an increased rate of β hydride elimination for the branched alkyl, thereby causing 2-octene formation as opposed to the branched aldehyde (Scheme 1 – 2).



Scheme 1 - 2. Hydroformylation of 1-octene with increased tendency for β hydride elimination.

In the enantioselective hydroformylation of styrene using a series of enantiopure ferrocenyl diphosphines (Figure 1 - 15), the highest rate and enantioselectivity were obtained using the electron poor diphosphine **1.25** (Table 1 – 4).[60] When these ligands were employed in the hydroformylation of 1-octene, the rate of reaction showed a strong correlation with the electronic character of the ligand (Table 1 – 5). In contrast with Casey's work, the highest rate was observed with the electronically dissymmetric ligand and there was virtually no effect on the regioselectivity.



1.23 : $R^1 = R^2 = OCH_3$
1.24 : $R^1 = R^2 = H_3$
1.25 : $R^1 = R^2 = CF_3$
1.26 : $R^1 = OCH_3$, $R^2 = CF_3$

Figure 1 - 15. Ferrocenyl diphosphines tested in the hydroformylation reactions.

Ligand	B:L	T.O.F (hr^{-1})	% ee
1.23	1.7	6	46 (S)
1.24	1.7	7	46 (S)
1.25	1.5	12	50 (S)
1.26	1.7	11	41 (S)

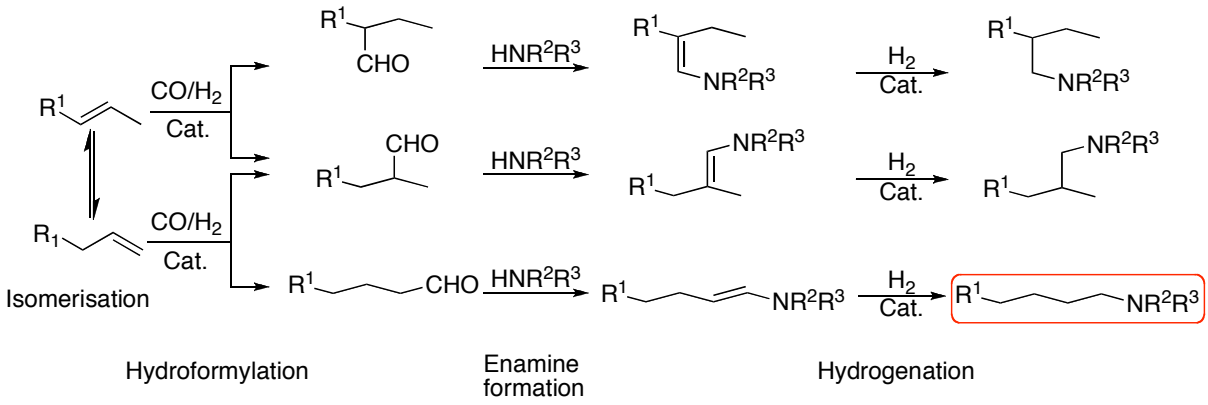
Table 1 - 4. Hydroformylation of styrene using enantiopure ferrocenyl diphosphines.

Ligand	L:B ratio	T.O.F (hr^{-1})
1.23	7.4	224
1.24	7.3	370
1.25	7.3	606
1.26	7.2	650

Table 1 - 5. Rates and selectivity for ferrocene derivatives in the hydroformylation of 1-octene.

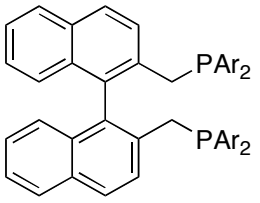
1.3.2. Hydroaminomethylation.

The use of the fluorinated NAPHOS derivative IPHOS as a ligand in this rhodium catalysed domino reaction is perhaps one of the most impressive uses of a fluorinated ligand in homogeneous catalysis, due to the range of functions that this catalyst system must perform and the high selectivity that it exhibits (Scheme 1 – 3).



Scheme 1 - 3. Possible pathways in the hydroaminomethylation reaction.

It has been found that the use of this ligand in this reaction results in high yields of linear amine, with a variety of internal olefins and amines.[61] This is mainly due to the high linear selectivity of the initial hydroformylation step, before reaction with amine to form an enamine (or imine). Testing showed that superior conversion to the linear enamine could be achieved with NAPHOS type ligands. However, only the more highly fluorinated IPHOS (**1.11**) ligand was found to be especially active in the hydrogenation step required to yield the linear amine (Table 1 – 6). This finding is in contrast with the results in many other homogeneously catalysed reactions, as it is often the case that less highly fluorinated ligands give better performance due to better coordination.



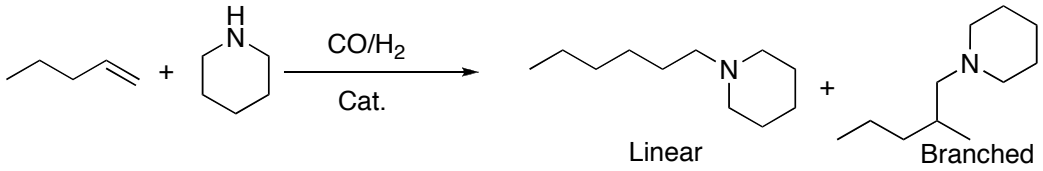
(1.10) Ar = Ph (NAPHOS)
(1.11) Ar = 3,5-$(CF_3)_2C_6H_3$, (IPHOS)
(1.27) Ar = 4-CF_3-C_6H_3,

Figure 1 - 16. Ligands for hydroaminomethylation.

Ligand	Conversion (%)	Total amine selectivity (%)	Linear Amine Selectivity (%)	L:B
1.10	50	6	6	>99:1
1.11	100	97	88	90:10
1.27	100	11	11	>99:1

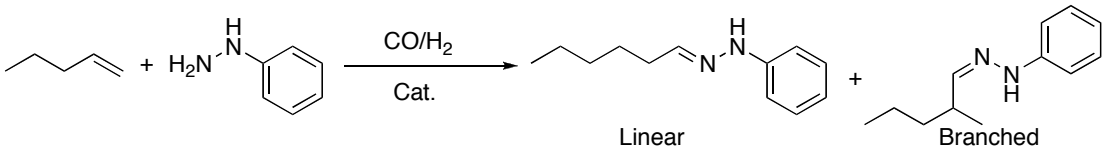
Table 1 - 6. Hydroaminomethylation of 2-butene.

Although the use of IPHOS has given superior results in the Rh catalysed hydroaminomethylation of internal alkenes, its use in reactions with terminal alkenes has been found to be inferior to a number of known ligands.[62] Despite very high selectivity for linear products the use of the less regioselective but more active Xantphos was found to be preferable for the hydroaminomethylation of pentene in the presence of piperidine (Scheme 1 - 4). In these tests, IPHOS gave lower conversion and led to the formation of by-products which reduced the yield of linear amine to 50% compared to 95% for Xantphos and 84% for NAPHOS.



Scheme 1 - 4. Hydroaminomethylation of pentene in the presence of piperidine.

In the reactions above, it was found that relatively moderate pressures (50 Bar H_2, 10 Bar CO) result in hydrogenation of the intermediate enamine product to the amine. So, it is remarkable that under lower pressures (H_2/CO, 1:1, 10 Bar) and otherwise similar conditions the same IPHOS based catalyst system can be used for the selective formation of the linear hydrazones (Scheme 1 - 5).[63] The linear selectivity in these reactions was higher than that seen for a range of well-known catalysts based on non-fluorine containing ligands including NAPHOS. The yields of hydrazone were close to 100 % for some substrates indicating a very low tendency toward hydrogenation.

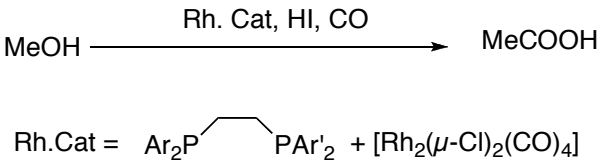


Scheme 1 - 5. Formation of hydrazones catalysed by NAPHOS derivatives.

This work was further developed to allow a convenient and remarkably selective one pot synthesis of indoles with yields of up to 85% from the starting olefin. However, in a separate report the use of IPHOS has been found to give inferior yields of enamines from terminal olefins to those achievable with NAPHOS.[64]

1.3.3. Methanol carbonylation.

In the carbonylation of methanol, which is one of the most important homogeneously catalysed reactions, a single report concerning the use of fluorinated phosphines has yielded some interesting results.[65] Several catalysts based on symmetrical and unsymmetrical analogues of DPPE with varying degrees of fluorine or trifluoromethyl substitution in *meta* or *para* positions were tested in this carbonylation reaction and were found to be active, with no signs of degradation under the harsh conditions used in industry (Scheme 1 – 6).



Scheme 1 - 6. Carbonylation of methanol.

The results show that the rate of methanol carbonylation for unsymmetrical diphosphines such as **1.32** is greater than for its symmetric counterparts and that the rate generally increases with the electron deficiency of the substituents, up to a point (Table 1 – 7). Whilst the initial increase in activity with greater fluorine content seems to be due to the increase in the ability of these ligands to act as π acceptors, the drop in activity at higher fluorine content may be due to poorer coordination, which often accompanies poorer σ donation.

Ligand	Ar	Ar'	Rate (mol l^{-1} hr^{-1})
1.28	Ph	C_6H_4OMe-4	6
1.29	Ph	C_6H_4F-3	45
1.30	Ph	$C_6H_4CF_3$-3	50
1.31	Ph	$C_6H_3F_2$-3,5	79
1.32	Ph	$C_6H_2F_3$-3,4,5	54
1.33	Ph	$C_6H_3(CF_3)_2$-3,5	31
1.18	Ph	Ph	4
1.35	C_6H_4F-3	C_6H_4F-3	13

Table 1 - 7. Rates for the carbonylation of methanol with a variety of ligands.

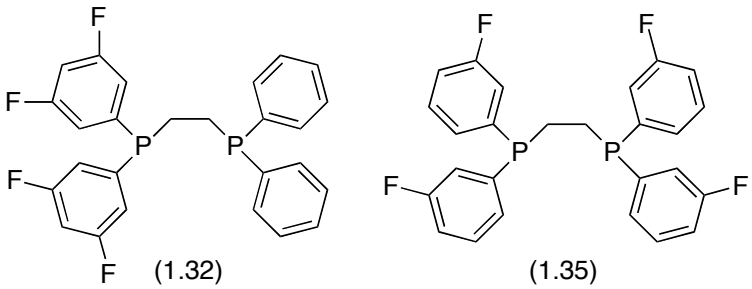
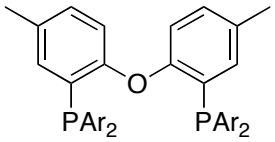


Figure 1 - 17. Fluorinated DPPE analogues which give superior results in the carbonylation of methanol.

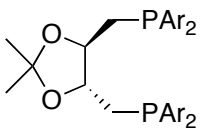
It is especially interesting that despite ligands **1.32** and **1.35** having the same number of *meta* fluorine atoms, **1.32** is over four times as active as **1.35**. These findings bear some similarity to Casey's work with hydroformylation, in which unsymmetric diphosphines show catalytic behaviour outside the range of their symmetric counterparts.[66]

1.3.4. Alkoxycarbonylation of alkenes.

A report, published whilst this project was in progress, on the palladium catalysed methoxycarbonylation of styrene has revealed that fluorinated analogues of DPEphos (Figure 1 – 18) give complexes which show increased selectivity for the commercially prized branched ester compared with the parent compounds (Table 1 – 8).[67] Indeed the selectivity for the branched ester is greater than that normally achievable in this reaction when it is catalysed by bidentate phosphine complexes.[68, 69]



1.36: Ar = Ph (DPEphos)
1.37: Ar = 3,5-(CF3)C_6H_3
1.38: Ar = *p*-MeOC_6H_4
1.39: Ar = 3,5 *t*-BuC_6H_3



1.40: Ar = Ph (DIOP)
1.41: Ar = 3,5-(CF3)C_6H_3

Figure 1 - 18. Fluorinated DPEphos and DIOP ligands tested in the alkoxycarbonylation of styrene.

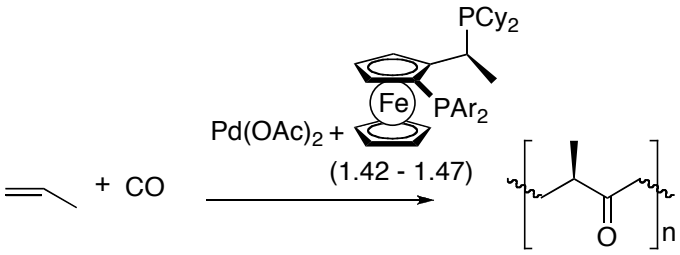
Ligand	Conversion (%)	B/L ratio	ee(%)
1.36	100	0.29	
1.37	99.4	2.86	
1.38	100	0.38	
1.39	99.9	0.40	
1.40	25	1.04	30
1.41	65	11.5	3

Table 1 - 8. Comparison of catalytic activity for a range of diphosphine ligands in the palladium catalysed methoxycarbonylation of styrene.

Suggested explanations for this unusual regioselectivity include an increase in the ability of the electron poor ligand to form trans coordinated species or even act as a monodentate ligand. Attempts to extend this work to a fluorinated enantioselective catalyst based on the DIOP scaffold resulted an even higher regioselectivity, however very little enantioselectivity was observed.

1.3.5. CO alkene polymerisation.

Gambs and co-workers have reported that the use of a series of fluorinated Josiphos (**1.42**) analogues as ligands in the palladium catalysed alternating copolymerisation of propene and CO (Scheme 1 – 7) has given improved productivity over more electron rich compounds (Figure 1 – 19).[70] Only when the fluorinated group was in the *ortho* position (**1.46**) was the productivity less than the parent compound. This is presumably due to a steric effect as the other CF_3 substituted isomers show far greater rates. The increased activity of fluorinated ligands is attributed to the increase in electrophilicty of the palladium centre, and hence any attached substrates. It is reasoned that this would allow alkenes to compete more effectively with CO for coordination sites than would be possible if the metal centre was ligated by a more electron rich diphosphine. There was almost no difference in the regioselectivity between the various ligands tested, with all polymer produced found to be >99% head to tail selectivity and of highly isotactic structure (>90%).



Scheme 1 - 7. Palladium catalysed CO propene copolymerisation using Josiphos analogues.

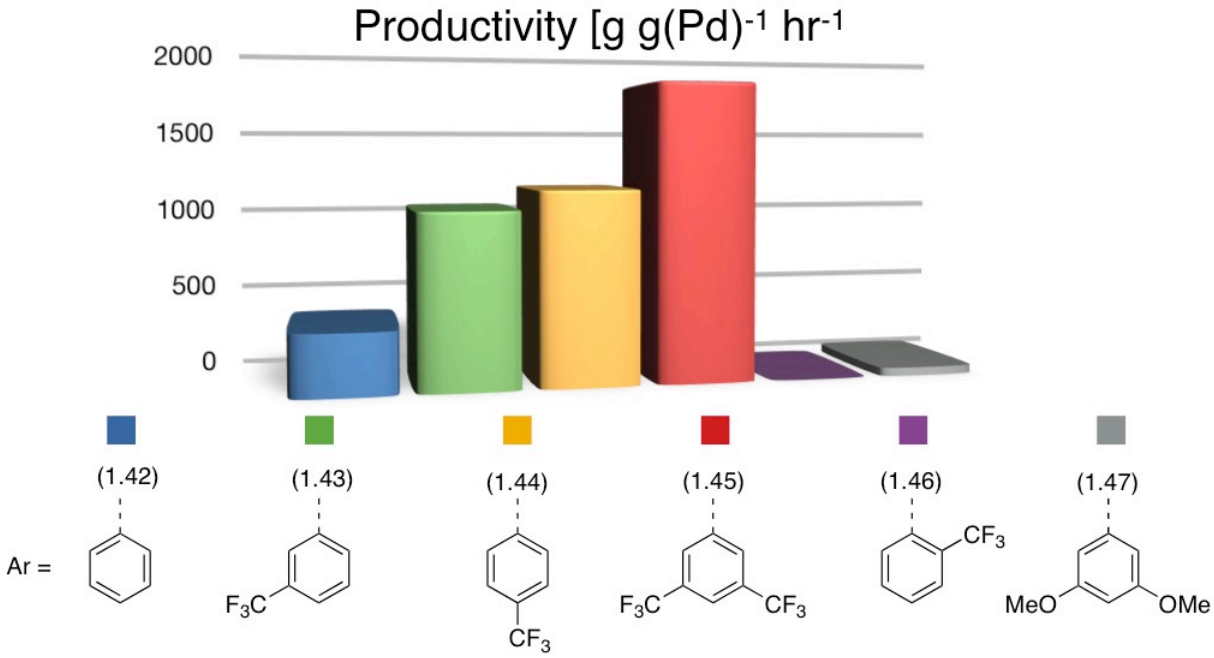
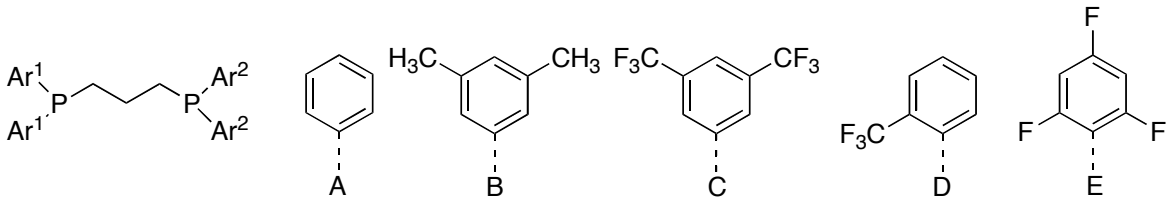


Figure 1 - 19. Productivity rates for various Josiphos analogues in CO ethene polymerisation.

In studies conducted into palladium catalysed CO ethene polymerisation it has been found that several unsymmetrical diphosphine complexes containing fluorine have a greater activity and produce polymer with higher molecular weights than symmetrical diphosphines (Figure 1 – 20).[70] A Pd complex of **1.51** was found to be 3 times more active than dppp and 6 times more active than the corresponding **1.49** complex. The **1.51** based complex also produced polymers of more than twice the molecular weight produced by its symmetrical counterparts or its 3,5 methyl analogue **1.49**. Very low activity was recorded when the sterically encumbered ligand **1.52** and the *ortho*-fluorinated ligand **1.53** were tested. These also gave low molecular weight polymers when compared to that produced by the dppp based catalyst.



(1.48) $Ar^1 = Ar^2 = A$ (DPPP)
(1.49) $Ar^1 = A$, $Ar^2 = B$
(1.50) $Ar^1 = C$, $Ar^2 = C$
(1.51) $Ar^1 = A$, $Ar^2 = C$
(1.52) $Ar^1 = A$, $Ar^2 = D$
(1.53) $Ar^1 = A$, $Ar^2 = E$

Figure 1 - 20. Diphosphines tested in CO ethene polymerisation.

It is interesting that in both the reports above the highest activity has been attained using ligands with one relatively electron rich phosphine subunit and one [bis[3,5-bis-(trifluoromethyl)phenyl]phosphine subunit linked by 3 carbon atoms, and that high molecular weight polymers were obtained using both of these ligands.

1.3.6. Polymerisation.

In the cobalt catalysed polymerisation of 1,3-butadiene a series of phosphines of the formula $P(C_6F_5)_n(C_6H_5)_{(3-n)}$, where n is an integer between 0 and 3, have been used as ligands (Figure 1 - 21).[71] The results show that the presence of fluorinated groups give higher conversions than PPh_3, due to the enhanced π acceptor character, with the exception of the highly fluorinated ligand $P(C_6F_5)_3$. This is likely due to poor coordination of this ligand. It is therefore perhaps surprising that, of the ligands which exhibited more π acceptor character than PPh_3, the largest molecular weight polymers were produced in reactions using $P(C_6F_5)_3$. However, it is thought that the molecular weight of polybutadiene produced is primarily determined by the intensity of the π acceptor character of the phosphine.

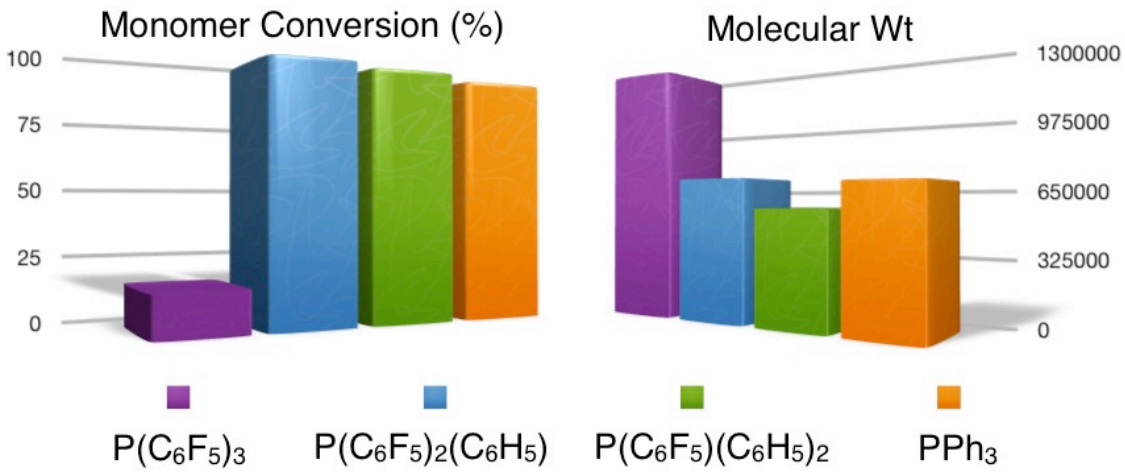
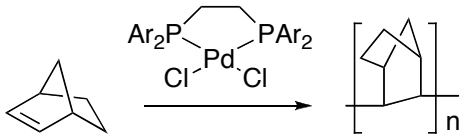


Figure 1 - 21. Monomer conversion and the molecular weights of the produced polymers for the cobalt catalysed polymerisation of 1,3 butadiene.



Scheme 1 - 8. Polymerisation of 2-norbornene.

A range of partially fluorinated bisphosphine ligands have been used as ligands in the palladium catalysed polymerisation of 2-norbornene (Scheme 1 - 8).[72] Similarly to the previously discussed results, the inclusion of fluorinated substituents has a beneficial effect on catalytic activity (Figure 1 – 22). However, the highly fluorinated pentafluorophenyl substituted ligand (**1.9**) gave a lower conversion than the other less highly fluorinated ligands.

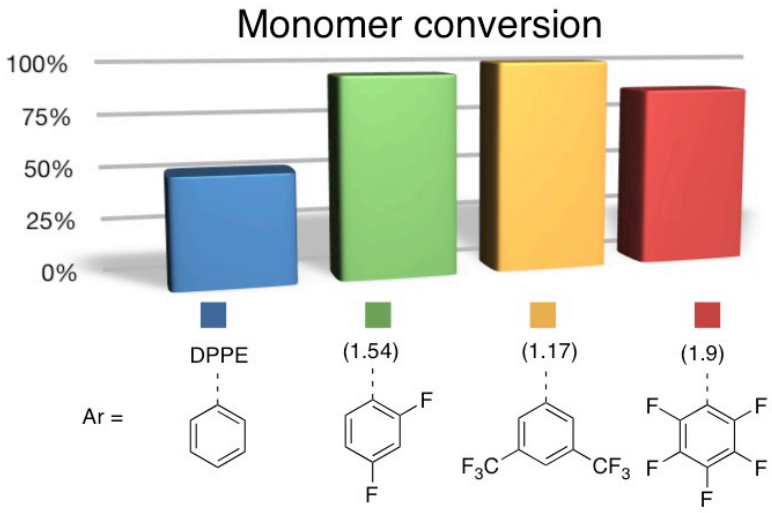
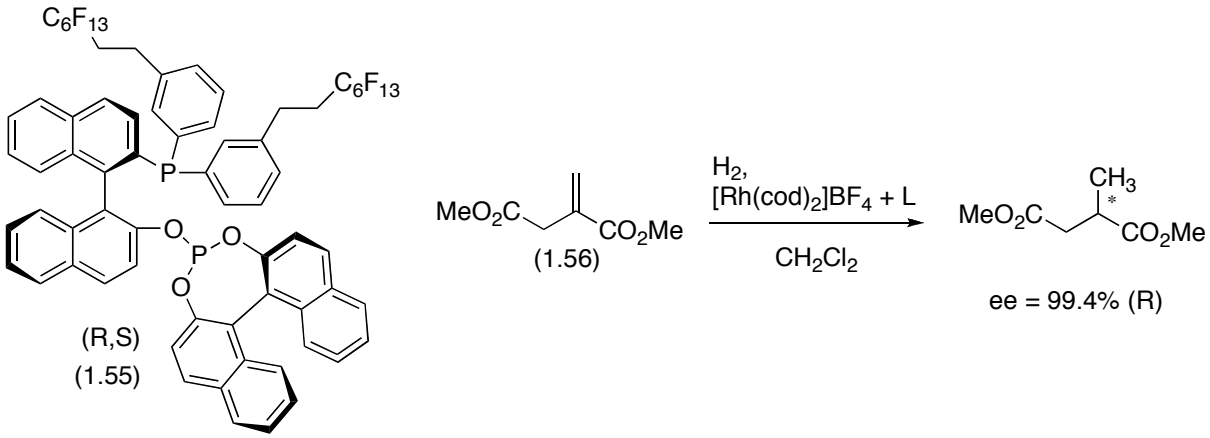


Figure 1 - 22. Monomer conversion in the polymerisation of 2-norbornene using a variety of DPPE analogue based catalysts.

1.3.7. Hydrogenation.

There are relatively few reports on the use of fluorinated phosphines in hydrogenation and those that do exist are mainly concerned with solubility in fluorous solvents or $scCO_2$, where there is considerable effort to insulate the site of catalysis from the electronic effects of the fluorous tags. It is thought that the reduction in electron density on the metal (caused by the presence of fluorinated ligands) decreases catalytic activity in hydrogenation reactions. However, a fluorous tagged analogue of BINAPHOS (**1.55**) has been used in the asymmetric hydrogenation of dimethyl itaconate (**1.56**) (Scheme 1 – 9) in a conventional solvent and achieved excellent conversion and enantioselectivity.[73] In this ligand phosphorus is likely to be exposed to at least some of the inductive withdrawing effect as it has been reported that complete insulation from fluorinated groups is not easily achieved.[42, 74] These results indicate that whilst the presence of fluorinated groups may not be beneficial for hydrogenation, in some cases it may not be disastrous.



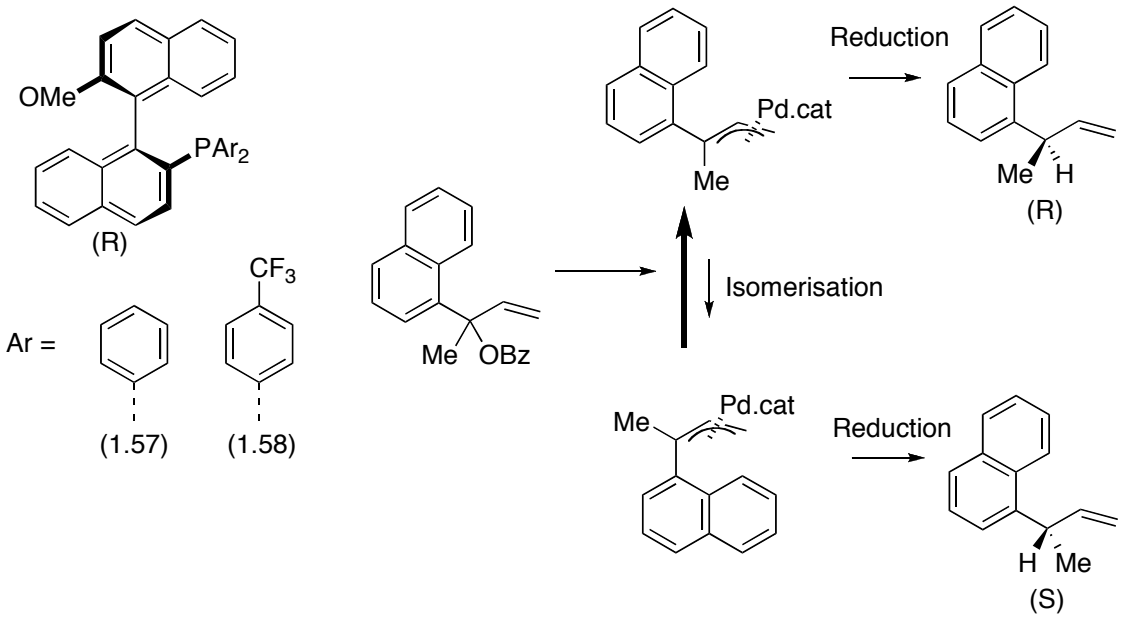
Scheme 1 - 9. Enantioselective hydrogenation of dimethyl itaconate using a fluorous tagged BINAPHOS derivative.

The Rh catalysed hydrogenation of styrene in fluorinated solvents using phosphines which have a combination of fluorous tags and a variety of insulating spacer units has been studied by Hope.[75] The results show that in this case the inductive effect of the fluorous tags has a detrimental effect on hydrogenation and the rate is greater for ligands where phosphorus is more effectively insulated from the fluorous groups (Table 1 – 9).

Ligand	Rate (mmol dm^{-3} h^{-1})
PPh_3	276
$P(4\text{-}C_6H_4\text{-}C_6F_{13})_3$	128
$P(4\text{-}C_6H_4\text{-}OCH_2C_7F_{15})_3$	201
PEt_3	177
$P(C_2H_4C_6F_{13})_3$	79
$Ph_2PCH_2CH_2PPh_2$	72
$(4\text{-}C_6H_4\text{-}C_6F_{13})_2PCH_2CH_2P(4\text{-}C_6H_4\text{-}C_6F_{13})$	66

Table 1 - 9. Comparison of rates for the Rh catalysed hydrogenation of styrene in the fluorous phase using phosphines with and without fluorous tags.

In the palladium catalysed asymmetric reduction of allylic esters using formic acid, a fluorinated phosphine ligand (**1.58**) has been found to provide greater yields and enantioselectivity than the non-fluorinated analogue (**1.57**) (Table 1 – 10).[76] The increase in enantioselectivity is thought to occur because of increased isomerisation rates for intermediate substrate-catalyst complexes which allows a preferential reduction to occur (Scheme 1 – 10).



Scheme 1 - 10. Allylic ester reduction showing isomerisation prior to enantioselection.

Ligand	Yield %	% ee
1.57	81	73
1.58	92	84

Table 1 - 10. The palladium catalysed asymmetric reduction on allylic esters using formic acid, effect of aryl ring substitution.

1.3.8. Cross-coupling.

Complexes based on fluorinated ligands have been studied by several workers as the reduction in the electron density surrounding palladium brought about by coordination with an electron poor phosphine can accelerate the rate of reductive elimination, which is often the rate-determining step in coupling reactions.[2, 44] Janssen studied the iridium catalysed allylic substitution of monosubstituted allylic derivatives and found that impressive results are achieved when the aryl rings attached to phosphorus have trifluoromethyl substitution (Figure 1 – 23).[77] A complex based on ligand **1.60** is significantly more selective than the phenyl substituted derivative **1.59,** giving 99% yield, 95:5 branched selectivity and 91 % *ee*. However for the more highly fluorinated 3,5-CF_3 substituted ligand (**1.61**) the results are less impressive. This suggests that in these reactions, as has been seen previously, there is an optimum fluorine content, beyond which the benefits cease.

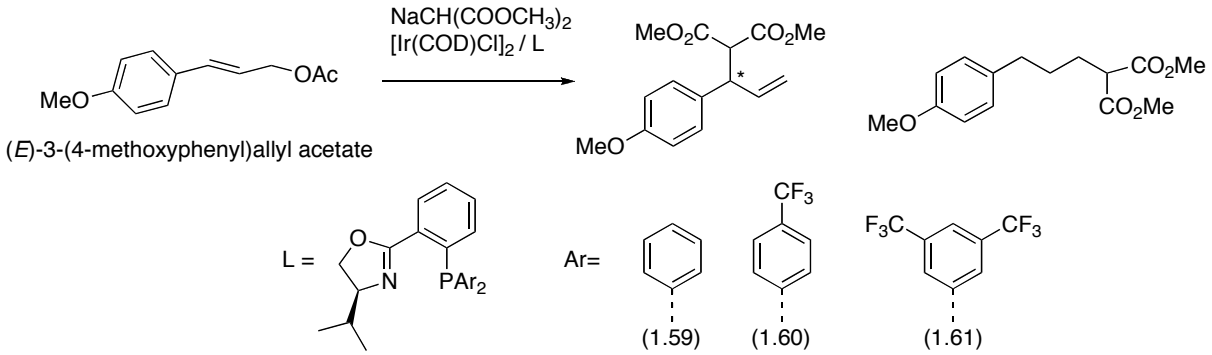
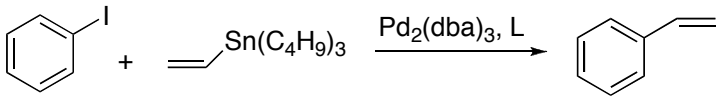


Figure 1 - 23. The iridium catalysed allylic substitution of (E)-3-(4-methoxyphenyl)allyl ethanoate with a variety of aryl substituted phosphines.

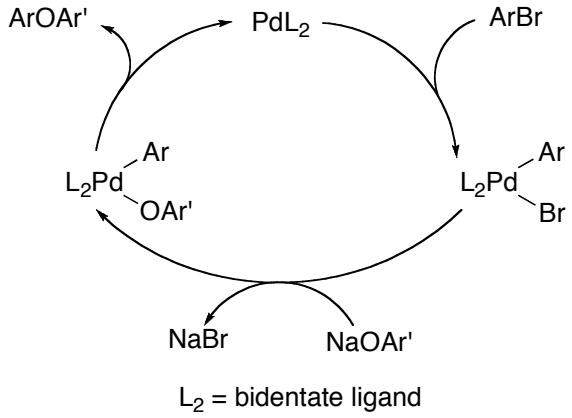


Scheme 1 - 11. palladium catalysed coupling of vinyl(tributyl)tin with aryl iodides.

Another C-C bond forming reaction where a fluorinated ligand has shown promise is in palladium catalysed Stille coupling which has been studied by Morita (Scheme 1 – 11).[78] In toluene the coupling of vinyl(tributyl)tin with aryl iodides was found to occur at almost double the rate when the reaction was performed using the 3,5-CF_3 substituted analogue of triphenyl phosphine, compared with the parent compound (Table 1 – 11).

L	Rate K/min-1
PPh3	0.034
$P(3,5\text{-}(CF_3)_2C_6H_3)_3$	0.057

Table 1 - 11. Rate of palladium catalysed coupling of vinyl(tributyl)tin with aryl iodides.



Scheme 1 - 12. Mechanism for the synthesis of biaryl ethers.

In the palladium catalysed formation of diaryl ethers (Scheme 1 – 12), which are important to the pharmaceutical industry, the effect of the electronic character of ligands based on DPPF has been investigated by Hartwig and co-workers (Figure 1 – 24).[2] It was found that by using a *para*-CF_3 substituted analogue yields of diaryl ethers synthesised from more difficult substrates could be increased. This is consistent with the facile reductive elimination expected for electron poor ligands. Indeed, the rate of reductive elimination has been shown to be twice as fast for **1.63** when compared to DPPF (**1.62**).

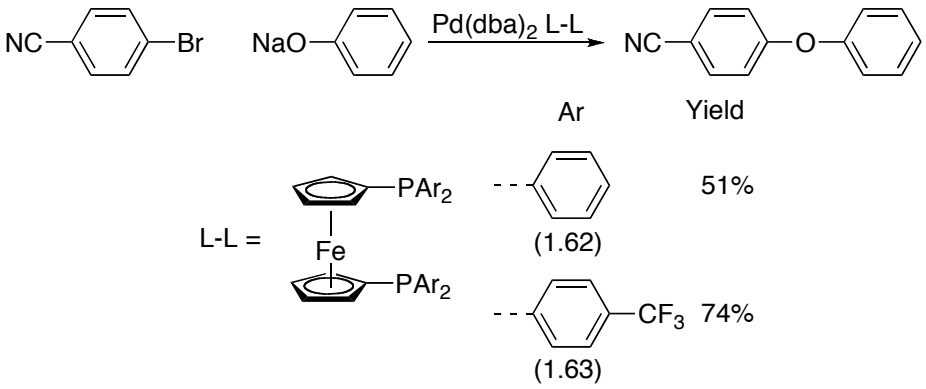


Figure 1 - 24. Palladium catalysed formation of diaryl ethers using DPPF analogues.

Palladium catalysed C-N bond forming reactions for the formation of aryl ureas, which have important applications such as drugs, pesticides and polymers, have been performed using a range of modified Xantphos (**1.64)** type ligands by Beletskaya and co-workers (Figure 1 – 25).[79, 80]

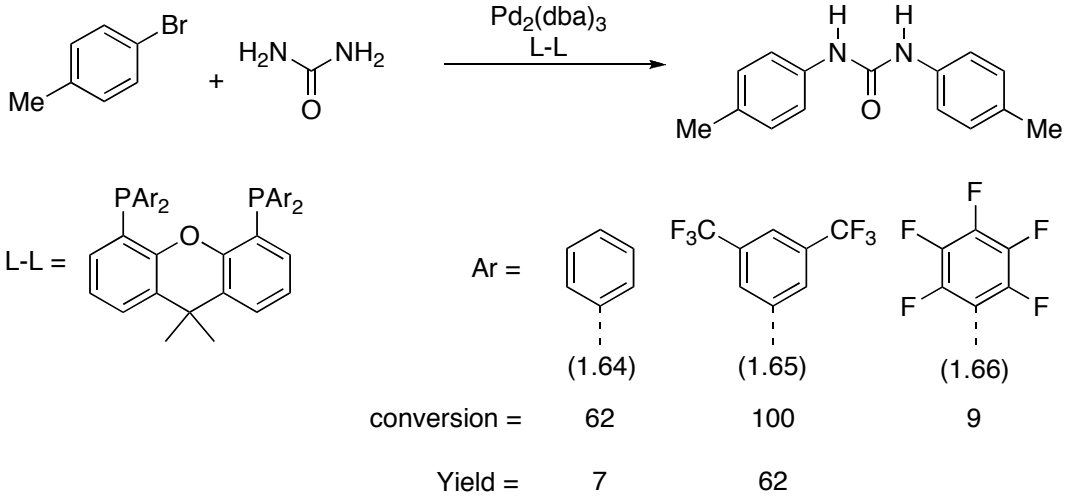


Figure 1 - 25. Palladium catalysed arylation of urea using a variety of Xantphos analogues.

The best performance in this reaction was achieved using fluorinated ligand **1.65**, It is however notable that FluoroXantphos (**1.66)** was found to be a poor choice of ligand for this reaction, with only 9% conversion achieved. This suggests that, as seen in previous examples, there is a subtle balance in the fluorine content, where σ donation of the lone pair to the metal is sufficient to form stable complexes yet the π accepting abilities of the ligand are great enough to influence the catalytic behaviour. **1.65** proved to be an effective ligand for these

transformations for most of the substrates tested in this study. Yields of up to 98% were achieved using only 1 mol% catalyst in the coupling of several hindered *ortho* substituted aryl halides which are considered to be more challenging. In comparison, Xantphos generally produced much lower yields despite the use of a greater amount of catalyst and longer reaction times.

1.3.9. Fluorine containing ligands in non-traditional solvents.

There is a great deal of interest in the use of fluorinated ligands in novel solvent systems such as perfluorocarbon solvents and $scCO_2$. Catalytic behaviour in these systems is often governed by the solubility characteristics of the ligands, and therefore outwith the scope of this project. However, in some cases there are significant stereoelectronic effects (due to the incorporation of fluorinated or fluorous moieties within ligands) which are worthy of a brief mention, especially in carbonylation reactions, where electron poor catalysts are often desirable.

1.3.9.1. Catalysis in fluorous solvents.

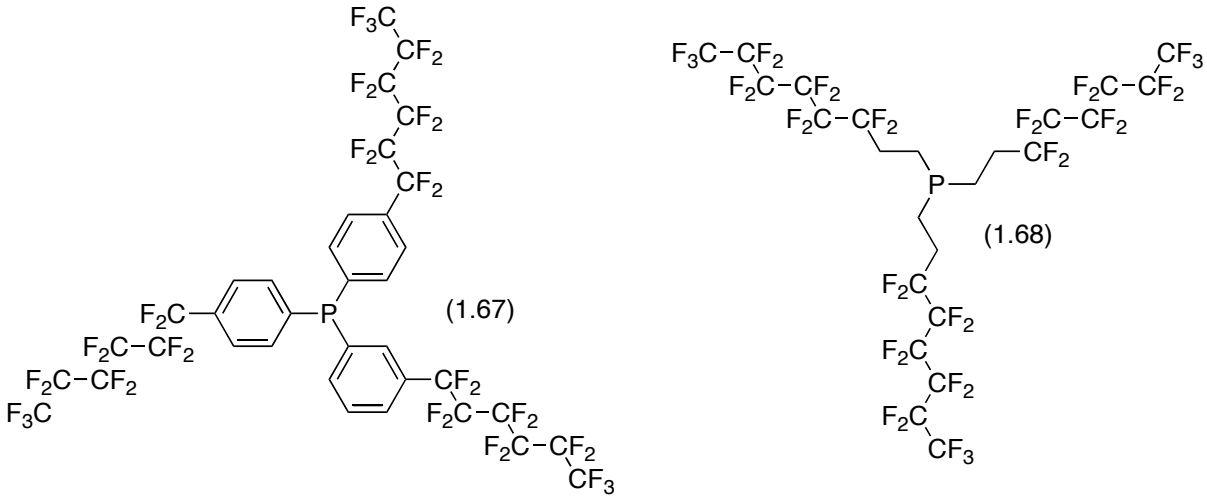


Figure 1 - 26. Phosphine ligands used in fluorous catalysis. The large fluorous domains are required for solubility in fluorous solvents.

The work of Horváth and Rabai first outlined the potential of fluorous biphasic catalysis and its applicability to the rhodium catalysed hydroformylation reaction.[81] Since then, much research effort has been expended in the field of fluorous chemistry.[42, 50, 75, 82-87] Under hydroformylation conditions, perfluorocarbon solvents and organic solvents form a single

phase, but on cooling the phases separate. Fluoroalkyl labels (Figure 1 – 26) allow the catalysts to be separated from the organics by virtue of their phase affinity for fluorous media. This separation technology potentially offers a method of recycling the costly catalysts used in homogeneously catalysed reactions. However, the attachment of fluorous labels to ligands can also induce significant changes in the ligand metal interactions, and thereby the catalytic behaviour of any complex. In the rhodium catalysed hydroformylation of 1-octene the use of ligand **1.67** in fluorous solvents has given a turnover frequency four times higher than PPh_3 in toluene, and also gives higher selectivity for the economically attractive linear isomer.[84] In the hydroformylation of propene, the work of Horvath and co-workers has shown that ligand **1.68** gives the same selectivity for the linear isomer as PPh_3, however the turnover frequency was found to be an order of magnitude lower.

1.3.9.2. Catalysis in supercritical CO_2.

Fluorinated ligands have also exhibited enhanced solubility in supercritical CO_2, a solvent which is currently being investigated as an ecologically benign, economically feasible reaction medium, which can replace conventional toxic, flammable organic solvents.[54, 73, 78, 86, 88-93] It should be noted that fluoroaryl ligands have more potential in this field due to the reduced degree of fluorination required to effectively solubilise catalysts in $scCO_2$. Attempts by Leitner and Ojima to achieve rhodium catalysed enantioselective hydroformylation of styrene derivatives in supercritical CO_2 have shown that when fluoroalkyl groups are present in ligands enhanced catalytic activity is possible.[73, 94] In conventional solvents, the fluorous-tagged derivative of BINAPHOS (**1.70)** achieves higher regioselectivity for the commercially valuable branched isomer, and good enantioselectivity, in a shorter period than its parent (**1.69**) (Table 1 - 12).

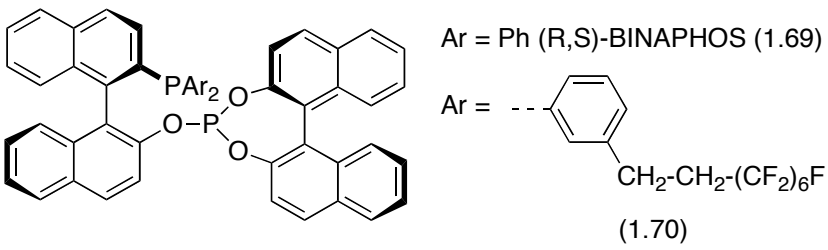


Figure 1 - 27. BINAPHOS systems tested in Rh catalysed hydroformylation reactions in organic and non conventional solvents.

Ligand	Time (hours)	Conversion (%)	Regioselectivity (% branched)	Ee (%)
1.69	43	>99	88	94
1.70	17	>99	92.7	90.6

Table 1 - 12. Rhodium-catalysed asymmetric hydroformylation of styrene in benzene

It seems, despite the presence of two methylene spacers to insulate phosphorus, the fluoroalkyl groups still have a pronounced effect on catalysis. The ability of fluoroalkyl chains to exert long range inductive effects, despite attempts to eliminate these, have been documented by others.[42, 74, 95] This phenomenon may limit the potential applications of fluoroalkyl tagged phosphines in non-conventional solvents if an electron rich ligand is required.

1.4. Summary

Fluorinated ligands have been used in a large variety of homogenously catalysed reactions. In these reactions they have often exhibited modified catalytic behaviour, with respect to their perprotio analogues due to their enhanced π acceptor character and larger steric profile. However, the coordination chemistry of these fluorinated ligands is also modified and this can be detrimental to the catalysis results.

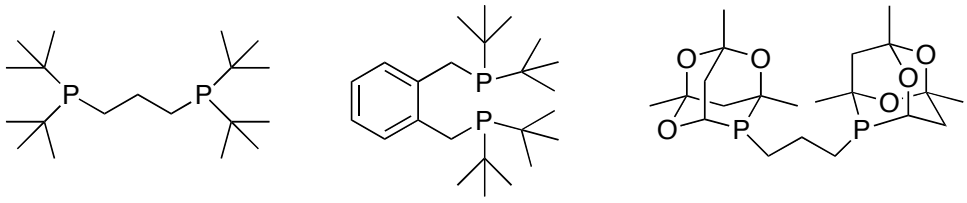
1.5. Aims.

The aim of this project was to synthesise novel fluorinated ligands for homogeneously catalysed carbonylation reactions. Two different strategies were to be employed for progress to towards this goal.

1.5.1. Bulky fluorinated ligands.

The use of catalysts based on highly sterically hindered ligands such as **1.71** and **1.72** in reactions such as alkoxycarbonylation has given extremely high activity and excellent product selectivity. Catalysts based on the adamantyl cage phosphines (**1.73**)[6] have been shown to exhibit an even more bulky steric profile, (Tolman cone angle, θ = 173°[1]) than that shown by those containing the bulky *tert*-butyl groups (θ = 155°).[96] It should be noted that this ligand includes electronegative oxygen atoms in its architecture which may be crucial to the

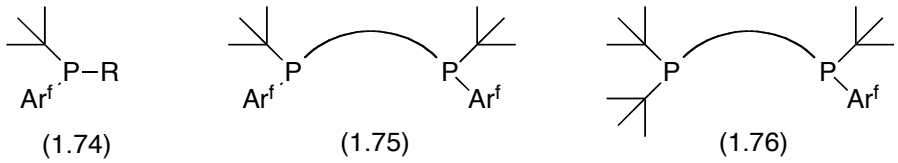
performance of catalysts based on this ligand in the tandem isomerisation-carbonylation reaction in alkoxycarbonylation.



(1.71) (1.72) (1.73)

Figure 1 - 28. Highly active ligands for alkoxycarbonylation.

As documented previously, attempts to use highly fluorinated phosphines as ligands have been hampered as these less electron rich and often more bulky structures often coordinate poorly to transition metals during catalysis.[28] Therefore the development of phosphines with a mixture of electron rich and electron poor substituents such as **1.74 – 1.76** may overcome this limitation (Figure 1 – 29).



(1.74) (1.75) (1.76)

Figure 1 - 29. General structures for proposed phosphine and diphosphines target compounds.

Our initial aim was to test the coordination chemistry of this type of novel architecture by tsynthesising a range of monodentate phosphines, and investigating the reactions of these with a selection of transition metal complexes. If these preliminary tests proved promising, the aim was to synthesise a range of bidentate phosphines (**1.75)** along the same lines as the monodentate phosphines. The coordination of these novel bidentate phosphines with transition metals was to be investigated, and any catalytic activity that these complexes exhibited in carbonylation reactions was to be explored. The development of electronically unsymmetrical ligands (**1.76**) was also a key aim of this project, as ligands of this type have been especially successful in several reactions, sometimes exhibiting higher activity and/or selectivity than either of their symmetric counterparts.[65, 66, 70]

1.5.2. Fluorinated Phosphacycles.

Phosphacycles such as phosphetanes[97] and phospholanes[98] have generated much interest in homogeneous catalysis. These ligands are highly electron rich and have been shown to be active and stereoselective in hydrogenations,[99-103] hydrosilation of olefins,[104] allylic alkylation,[105] methoxycarbonylation,[106] and the isospecific alternating copolymerisation of α-olefins with carbon monoxide,[107] which is closely related to the alkoxycarbonylation reaction.[108] The fact that the steric environment surrounding phosphorus is very well controlled when it is incorporated into a cyclic structure is a key feature of these ligands. This is thought to be crucial to the efficient transfer of chiral information. A feature of the phosphetane ligands is the geometry imposed by the four membered ring, which causes distortion of the orbitals of phosphorus leading to greater S character in the lone pair. This in turn may lead to novel catalytic behaviour. This right angular geometry is also shared with **1.72** and may contribute to this ligand's success in homogeneously catalysed reactions, although importance of the C-P-C angle for effective catalysis has been questioned for larger phosphacycles.[109] Only a few reports have appeared concerning the synthesis of highly fluorinated phosphacycles[110-112] (**1.75** – **1.77**) and the author is not aware of any reports in the literature of the use of any fluorinated phosphacycles in homogeneous catalysis. It should be noted that high degree of fluorination in compounds **1.75** – **1.77** makes it unlikely that these would form complexes stable enough for use in catalysis.

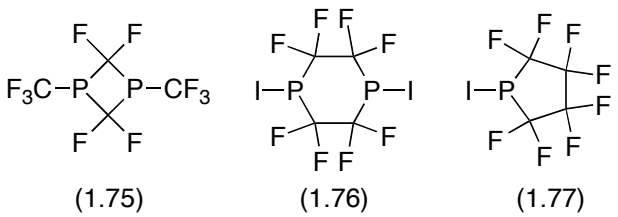


Figure 1 - 30. Highly fluorinated phosphacycles which have been synthesised in previous studies.

Therefore, another of the aims of this project was to discover suitable methods for the synthesis of less highly fluorinated phosphacycles yet with the fluorine atoms attached directly to the ring, so as to ensure a significant stereoelectronic effect (Figure 1 – 31).

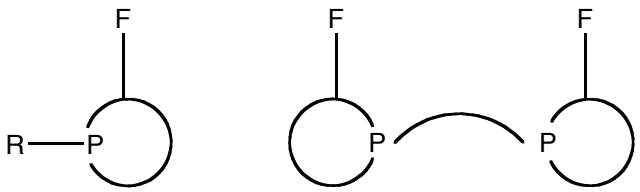
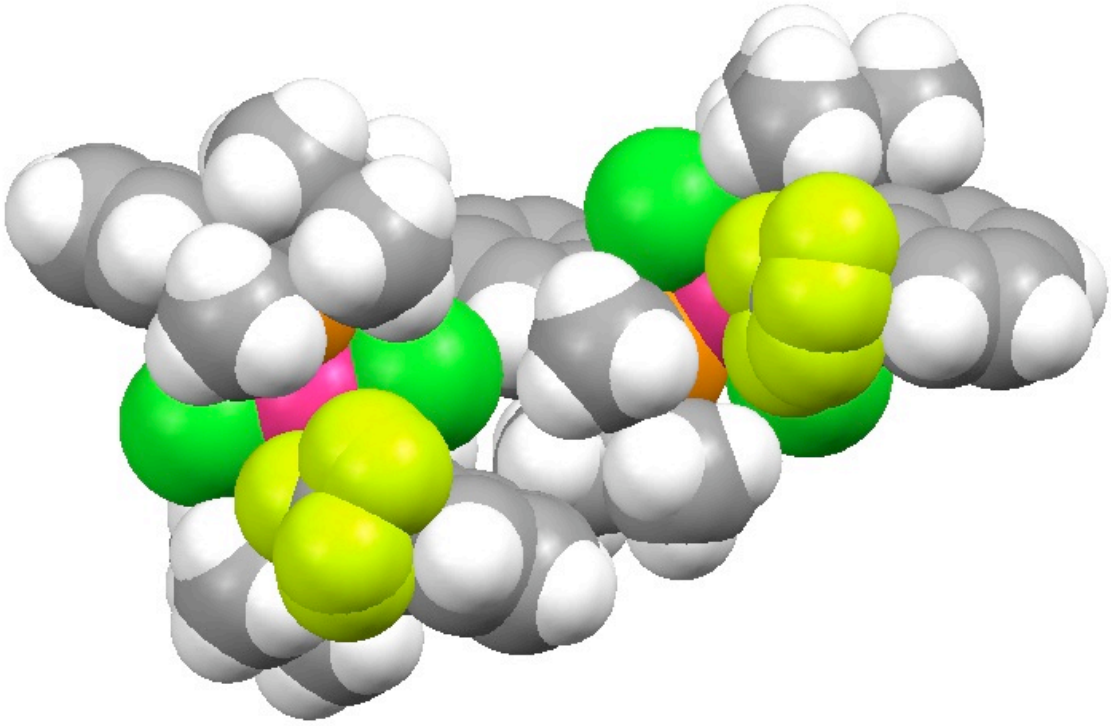


Figure 1 - 31. General architecture of proposed fluorinated phosphacycles.

It is hoped that the inclusion of this electronegative element would broaden the scope of reactions for which phosphacycles can be used effectively as ligands, especially in carbonylation reactions where electron poor ligands are known to have performance advantages.[28, 113, 114] The coordination chemistry and any catalytic activity exhibited by any resulting complexes were also to be investigated.

2. Synthesis of Monophosphine Compounds.

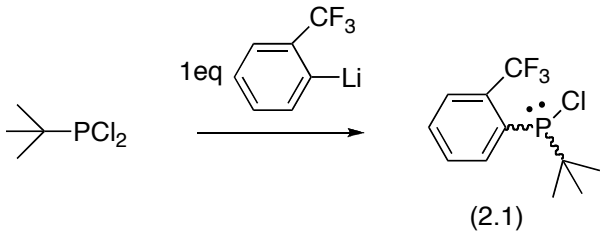


sasol
reaching new frontiers

In order to pursue the aims of investigating the chemistry of bulky fluorine containing ligands containing fluorine containing aryl groups it was decided to synthesise the chlorophosphines **2.1**, **2.2** and **2.3**. These, and other chlorophosphines, were considered versatile enough to be the starting point for producing a variety of monodentate and bidentate phosphines.

2.1. Synthesis of Chlorophosphines.

2.1.1. *Tert*-butylchloro(*ortho*-(trifluoromethyl)phenyl)phosphine (2.1).[115]

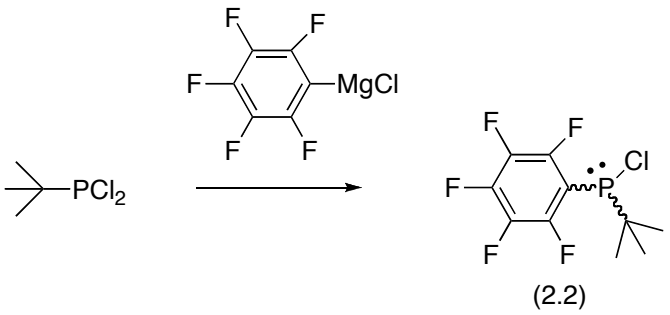


Scheme 2 - 1. Synthesis of 2.1.

The synthesis of **2.1** was achieved by transmetallation of the corresponding aryl bromide using *n*-butyllithium at low temperature, followed by reaction of the resulting aryl lithium with *tert*-butyldichlorophosphine (Scheme 2 – 1). This yielded the almost completely pure chlorophosphine (as judged by $^{31}P\{^{1}H\}$ NMR). The spectrum showed the chlorophosphine as a quartet at 101.5 ppm with a phosphorus-fluorine coupling constant of 72.5 Hz. The size of this coupling constant is extremely large for a ^{4}J coupling, however this large coupling can be explained by an interaction of the three highly electronegative fluorine atoms with the phosphorus lone pair. Such "through space" couplings have been observed previously for *ortho*-derivatised triaryl phosphines.[50, 116] These interactions are known to occur when orbital overlap is imposed due to geometric constraints[13] and fluorine in particular is known to be susceptible to such interactions.[117] Another very small quartet, which appears at 96.5 ppm, is assigned to the presence of traces of the bromide due to the chemical shift. It was particularly convenient that in these reactions only traces of the diaryl product (**2.13**) were observed. It appears that the bulky structure of the reactants is effective in controlling the reaction, allowing the selective formation of the mono-aryl product, in contrast to other less sterically demanding dichlorophosphines which require protecting groups.[118, 119] The optimised synthesis of **2.1** gave a yield of 70% of the pure product after vacuum distillation. However, as the $^{31}P\{^{1}H\}$ NMR spectrum showed the crude reaction product to be of high purity, it was

routinely used in further synthesis without further purification other than the removal of salts by precipitation followed by filtration.

2.1.2. *Tert*-butylchloro(perfluorophenyl)phosphine (2.2).[115]

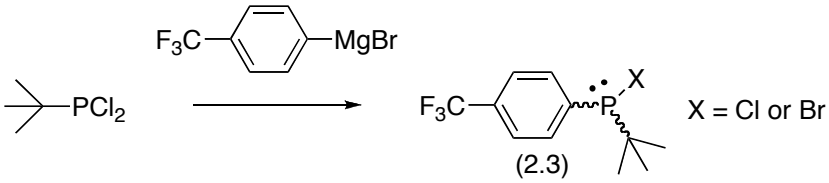


(2.2)

Scheme 2 - 2. Synthesis of 2.2.

As the addition of *n*-butyllithium to C_6F_5Cl did not give a lithium reagent which was stable enough to be of practical use in the synthesis, the highly fluorinated pentafluoro phosphine chloride was synthesised by use of a Grignard reagent prepared from this aryl chloride. This allowed the preparation of the chlorophosphine (Scheme 2 – 2), which was of high purity as judged by $^{31}P\{^1H\}$ NMR, where it was observed as a triplet at 94.4 ppm, with a ^3J phosphorus fluorine coupling constant of 55 Hz. The yield achieved after distillation was only 42%, which is disappointing when one considers the apparent purity of the crude product observed in the $^{31}P\{^1H\}$ NMR spectrum. However, this synthesis was not optimised as the development of diphosphines based on this compound was complicated by the poor stability of the secondary borane (**2.5**). Therefore, it is quite possible that this yield may be improved. A small amount of a compound which gave rise to a pentet at 17.5 ppm, with a coupling constant of 31 Hz, was observed in the spectra. The position and multiplicity are consistent with the resonance which would be expected for (*tert*-Bu)$(C_6F_5)_2P$, but this novel compound has not been further investigated here.

2.1.3. *Tert*-butylchloro(*para*-(trifluoromethyl)phenyl)phosphine (2.3).



Scheme 2 - 3. Synthesis of 2.3.

In order to decouple the steric effect of *ortho* substitution from the electronic effect of trifluoromethyl substitution of the aryl ring, **2.3** was synthesised. This was achieved by the reaction of a Grignard reagent prepared from *para*-$CF_3(C_6H_4)Br$, with *tert*-butyldichlorophosphine (Scheme 2 – 3). In this reaction, there was considerable by-product formation, which led to excess Grignard being required for full conversion of the dichlorophosphine. This is partly explained by the fact that a significant amount of 4,4'-bis(trifluoromethyl)biphenyl was isolated as a fraction during flash chromatography of **2.6** which was subsequently synthesised from **2.3**. In contrast to the reaction of **2.1**, a considerable amount of transmetallation occurred during the arylation of the dichloride, resulting in the product being synthesised as a mixture of the bromo and chloro compounds (since the magnesium bromide was used in its synthesis). As success had been achieved in the one pot synthesis of **2.4** no attempt was made to isolate **2.3**, however the chemical shifts observed in the $^{31}P\{^1H\}$ NMR spectrum at 107.3 ppm and 103.9 ppm are very similar to those observed above for **2.1** and **2.2**. Additionally, the observation of an isotopomer shift (see below) for the signal at 107.3 ppm is compelling evidence that this is indeed the chloride. As flash chromatography was to be performed in subsequent synthesis steps, the products synthesised here were used without further purification.

2.1.4. Isotopomer shifts of Chlorides.

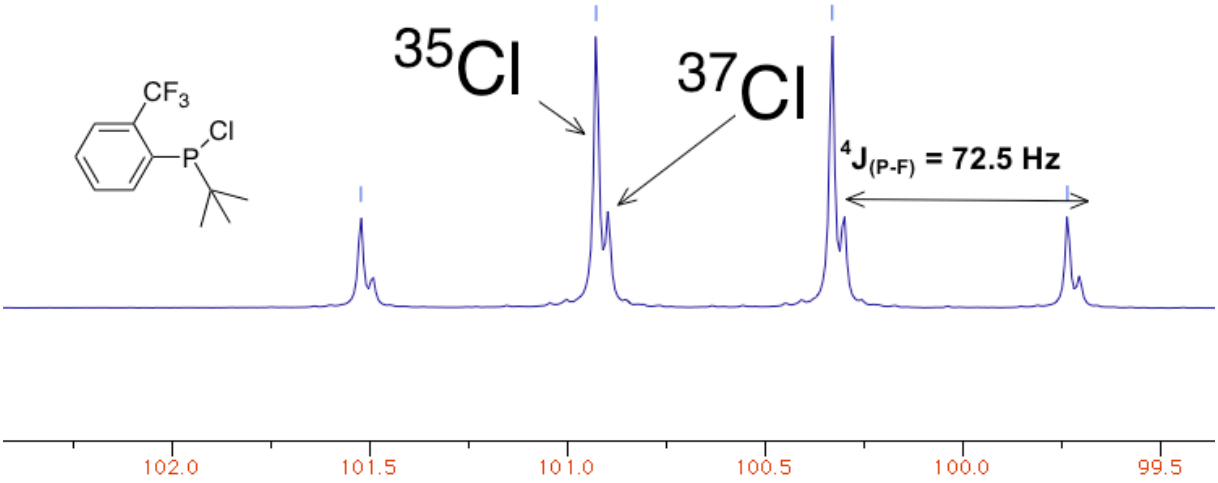


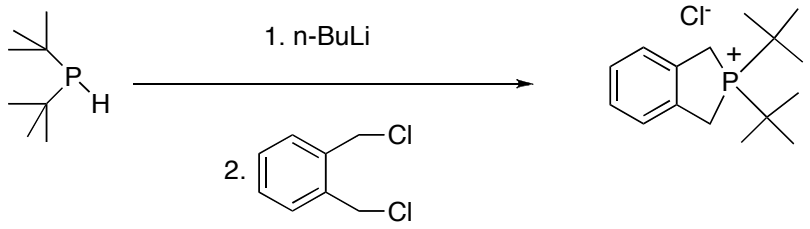
Figure 2 - 1. $^{31}P\{H\}$ spectrum of 2.1 showing an isotopomer shift.

An interesting and rarely observed phenomenon, which is apparent in the phosphorus spectra of both phosphine chlorides **2.1** and **2.3,** is the isotopomer shift (Figure 2 – 1).[120] This slight difference in chemical shift (around 0.025 ppm) is due to the fact that P is bonded directly to chlorine, so there are differences in nuclear shielding and anharmonicity between molecules of a compound consisting of different isotopes. The ratio of the two resonances as found by deconvolution of the signals is 3:1 for the spectra of both **2.1** and **2.3**, which corresponds well with the natural abundance of ^{35}Cl (75.77%) and ^{37}Cl (24.23%) respectively. The observation of isotopomer shifts is also additional evidence that distinguishes the ^{31}P NMR signal of the chloride from the signal of the bromide, which has a symmetrical shape due to the near equal abundance of ^{79}Br and ^{81}Br.

2.2. Synthesis of phosphine boranes as precursors for bidentate phosphines.

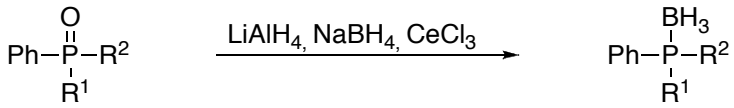
In order to synthesise these bidentate compounds a modular approach was employed. A selection of subunits from which nucleophiles could be generated was envisaged. The reaction of these nucleophiles with electrophilic bridging units was planned to give access to a range of bidentate ligands with varying stereoelectronic character, which could be used to probe the how the stereoelectronic character effects the outcome of the catalysis.

Some phosphines, particularly primary and secondary phosphines containing alkyl groups are known to be corrosive, have a strong tendency to oxidize, and can be extremely difficult to work with and purify. Phosphines are often liquids with a painfully pungent vapour that most chemists would prefer to avoid. Also, it has been found that phosphines containing alkyl groups have a tendency to quaternise, yielding stable cyclic products rather than the desired bidentate ligands[121] (Scheme 2 - 4). In addition, it has been found that strongly basic diaryl and dialkyl metallophosphides can give rise to base mediated elimination products.



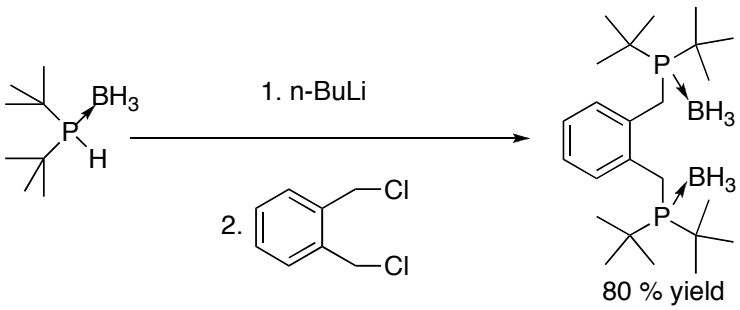
Scheme 2 - 4. An example of a quaternation reaction of an alkyl phosphine.

To avoid these complications it was decided that phosphine boranes would be employed as the building blocks for the bidentate ligands that were to be synthesised in this study. Phosphine borane complexes were first synthesised in 1965 by Frisch,[122] yet they received little attention until Imamoto and co-workers reported a convenient one step procedure for their preparation. Phosphine oxides were converted into the corresponding phosphine boranes in good yield using a combination of $LiAlH_4$, $NaBH_4$ and $CeCl_3$ without the isolation of the intermediates (Scheme 2 – 5).[123]



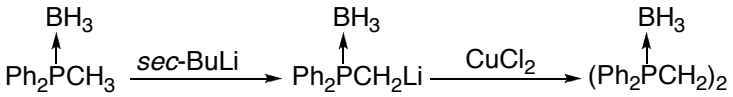
Scheme 2 - 5. Synthesis of phosphine boranes from phosphine oxides.

Phosphine boranes have been efficiently deprotonated by a range of bases to yield nucleophilic but mildly basic anions, which react with a selection of electrophiles to produce the corresponding bidentate tertiary phosphine boranes (Scheme 2 – 6).[43, 124, 125]



Scheme 2 - 6. Synthesis of a diphosphine by deprotonation of secondary phosphine boranes.

Imamoto's work, also showed it is possible to deprotonate the methyl group of phosphine boranes to produce bidentate phosphines (Scheme 2 – 7).



Scheme 2 - 7. Synthesis of a diphosphine by copper mediated coupling.

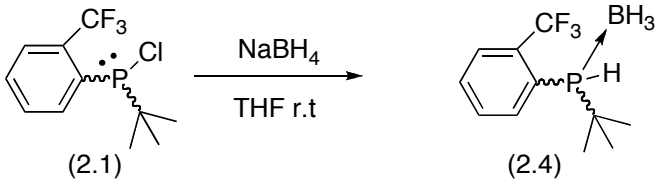
The use of methods based on phosphine boranes have become popular in diphosphine synthesis[60, 126-128] due to the following advantages:

- They are generally easier to work with than unprotected phosphines.
- Oxidation is prevented as the borane acts as a protecting group for the phosphorus lone pair allowing for easier handling and storage requirements.
- The protection of the lone pair also avoids the problems of quaternisation and over alkylation.
- The mild basicity of the anions derived from these complexes prevents elimination reactions.
- Purification methods such as flash chromatography and, if the phosphine borane is a solid, crystallisation can be used under atmospheric conditions.

Synthesis of phosphine boranes can be achieved by several methods. The two methods used in this work are, the synthesis from halophosphines by the use of $NaBH_4$, and synthesis from tertiary phosphines by the addition of BH_3-donating complexes such as BH_3.THF or BH_3.$SiMe_2$. It is noteworthy that $NaBH_4$ does not by itself facilitate the boronation of tertiary phosphines. It does however perform a convenient 1-pot reduction-boronation reaction with

halophosphines without the need to isolate the intermediates. During the first step, the reduction of the halophosphine by loss of a hydride generates the "free BH_3," which is then coordinated by the secondary phosphine to yield the secondary phosphine borane.

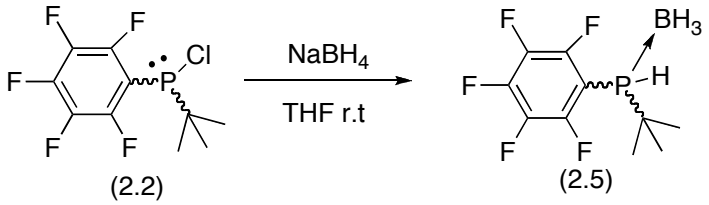
2.2.1. *Tert*-butyl(*ortho*-(trifluoromethyl)phenyl)phosphineborane (2.4).



Scheme 2 - 8. Synthesis of 2.4.

The synthesis of this phosphine borane was achieved by the addition of 3-5 equivalents of $NaBH_4$ to a THF solution of the chlorophosphine (Scheme 2 – 8). This reaction was initially performed using samples of chlorophosphine **2.1** that had been purified by distillation. However, this was found to be unnecessary and later reactions were performed using crude **2.1** resulting in isolated yields of up to 87% (from **2.1**), after flash chromatography. These results were further improved upon by the use of a "one pot" strategy where $NaBH_4$ was added directly to the reaction mixture after the synthesis of **2.1**. This resulted in a 91.5% yield (from dichloro(*tert*-butyl)phosphine) after work up and recrystallisation from hexane at low temperature. Whilst the synthesis of this compound was judged complete when monitored by $^{31}P\{^1H\}$ NMR after less than 20 hours on some occasions, on other occasions no detectable conversion of the chloride had occurred after 24 hours. In cases where the reaction was found to be sluggish, additional THF and/or additional $NaBH_4$ was found to increase conversion to **2.4**, whereas heating the mixture had little or no effect on conversion. On occasions when the reaction was incomplete the $^{31}P\{^1H\}$ NMR showed a quartet at -16 ppm, which corresponds to the secondary phosphine. The $^{31}P\{^1H\}$ NMR spectrum of pure **2.4** shows a broad multiplet at 18 ppm which is consistent with coupling to boron, however no fine detail is observed which may be a symptom of weak bond strength. ^{31}P spectrum shows a doublet with a large 386 Hz coupling constant, which corresponds to a doublet of multiplets seen in the proton spectrum centred around 5.6 ppm. This collapses to a single multiplet in the $^1H\{P\}$ spectrum. The ^{19}F spectrum shows no discernible P-F coupling, supporting the contention that the P-F coupling seen in free phosphines with an *ortho*-CF_3 subunit is indeed a through space interaction which is only transmitted by an unbound lone pair. An annotated ^{13}C spectrum is included in the appendix (i), and all resonances are consistent with the structure.

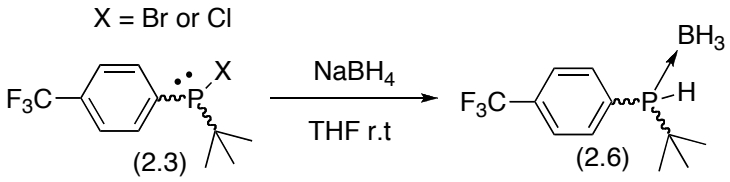
2.2.2. *Tert*-butyl(perfluorophenyl)phosphineborane (2.5).



Scheme 2 - 9. Synthesis of 2.5.

The synthesis of **2.5** was attempted in a same manner as **2.4** (Scheme 2 – 9). The $^{31}P\{^{1}H\}$ NMR spectrum showed a broad multiplet at 6 ppm, as is typically observed for phosphine boranes, and electrospray mass spectrometry shows a peak at 269.1 (M - H) as well as 295,0 (M oxide + Na). This evidence suggests that this compound was formed, although it decomposed during purification attempts by flash chromatography, and during recrystallisation. When the remaining material was analysed using $^{31}P\{^{1}H\}$ NMR a large peak at -60ppm was present. This is likely to be the signal for the secondary phosphine, which appears to have resisted oxidation despite being exposed to the atmosphere. If this is indeed the secondary phosphine, the absence of any significant resonance further down field indicates that this compound is reasonably air stable. Due to the instability of the phosphine borane, it was thought that further synthesis work using this compound would be unsuccessful or more difficult, so it was abandoned in favour of more stable phosphine boranes.

2.2.3. *Tert*-butyl(*para*-(trifluoromethyl)phenyl)phosphineborane (2.6).

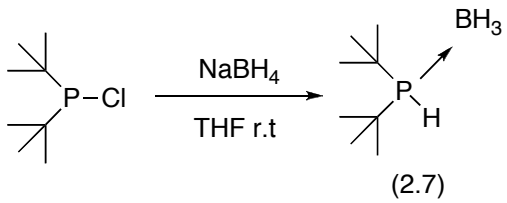


Scheme 2 - 10. Synthesis of 2.6.

The *para* isomer (**2.6**) was prepared by adding a 3 fold excess of $NaBH_4$ directly to the halophosphine mixture formed in Scheme 2 – 3 (Scheme 2 – 10). However in contrast to the other phosphineboranes mentioned above, the synthesis of this compound was always extremely slow, taking up to a week to go to completion. Attempts to speed up the reaction

using large excesses of $NaBH_4$, or heating the reaction mixture, resulted in decomposition to unknown products. The reaction was monitored by $^{31}P\{^1H\}$ NMR, and showed two characteristically broad borane peaks. The first is at 30 ppm, which is the secondary phosphine borane, and a second at 125 ppm which, due to its position, appears to be a halophosphine borane. Over time, the resonance at 125 gets smaller, presumably due to reduction of the P-halogen bond, and the signal at 30 ppm gets progressively larger. There are several other small signals upfield of 0 ppm the origin of which is not known, but presumably it is during the formation of these products that the "free BH_3," which then goes on to be coordinated by P, is produced. When the reaction is complete, the predominant signal is that of the secondary phosphine borane, which was purified by flash chromatography resulting in 62.5% yield of clear viscous oil.

2.2.4. Di-*tert*-butylphosphineborane (2.7).

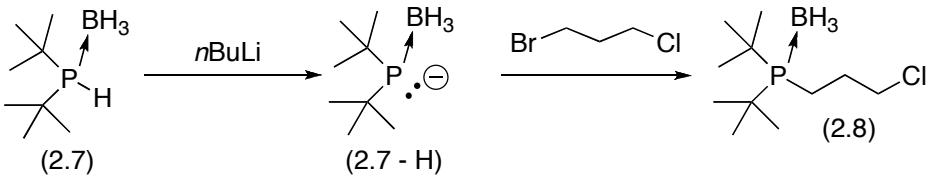


(2.7)

Scheme 2 - 11. Synthesis of 2.7.

Di-*tert*-butylphosphineborane (**2.7**) is a known compound[129] and its synthesis is only discussed here for comparison with that of the other phosphine boranes presented here. The addition of three equivalents of $NaBH_4$ (Scheme 2 – 11) resulted in an incomplete conversion to the secondary phosphine borane after 24 hours. The two additional signals that are present in the $^{31}P\{^1H\}$ NMR spectrum are the singlet at 20 ppm which corresponds to the secondary phosphine,[130] a broad multiplet at 47ppm which corresponds to the product. Another signal is visible at 151 ppm, which is the correct position and peak shape for the chloro borane. There is no signal attributable to the chlorophosphine, suggesting that the chloro phosphine has a higher affinity for borane than the secondary phosphine. This material was easily isolated by recrystallisation with a yield of 86%.

2.2.5. Di-*tert*-butyl(3-chloropropyl)phosphineborane (2.8).



Scheme 2 - 12. Synthesis of 2.8.

The synthesis of **2.8** was performed by the reaction of an anion (**2.7 – H**) generated from **2.7** by deprotonation, with *n*-butyllithium with one equivalent of 1-bromo-3-chloropropane (Scheme 2 – 12). The product was isolated by flash chromatography as a crystalline solid in 58% yield. This material was found to be highly stable, even when stored for over 1 year at room temperature. This makes it a convenient intermediate from which it is possible to synthesise bidentate phosphines given a sufficiently strong nucleophile. No exceptional bond lengths or angles were present in the solid-state structure.

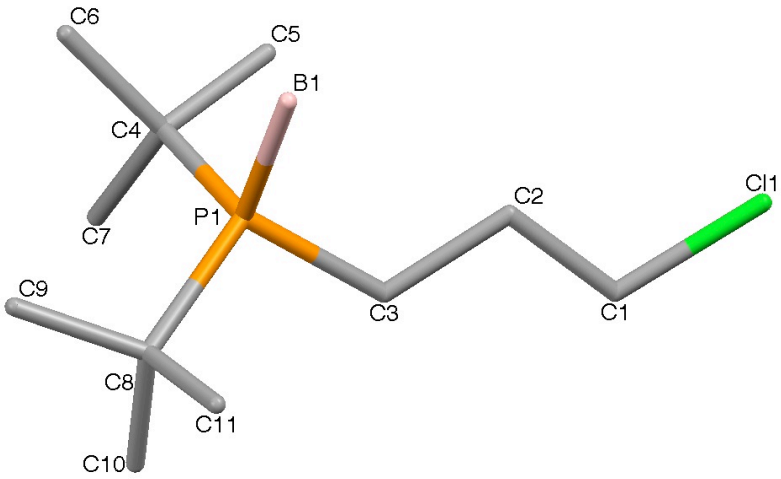
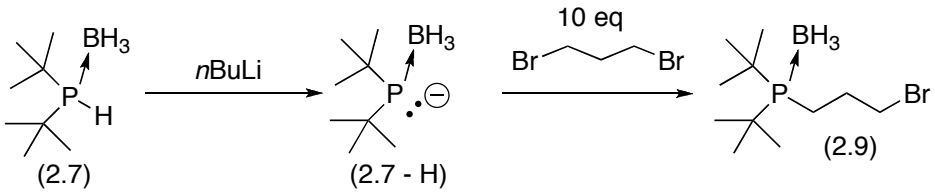


Figure 2 - 2. X-ray structure of 2.8. H atoms omitted for clarity.

Table 2 - 1. Selected bond lengths (Å) and angles (°) for 2.8, with estimated standard deviations in parentheses.

P(1)-C(3)	**1.832(6)**	**C(3)-P(1)-B(1)**	**111.9(3)**
P(1)-C(4)	**1.850(6)**	**C(4)-P(1)-B(1)**	**110.9(3)**
P(1)-C(8)	**1.860(6)**	**C(8)-P(1)-B(1)**	**110.1(3)**
P(1)-B(1)	**1.930(7)**		

2.2.6. Di-*tert*-butyl(3-bromopropyl)phosphineborane (2.9).



Scheme 2 - 13. Synthesis of 2.9.

2.9 was synthesised by the rapid addition of a ten fold excess of 1,3-dibromopropane to a solution containing the phosphide (**2.7 – H**) (Scheme 2 - 13). When the reaction was complete, the additional dibromopropane was removed under vacuum and the product purified either by chromatography or recrystallisation. The yield for this reaction was up to 78%, and the product was obtained as crystalline solid which showed no sign of degradation even after 6 months of storage with no special precautions. It may be possible to produce a variety of highly stable compounds of this type using electron rich phosphine boranes and excesses of dielectrophile. No attempt has been made to synthesise the iodo analogue, or to mono-substitute other dihalides to vary the bridging unit, which may extend the range of unsymmetrical bidentate phosphines that it is possible to synthesise from compounds of this type.

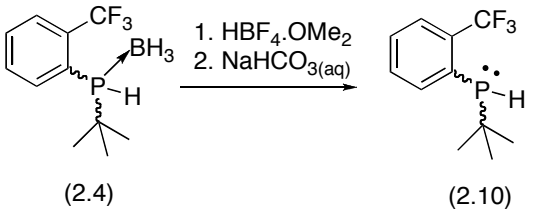
2.2.7. Stability of phosphine boranes.

The stability of phosphine borane bond varies markedly in the compounds discussed here. (**2.7)** and its derivatives are remarkably stable despite the steric bulk that one would assume repels the borane moiety. In this case, the stronger donation of the lone pair induced by the three electron rich alkyl groups overrides these steric repulsions. At the other end of the scale is **2.5**, in which the weaker electron donation caused by the presence of the pentafluorophenyl group is enough to weaken the coordinate bond and (despite the reduction in steric demand) make this compound unstable. The less highly fluorinated, though arguably more bulky, **2.4** is more stable. However, a sample of this material was found to be over 50% decomposed to the secondary phosphine and the resulting oxide after storage for 3 months. Later samples, which were stored at low temperature showed far less evidence of decomposition. One might expect that **2.6** would be significantly more stable than **2.4** due to the reduced steric demand; however this is not the case and some traces of decomposition were detected during TLC. It seems that the lower donor strength caused by the presence of fluorinated groups decreases

the stability of the P-B bond in these bulky phosphines, regardless of the position of the trifluoromethyl substituent. Others have found that steric crowding around phosphorus can lead to instability in phosphine borane complexes of aryl phosphines which are relatively electron rich.[128]

2.3. Synthesis of novel fluorinated mono-phosphines.

2.3.1. Tert-butyl(*ortho*-(trifluoromethyl)phenyl)phosphine (2.10).[115]

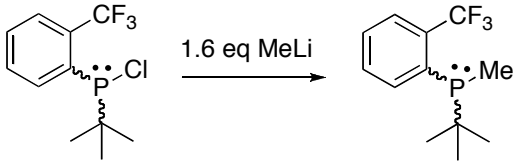


(2.4) (2.10)

Scheme 2 - 14. Synthesis of 2.10.

Deprotection of **2.4** by the use of $HBF_4.OMe_2$ followed by workup with aqueous $NaHCO_3$, as per the methods developed by Livinghouse,[43, 125] allowed the formation of the secondary phosphine **2.10** (Scheme 2 – 14). The $^{31}P\{^1H\}$ NMR spectrum for this compound shows a quartet at -16.3 ppm ($^4J_{P\text{-}F}$ = 27 Hz) and all other data is consistent with the structure.

2.3.2. *Ortho*-trifluoromethylphenyl)(*tert*-butyl)methylphosphine (2.11).



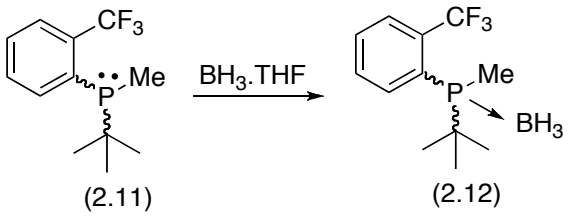
(2.1) (2.11)

Scheme 2 - 15. Synthesis of 2.11.

It was envisaged that by synthesising **2.11** and performing complexation reactions with selected transition metals, it would be possible to gain some insight into the possible coordination behaviour of the bidentate phosphines that were to be produced in this study. **2.11** was prepared from the chlorophosphine (**2.1**) by the addition of an excess of methyllithium (Scheme 2 – 15). The reaction proceeded cleanly and the ^{31}P NMR spectrum showed little evidence of significant impurities. The ^{19}F NMR spectrum displays a doublet at 55.23 ppm due to the ^4J "through space" coupling to phosphorus ($J_{F\text{-}P}$ = 56.9 Hz). The

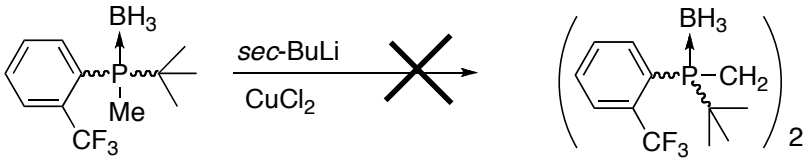
corresponding coupling is seen in the quartet observed in the $^{31}P\{^{1}H\}$ NMR spectrum at -20.0 ppm (J_{P-F} = 58.6Hz).

2.3.3. *Ortho*-trifluoromethylphenyl)(*tert*-butyl)methylphosphineborane (2.12).



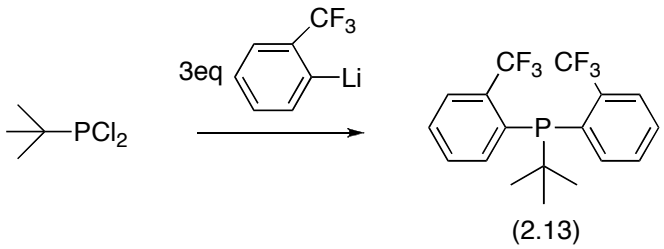
Scheme 2 - 16. Boronation of 2.11.

Although **2.11** was pure enough for synthetic application when it was prepared, it was thought that further purification of this air sensitive compound could be achieved by forming a borane adduct, which would be suitable for column chromatography under atmospheric conditions. The methyl phosphine was easily converted to the borane by the addition of a slight excess of BH_3.THF, (Scheme 2 – 16) and on the first attempt the borane was successfully isolated. However, it became evident in subsequent attempts that the material is prone to deprotection during isolation procedures. It was also hoped that bidentate ligands could be synthesised using the methyl phosphine borane **2.12**, as Imamoto has shown that borane moieties can act as activating groups allowing selective deprotonation of methyl substituents.[131] However, despite several attempts there was no evidence to support the formation of the desired bidentate phosphine (Scheme 2 – 17).



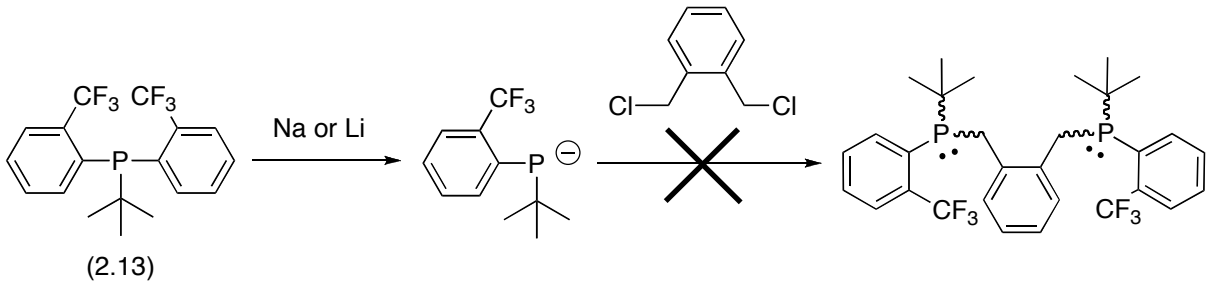
Scheme 2 - 17. Attempted diphosphine synthesis using 2.12.

2.3.4. Bis(*ortho*-trifluoromethylphenyl)(*tert*-butyl)phosphine (2.13).



Scheme 2 - 18. Synthesis of 2.13.

A decision was taken to synthesise **2.13**, which had previously been produced as a trace by-product in the synthesis of **2.1**, as this was recognised as a compound which could be used to further investigate the complexation behaviour of bulky fluorinated ligands with transition metals. **2.13** was synthesised in an analogous fashion to **2.1**. In this case however, a three-fold excess of the lithium reagent was used (Scheme 2 – 18). The relatively air stable solid product was isolated by recrystallisation from ethanol in 82% yield. This compound shows the expected septet, due to the interaction of the phosphorus lone pair with the two fluoromethyl groups, at 2.6 ppm ($^{4}J_{P\text{-}F}$ = 51.2 Hz) in the $^{31}P\{H\}$ spectrum. Literature reports had shown that it was possible to selectively cleave a single phenyl group from (*ortho*-aminophenyl)diphenylphosphine using alkali metal to yield a phosphide nucleophile.[132] We wished to emulate this approach for bidentate phosphine synthesis (Scheme 2 – 19).



Scheme 2 - 19. Attempted diphosphine synthesis using 2.13.

Despite numerous attempts under varying conditions we were unable to successfully generate diphosphines using **2.13**. No reaction was observed with lithium, and reaction with sodium gave an extremely complicated mixture of phosphorus containing products, in which it was impossible to positively confirm any formation of the desired diphosphine.

2.4. Monodentate complexes from palladium and platinum precursors.

Tris(*ortho*-trifluoromethylphenyl)phosphine does form a complex with rhodium,[49] but it does not however form mono-ligated complexes with palladium and platinum. This behaviour is probably due to the combination of its very bulky steric profile and the lower σ donor strength caused by the presence of three electronegative groups. To ascertain if a similar behaviour would be exhibited by the bulky electron poor ligands synthesised in this study, a series of coordination chemistry experiments was performed with a variety of transition metal precursors. It was hoped that the presence of the electron rich *tert*-butyl substituent would enhance the donor strength of the phosphorus lone pair and result in the formation of stable complexes.

2.4.1. Zeise's salt.

The reaction of **2.13** with 1 equivalent of Zeise's salt at room temperature gave full conversion to a complex which has defied attempts at characterisation. The electrospray mass spectrum was consistent with the ligand retaining its composition and being bound to Pt in a 1:1 ratio. The $^{31}P\{H\}$ NMR spectra indicate the presence of four similar phosphorus environments, each displaying the characteristic Pt satellites on either side of the central signals (Figure 2 - 3).

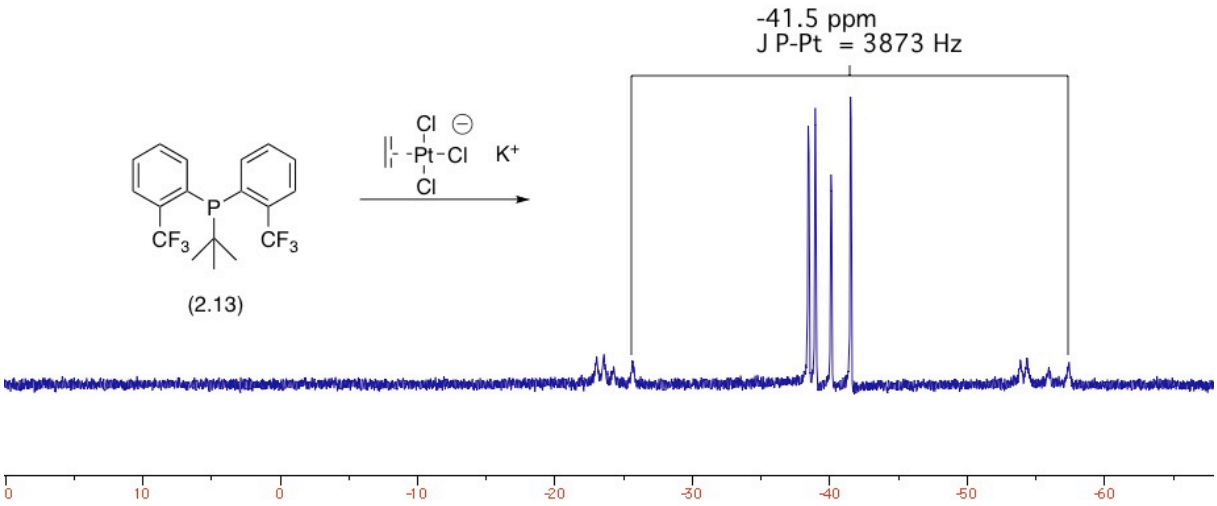
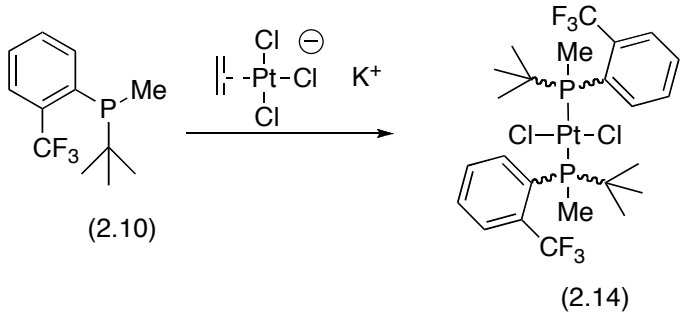


Figure 2 - 3. $^{31}P\{H\}$ NMR of the product of the reaction between 2.13 and Zeise's salt.

The value of the Pt-P coupling constants, at about 3870 Hz, are consistent with the formation of complexes with the phosphine ligand trans to chloride.[133] The coordination chemical shift of the new species are around - 40 ppm and is in the opposite direction to that usually seen in complexation reactions of this type. A coordination chemical shift of this magnitude is

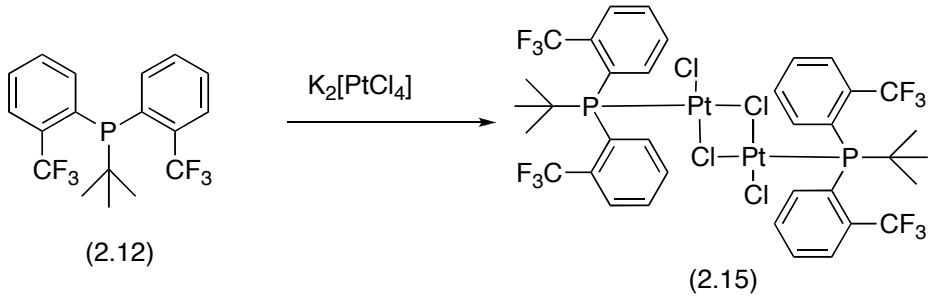
consistent with the formation of a four membered ring,[134] and *tert*-butyl substituted phosphines are known to form internally metalated four membered rings in reactions with platinum precursors.[135] Despite several attempts, crystals suitable for X-ray analysis could not be obtained.

Ligand **2.10** also gave a complex when stirred in the presence of Zeise's salt (Scheme 2 – 20). The $^{31}P\{H\}$ NMR spectrum indicates the presence of a complex with a resonance at 25.1 ppm with the characteristic Pt satellites. The value of the coupling constant at $^{1}J_{P\text{-}Pt} = 2587$ Hz is consistent with a *trans* complex,[133] as may be expected for this bulky phosphine. The mass spectrum indicates the existence of a complex with the formula $[PtCl_2(C_6H_4(CF_3)C_4H_9MeP)_2]$ (**2.14)**.



Scheme 2 - 20. Reaction of 2.10 with Zeise's salt.

2.4.2. $K_2[PtCl_4]$.

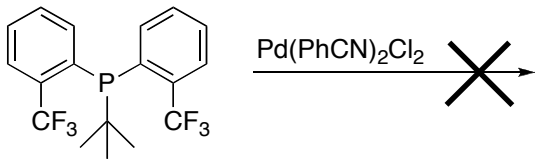


Scheme 2 - 21. Reaction of 2.12 with $K_2[PtCl_4]$.

2.12 only reacted partially with $K_2[PtCl_4]$ (Scheme 2 – 21). The ^{31}P $\{^{1}H\}$ NMR spectrum of the complex displays a quartet in which the $^{4}J_{P\text{-}F}$ coupling constant of 5 Hz can be seen. The characteristic ^{195}Pt satellites are also evident and the value of this coupling ($^{1}J_{P\text{-}Pt} = 3324$ Hz,) is considered relatively low for a P-*trans*-Cl complex [*cis*-$Pt(PPh_3)_2Cl_2$] ($^{1}J_{P\text{-}Pt} = 3676$ Hz).[133] This is however significantly larger than $^{1}J_{P\text{-}Pt}$ seen in the P-*trans*-P complexes $[PtCl_2(PPh_3)_2]$ (2635 Hz),[133] $[PtCl_2(PPh_2(2\text{-}C_6H_4CF_3))_2]$ ($^{1}J_{P\text{-}Pt}$=2805 Hz)[50] and $[PtCl(C_4H_8P(t\text{-}Bu)_2P(t\text{-}Bu)_3]$

($^1J_{P\text{-}Pt}$ = 2680, 2360 Hz).[135] Mass spectral data show a strong signal corresponding to $[Pt((C_6H_4(CF_3))_2C_4H_9P)Cl_2]$, however a peak can be seen at the higher range of the spectrum corresponding to the dimer (**2.15**).

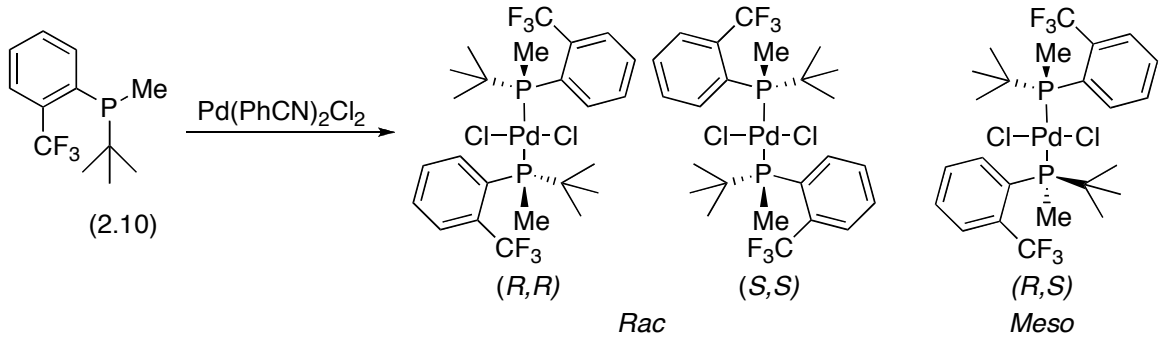
2.4.3. $[Pd(PhCN)_2Cl_2]$.



(2.12)

Scheme 2 - 1. Reaction of 2.12 with $[Pd(PhCN)_2Cl_2]$.

There was no discernable evidence of reaction between **2.12** and $[Pd(PhCN)_2Cl_2]$ even after extended heating (Scheme 2 – 22). However, a complex did form between **2.10** and this Pd precursor (Scheme 2 – 23). A crystal structure of the *meso* isomer was successfully obtained and this shows that a 2:1 complex forms between the ligand and palladium (Figure 2 – 4).



(2.10)

(*R,R*) (*S,S*) (*R,S*)

Rac *Meso*

2 diastereomers

(2.16)

Scheme 2 - 22. Reaction of 2.10 with $Pd(PhCN)_2Cl_2$ showing the three possible stereoisomers.

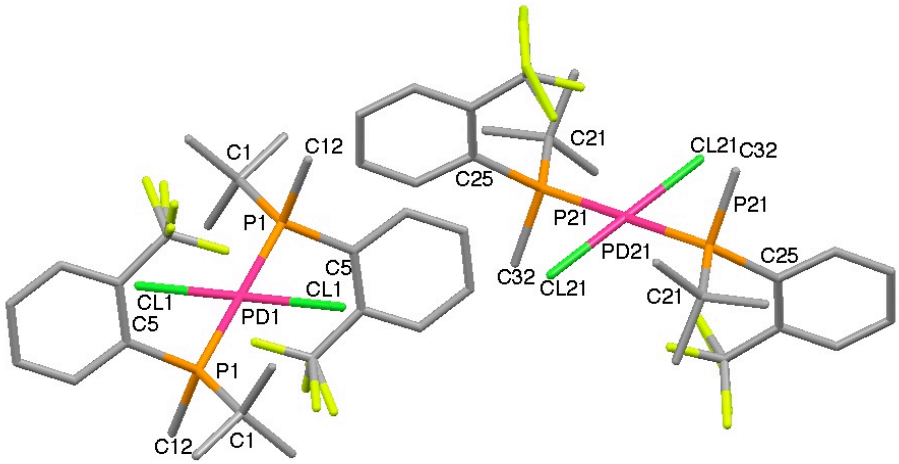


Figure 2 - 4. Solid state structure of 2.16 *meso*. Hydrogens omitted for clarity.

Table 2 - 2. Selected bond lengths (Å) and angles (°) for 2.16, with estimated standard deviations in parentheses.

Pd(1)		Pd(21)	
C(12)-P(1)-Pd(1)	103.82(16)	C(32)-P(21)-Pd(21)	103.59(17)
C(5)-P(1)-Pd(1)	111.84(14)	C(25)-P(21)-Pd(21)	115.45(15)
C(1)-P(1)-Pd(1)	125.74(16)	C(21)-P(21)-Pd(21)	124.43(17)
Cl(1)#1-Pd(1)-P(1)	95.28(5)	Cl(21)-Pd(21)-P(21)	96.02(5)
Cl(1)-Pd(1)-P(1)	84.72(5)	Cl(21)#2-Pd(21)-P(21)	83.98(5)
Pd(1)-Cl(1)	2.3240(11)	Pd(21)-Cl(21)	2.3172(12)
Pd(1)-P(1)	2.3315(13)	Pd(21)-P(21)	2.3606(13)

The unit cell of the complex consists of two distinct molecules with slightly different dimensions. Both molecules are made up of two phosphorus ligands that are of opposite optical rotation and arranged *trans* to each other. They adopt a staggered conformation about the P-Pd-P axis such that each of the substituents on phosphorus is at 180° to its counterpart when viewed along this axis. The arrangement of ligands around Pd is distorted from square planar with two acute and two obtuse Cl-Pd-P angles. The Pd-P-C angles seem to reflect the effective steric bulk of the substituents with the smallest for methyl, and the largest for *tert*-butyl. There is some disorder in all of the trifluoromethyl groups. The distance from Pd to the closest F atoms at 2.898 Å is just close enough for an electrostatic interaction to be possible.

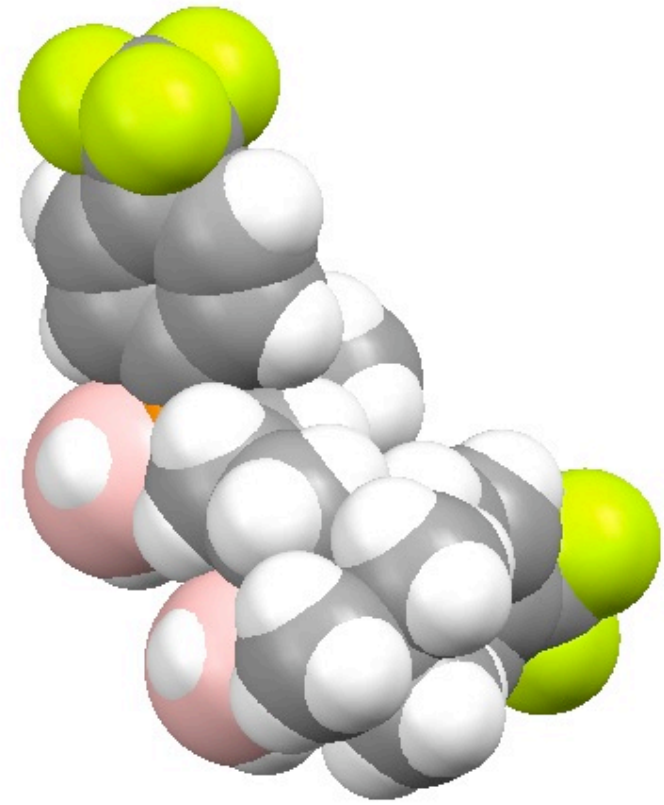
Although the diastereomer which crystallised out was the *meso* isomer, in which both phosphine units are of the opposite optical rotation, the *rac* isomer in which the phosphines are of the same optical rotation also appears to be present in solution (judging by the ^{31}P NMR

spectrum), in a 1:2.5 ratio (*rac*:*meso*). P-F coupling is seen in the ^{19}F and ^{31}P NMR spectra in contrast to other compounds in this study where there is no free lone pair such as boranes or oxides. However, the ^{19}F spectrum does not display a simple first order d or dd coupling pattern. Instead, each diastereomer gives rise to a virtual triplet due to the apparent equivalence of the two strongly coupled *trans* phosphorus atoms, i.e. this is an $A_3A'_3XX'$ system. These observations are mirrored in the ^{1}H and ^{13}C spectra where the methyl and *tert*-butyl groups also give rise to virtual triplets. Similar observations have been made previously for related systems.[50]

2.5. Summary.

Novel halophosphines containing a mixture of bulky alkyl and fluorine containing aryl groups have been successfully synthesised. A range of phosphine borane building blocks for diphosphine synthesis, were also successfully prepared. However, some of the bulky fluorinated phosphine boranes have been found to be significantly less stable than alkyl phosphine boranes. Two novel bulky fluorinated monophosphine ligands were synthesised and were found to react with some Pd and Pt precursors to form complexes.

3. Synthesis of Bulky Fluorinated Diphosphine Compounds.



sasol
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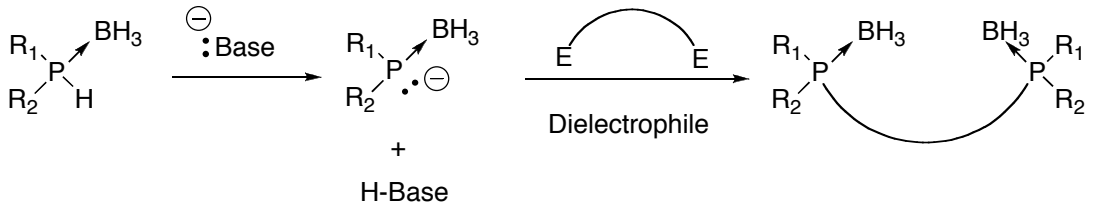
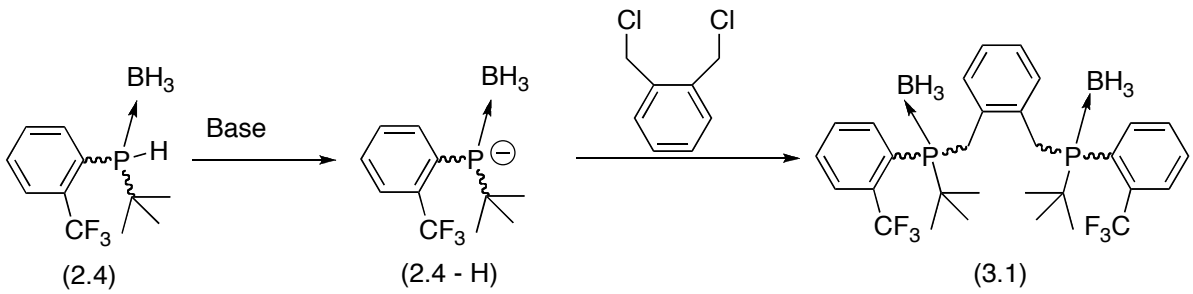
3.1. Deprotonation of secondary phosphine boranes for bidentate phosphine synthesis.



Scheme 3 - 1. Outline of strategy for the synthesis of bidentate phosphines.

It was decided that to synthesise bridged bidentate phosphines based on **2.4** the phosphine borane strategies developed by Imamoto and co-workers would be employed (Scheme 3 – 1).[123, 131, 136] These techniques have proved popular and successful for the synthesis of diphosphines.[43, 127, 137]

3.1.1. Problems in secondary boranophosphide (2.4 – H) formation.



Scheme 3 - 2. Synthesis of 3.1

An initial small-scale attempt to deprotonate **2.4** using KO*t*-Bu and subsequent addition of dichloroxylene (Scheme 3 - 2) failed to give **3.1** in a satisfactory yield. It was therefore decided that the deprotonation process should be investigated.

3.1.2. NMR studies of deprotonation.

Deprotonation with KO*t*-Bu resulted in very little of the desired anion (**2.4 – H**) and large amounts of a product which gave a quartet at -16 ppm in the ^{31}P-NMR spectrum. This was later identified as the secondary phosphine (**2.10**).[138] Surprisingly, **2.4** was present in significant quantities despite 1.1 equivalents of base being added (Figure 3 - 1).

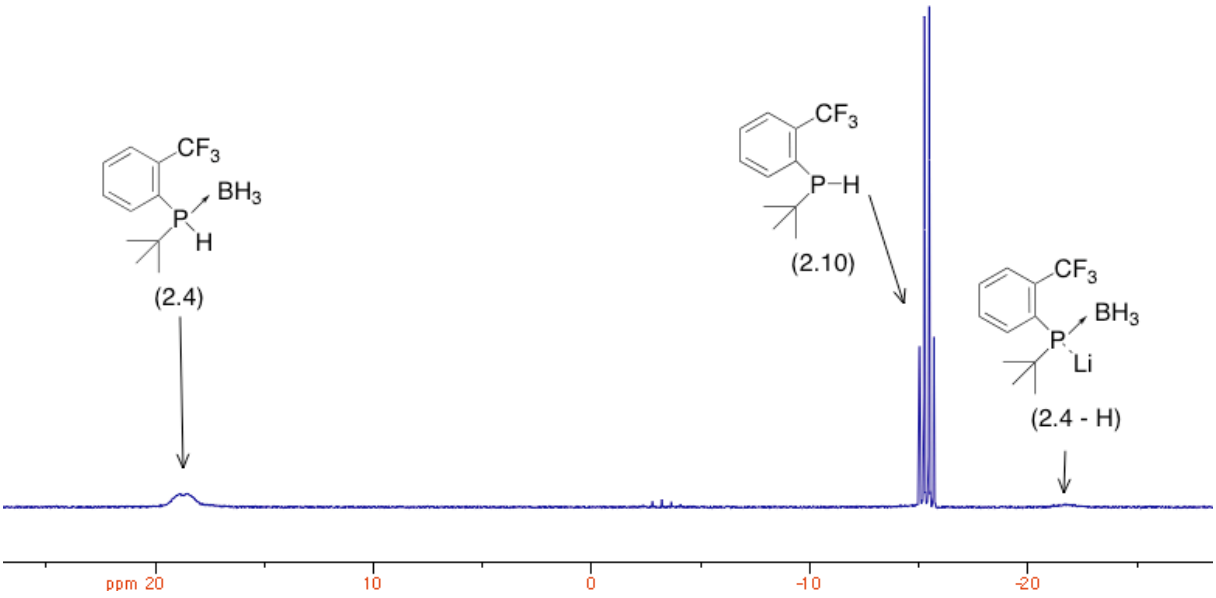


Figure 3 - 1. $^{31}P\{H\}$ spectrum observed within 1 hour of the addition of 1.1 equivalents of KO*t*-Bu to a THF solution of 2.4.

At this stage, a range of different bases were tested and *n*-butyllithium was found to give the best conversion to the anion (**2.4 – H)**. However, the formation of this was also accompanied with significant amounts of **2.10**. Again, residual **2.4** was also present, despite an excess of *n*-butyllithium being used (typically 1.1 equivalents). Repeated reactions gave the same results despite the use of freshly purchased *n*-butyllithium (the concentration of which was confirmed by titration) and dry solvents from a variety of sources. The anion (**2.4 – H)** was characterised using a variety of NMR techniques (Figure 3 – 2). The $^{31}P\{H\}$ NMR spectrum shows a complex multiplet in which the 50 Hz P-F, and the 36 Hz P-B couplings, that are evident in the ^{11}B and ^{19}F spectra can just be discerned. The lack of any P-Li coupling in the ^{7}Li NMR spectrum may be an indication that Li is fully dissociated in this solvent.

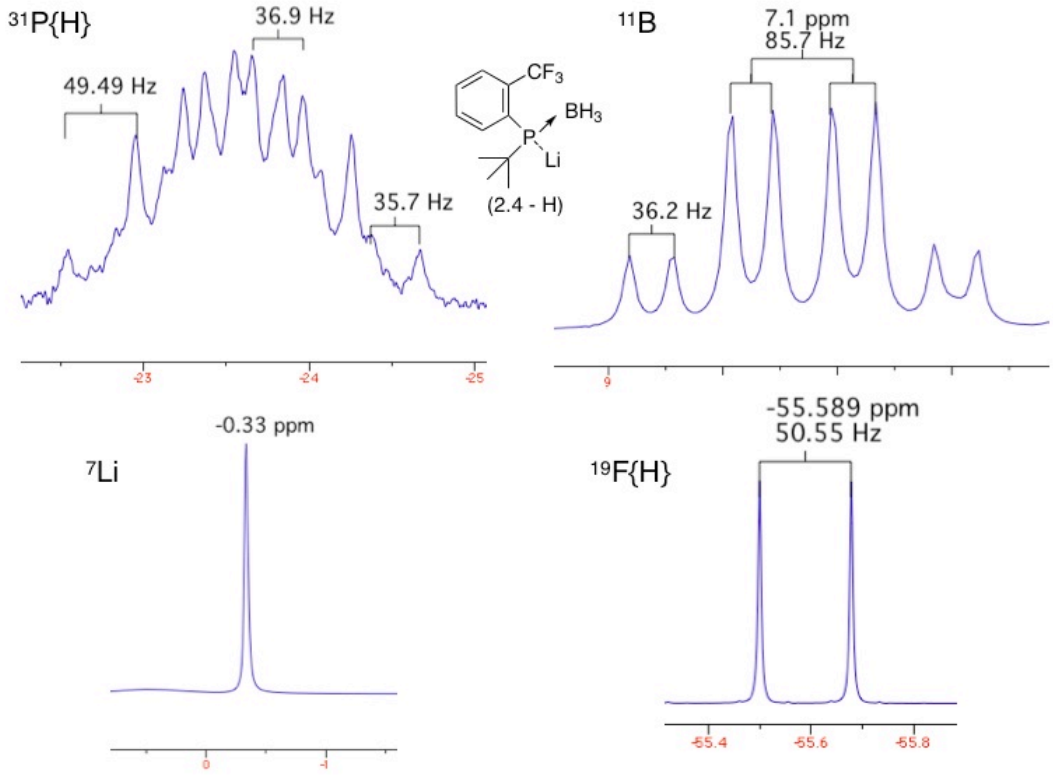


Figure 3 - 2. NMR spectra of the anion derived from 2.4 (2.4 – H).

The behaviour observed during deprotonation of **2.4** is in sharp contrast to that of **2.7** which, is robust during deprotonation and requires no special precautions. The addition of a small excess of *n*-butyllithium fully deprotonates **2.7** cleanly, with no phosphorus-containing side products being formed. The $^{31}P\{H\}$ and ^{11}B spectra of the anion (**2.7 – H)** are shown in Figure 3 - 3.

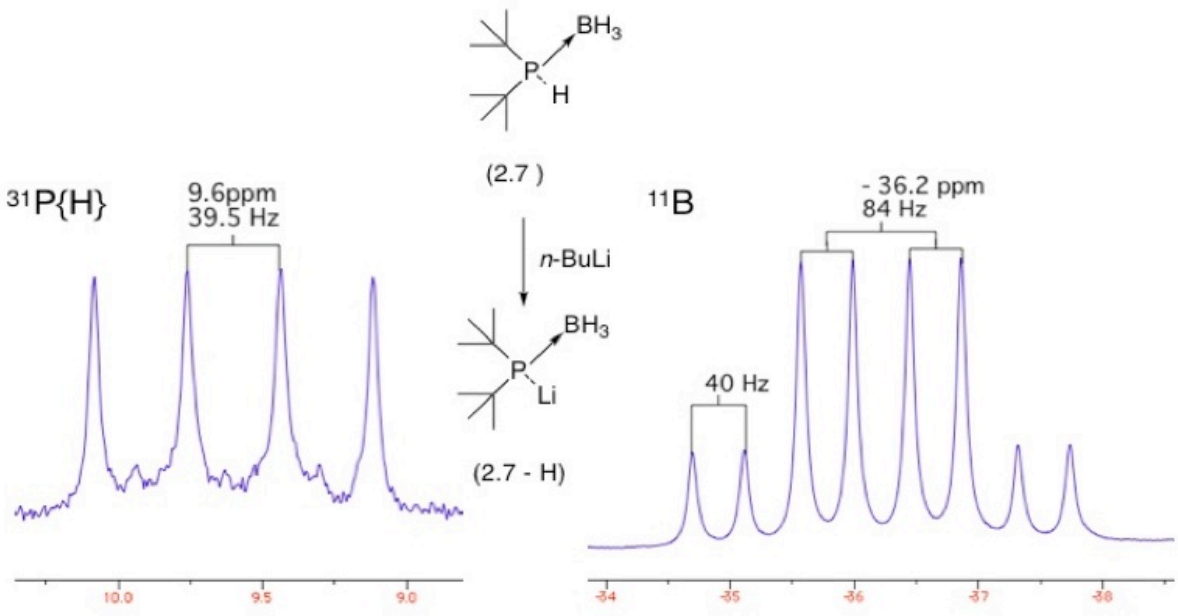


Figure 3 - 3. NMR spectra of 2.7 – H.

Comparison of NMR data for secondary boranes and phosphides.

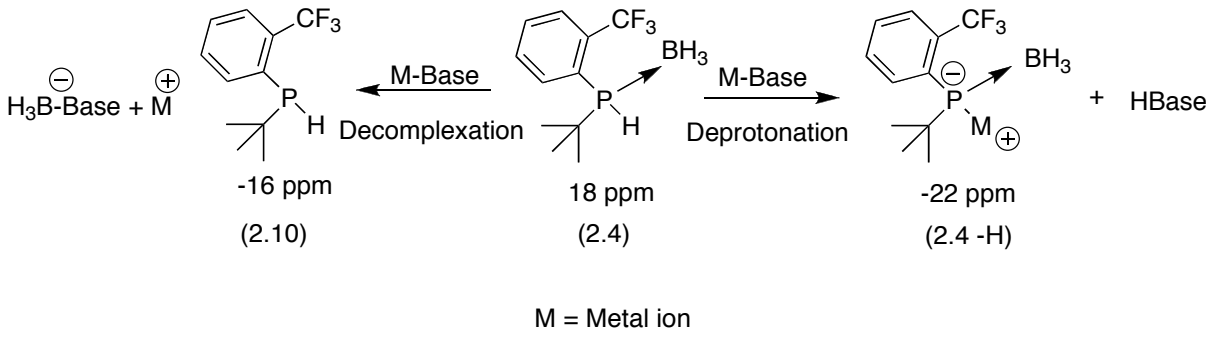
Table 3 - 1. Boron NMR data for selected species.

Species	δ^{11}B ppm	J_{P-B} Hz	J_{B-H} Hz
2.4	42.5	40	100
2.4 - H	7.1	36	85
2.7	-42.7	47	75.5
2.7 - H	-36.2	40	84
PF_3BH_3	66.6	39	107[139]
$(CH_3)_3PBH_3$	54.2	54	97.4[139]

Comparison of the P-B coupling constants shows that the lowest J_{P-B} value is observed for **2.4 –H** (Table 3 -1), lower even than PF_3BH_3, which does not form stable borane complexes. The value of P-B coupling constants is a qualitative indication of bond strength,[139, 140] and both the anions (**2.4 – H** and **2.7 – H)** have lower values than their parent phosphine boranes.

3.1.3. Decomplexation of 2.4 during deprotonation.

The formation of secondary phosphine during the reaction of **2.4** with bases shares many of the characteristics of the amine-mediated decomplexation reactions used to deprotect phosphine boranes. It is now thought that the addition of a base results in the formation of free phosphine, and higher temperatures increase the tendency towards decomplexation. The deprotonation and the competing decomplexation reaction are shown in Scheme 3 - 3.

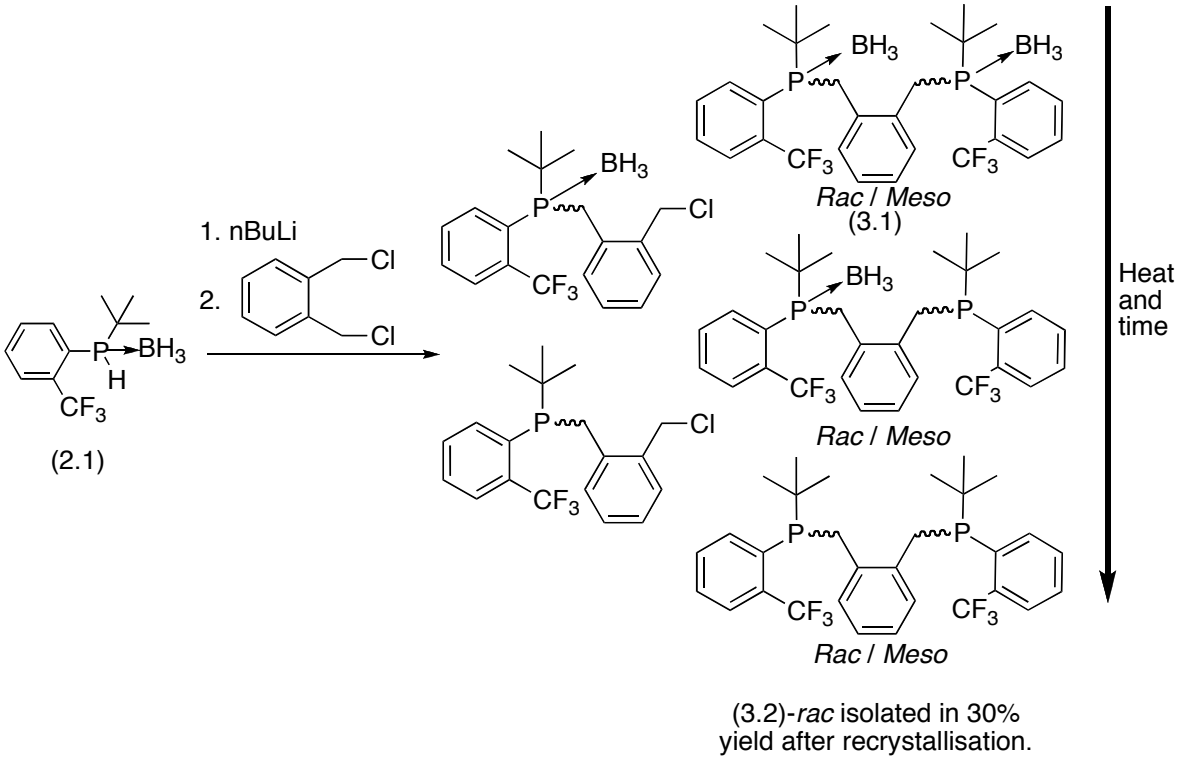


Scheme 3 - 3. Reaction of 2.4 with bases showing a possible decomplexation reaction.

Attempts were made to optimise reaction conditions based on the results of these investigations. Through the use of low temperatures and extremely slow addition of diluted *n*-butyllithium to freshly recrystallised **2.4**, significantly improved yields of (**2.4 – H**) were observed. However, some decomposition could not be prevented.

3.2. Symmetrical bidentate ligand synthesis.

3.2.1. Synthesis of 3.2-*rac*.



Scheme 3 - 4. Synthesis and decomplexation reactions leading to 3.2 formation.

The reaction of the anion (**2.4 – H)** with dichloro xylene did not give the expected diphosphine diborane in significant yield as judged by ^{31}P NMR spectroscopy, instead a complicated mixture was produced in which the expected product was a minor component (Scheme 3 – 4). Other components of this mixture did not show the characteristic P-B coupling. Our first attempt at purification was to treat the mixture with BH_3.THF to reboronate the products in order to protect the lone pair, before recrystallisation and chromatography but this resulted in similarly complicated mixtures. It became clear that the product was spontaneously decomplexing, leading to a mixture that contained *meso* and *rac* isomers of the diborane, monoborane and unboronated forms of the diphosphine, as well as the boronated and unboronated mono phosphine. Prolonged heating of this mixture resulted in further decomplexation, and the mixture gradually simplified to yield the two diastereomers of the diphosphine in approximately 1:1 ratio, as well as the monophosphine as a minor component. Recrystallisation of the free diphosphine (**3.2-*rac***) from CH_2Cl_2/ethanol provided the diphosphine as clear needles suitable for X-ray analysis in 30% yield (Figure 3 - 4), and this confirmed the stereochemistry of the recrystallised ligand.

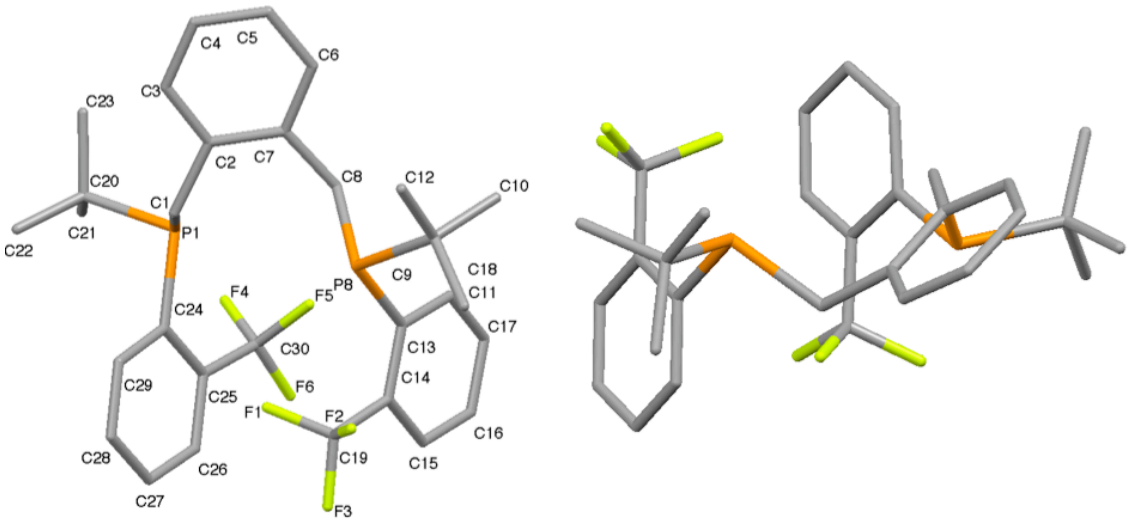
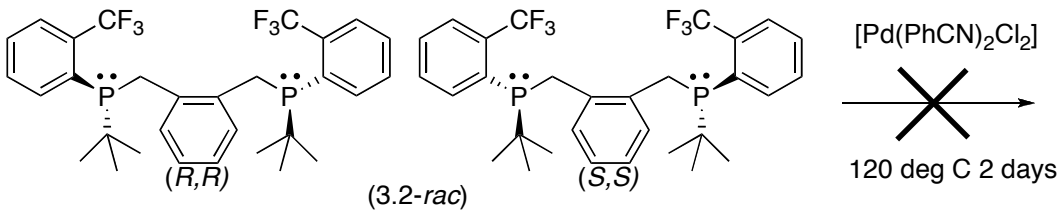


Figure 3 - 4. X-ray crystal structure of 3.2-*rac*. All hydrogen atoms have been omitted for clarity.

Table 3 - 2. Selected bond lengths (Å) and angles (˚) for 3.2-*rac*, with estimated standard deviations in parentheses.

P(1)		P(8)	
P(1)-C(24)	1.8646(16)	P(8)-C(13)	1.8646(16)
P(1)-C(1)	1.8770(16)	P(8)-C(9)	1.8931(17)
P(1)-C(20)	1.8909(17)	P(8)-C(8)	1.8752(16)
C(24)-P(1)-C(1)	98.33(7)	C(13)-P(8)-C(8)	98.18(7)
C(24)-P(1)-C(20)	102.78(7)	C(13)-P(8)-C(9)	102.28(7)
C(1)-P(1)-C(20)	105.62(7)	C(8)-P(8)-C(9)	105.67(7)

The molecule is *C2* symmetric with no significant differences between either of the phosphorus subunits. P-C bond lengths are unexceptional. The phosphorus lone pairs are oriented away from each other in opposite directions, and the bulky *ortho*-CF_3 substituted aryl groups are oriented so that the trifluoromethyl groups are aligned with the lone pair. This arrangement, coupled with the proximity of the *tert*-butyl and xylyl CH_2 groups, results in considerable steric hindrance around phosphorus. If similar geometry is adopted in the solution phase, this may help to explain why no palladium complex of this diphosphine was observed during this project, despite the use of elevated temperatures (Scheme 3 -5).

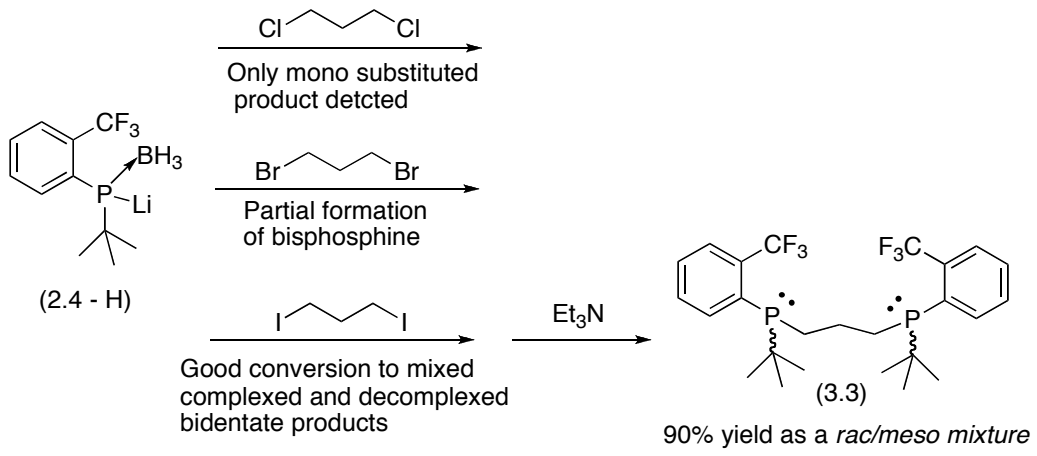


Scheme 3 - 5. No observable reaction between 3.2-*rac* and $[Pd(PhCN)_2Cl_2]$ despite extended reaction times and elevated temperatures.

3.2.2. Synthesis of 3.3.

It was decided to synthesise a propyl bridged bidentate phosphine by the reaction of **2.4 –H** with a 1,3-propyl dihalide (Scheme 3 – 6). Initial attempts to perform this reaction using the dichloride produced only traces of the expected product, observed as a broad signal at 34 ppm in the $^{31}P\{H\}$ NMR spectum. Several new quartets were apparent between -7.5 and -10.5 ppm, due to the presence of decomplexed tertiary phosphine moieties. In further reactions using a dibromide electrophile, the phosphide reacted more fully, however these reactions frequently resulted in unsatisfactory yields of bidentate product. The use of 1,3-propyldiiodide with a carefully optimised deprotonation procedure involving very slow addition of *n*-butyllithium eventually resulted in good conversion to mixed complexed and decomplexed diphosphines. The addition of triethylamine to this mixture resulted in full decomplexation to the free diphosphine (**3.3**). After aqueous workup, attempts were made to recrystallise this material and some solid material did form in hexane at low temperatures (-78 °C). However, this method of purification was judged unsuitable.

The decision was taken to isolate this material by chromatography under inert gas, using degassed solvent with fraction collection into round-bottomed flasks under a stream of argon. The fractions were then reduced on a standard rotary evaporator before being quickly restored to an inert atmosphere. The purity of fractions was assessed using ^{31}P NMR. Using this rather laborious method, it was possible to obtain the phosphine in relatively high purity with the only other signals present being attributed to the phosphine oxides (49.8 and 50.1 ppm, 1-2%), which probably formed at elevated temperatures during solvent removal, as this material has been found to be relatively air-stable at room temperature. Although the ligand was isolated as a diastereomeric mixture, a small degree of enrichment was observed. However obtaining pure diastereomers by this method was judged impractical.

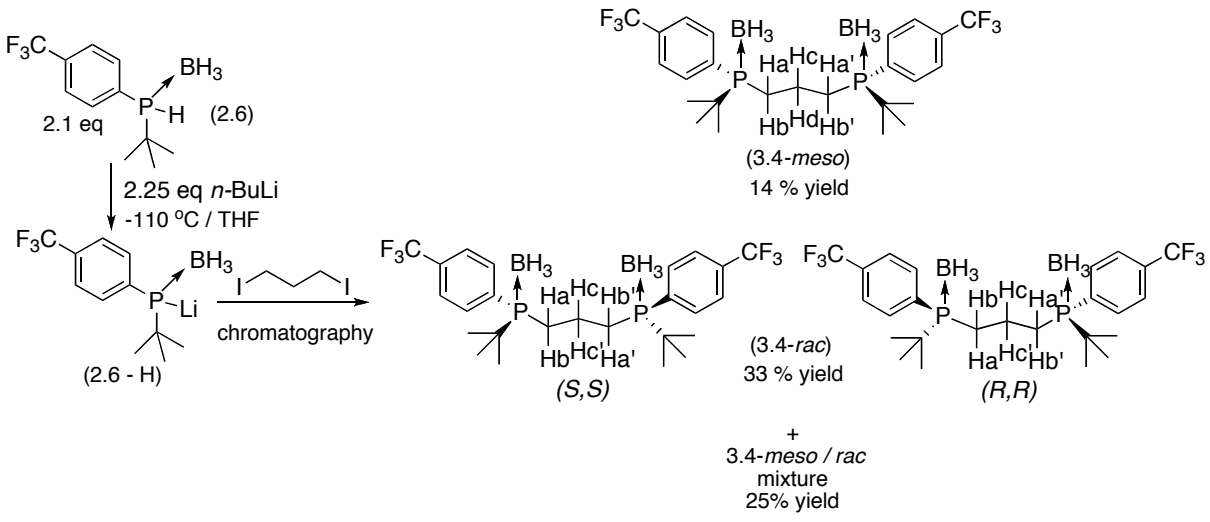


Scheme 3 - 6. Synthesis of 3.3.

The ^{31}P NMR shows two quartets which, due to the diastereomeric enrichment, are assigned by correlation with the ^{1}H spectrum. The signal at -8.6 ppm is assigned as the *rac* and the *meso* isomer is apparent at 10.2 ppm. The "through space" interaction leads to a 57 Hz P-F coupling constant which is also seen in the ^{19}F spectrum at 57.1 ppm for the *meso* and 58.0 ppm for the *rac*. All other data is wholly consistent with the structure.

3.2.3. Synthesis of 3.4-*rac* and *meso*.

To evaluate the catalytic importance of the *ortho* substitution of the CF_3 group on the phenyl ring the *para* isomer was synthesised (Scheme 3 -7). It was reasoned that, due to the reduced steric demand, the borane complex of this ligand would be more stable and therefore purification and handling would be a good deal easier. Initially it was hoped that the deprotonation of the **2.6** would also be a more forgiving procedure, similar to the deprotonation of the dialkylphosphineborane (**2.7)**, but in practice, significant amounts of by-products were formed. $^{31}P\{^{1}H\}$ NMR of the reaction mixture showed a sharp singlet at -5.6 ppm, which is attributed to the secondary phosphine, as well as several other signals which due to their broad profile are attributed to fluxional species. Despite the formation of these by-products it was possible to successfully generate the desired anion (**2.6 – H)**, which was observed as a broad multiplet at -10.7 ppm, by the very slow addition of *n*-butyllithium to a solution of the secondary borane maintained at -110° C.



Scheme 3 - 7. Synthesis of 3.4.

Addition of 1,3-diiodopropane to this solution resulted in good conversion to the bisborane complexed diphosphine ligand (**3.4**), however it should be noted that an excess of the anion was required to achieve acceptable yields in this reaction. In contrast to **3.1**and **3.3** this borane

complex was considered to be stable enough for isolation by flash chromatography under atmospheric conditions. TLC showed the two spots which were proved to be separable by careful control of polarity. Crystals suitable for x-ray analysis were obtained from the pure fractions, which gave only a single spot by TLC, and these were found to be the isomers (**3.4-*meso***) and (**3.4-*rac***). By recrystallisation of mixed fractions, the isolation of the *meso* and *rac* isomers was achieved in 14% and 33% yield respectively, with the remainder of the 72% total yield being a made up of a mixture of the two diastereomers. The borane complex of this compound was found to be reasonably stable when refrigerated, with only a small (1-2%) conversion to the phosphine oxide in 8 weeks.

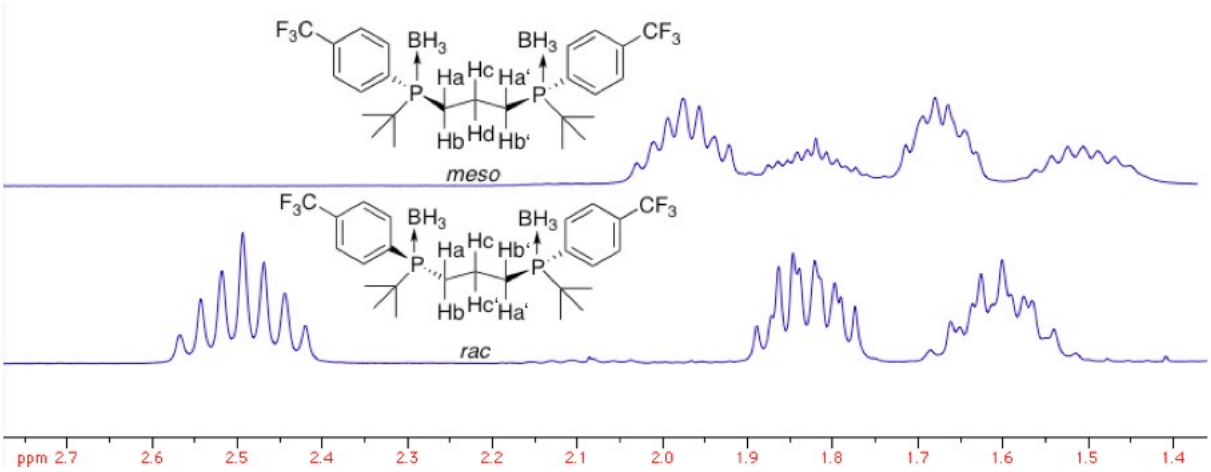


Figure 3 - 5. ^{1}H spectra of the bridging methylene protons for the two diastereomeric forms of 3.4.

The ^{31}P NMR spectrum shows characteristic broad multiplets at 34 ppm for both diastereomers as would be expected for phosphine boranes. However, the most significant differences between the diastereomers are seen in the proton NMR spectrum, with the *meso* isomer giving rise to four multiplets which correspond to the proton environments in the propyl bridge, and the *rac* isomer giving rise to only three (Figure 3 - 5). The solid state structures confirm the structures of the two diastereomers.

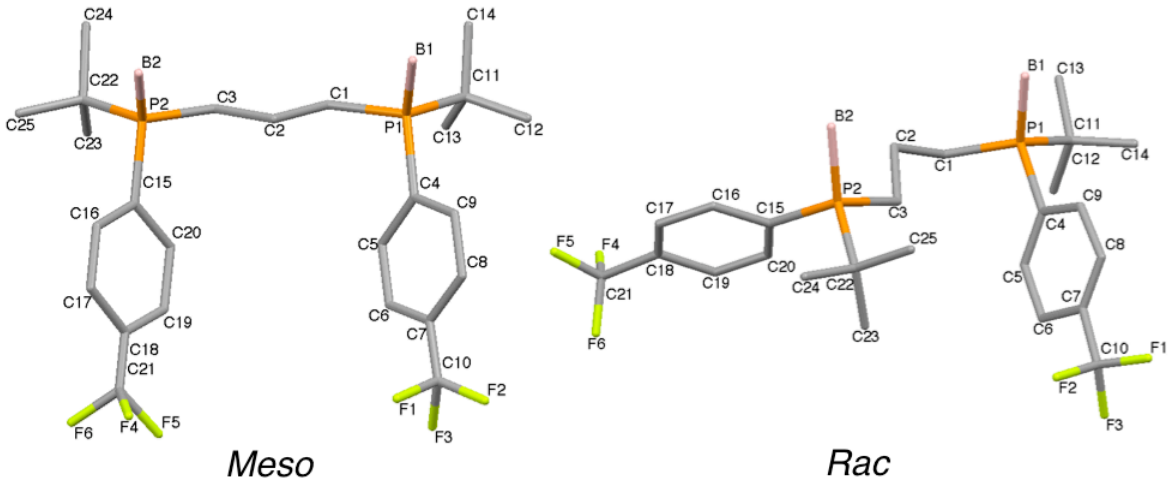


Figure 3 - 6. X-ray crystal structures of 3.4-*meso* and 3.4-*rac*. All hydrogen atoms have been omitted for clarity.

Table 3 - 3. Selected bond lengths (Å) and angles (°) for 3.4-*meso*, with estimated standard deviations in parentheses.

Meso			
P(1)-B(1)	1.929(18)	P(2)-B(2)	1.96(3)
P(1)-C(1)	1.899(15)	P(2)-C(3)	1.82(2)
P(1)-C(4)	1.841(16)	P(2)-C(15)	1.841(17)
P(1)-C(11)	1.88(2)	P(2)-C(22)	1.785(17)
C(1)-P(1)-B(1)	110.8(7)	C(3)-P(2)-B(2)	114.0(11)
C(4)-P(1)-B(1)	112.7(7)	C(15)-P(2)-B(2)	111.7(10)
C(11)-P(1)-B(1)	114.0(9)	C(22)-P(2)-B(2)	114.7(10)

Table 3 - 4. Selected bond lengths (Å) and angles (°) for 3.4-*rac*, with estimated standard deviations in parentheses.

Rac			
P(1)-B(1)	1.858(19)	P(2)-B(2)	1.89(2)
P(1)-C(1)	1.826(14)	P(3)-C(2)	1.820(14)
P(1)-C(4)	1.839(14)	P(2)-C(15)	1.853(15)
P(1)-C(11)	1.884(17)	P(2)-C(22)	1.857(15)
C(1)-P(1)-B(1)	111.9(8)	C(3)-P(2)-B(2)	110.9(8)
C(4)-P(1)-B(1)	111.5(7)	C(15)-P(2)-B(2)	113.4(8)
C(11)-P(1)-B(1)	115.6(8)	C(22)-P(2)-B(2)	117.5(8)

3.2.4. Synthesis of 1,3-bis(di*tert*-butyl)phosphinodiborane (3.5).

The diphosphine **3.5** was synthesised, as a it was desirable to compare the catalytic performance of complexes based on the novel ligands synthesised in this project with a known bulky, yet electron rich ligand. The synthesis of **3.5** has not previously been reported in the open literature and is worthy of mentioning for comparison with the synthesis of the bidentate phosphines discussed above. Only 2 signals were observed in the ^{31}P NMR spectrum (Figure 3- 7) after the reaction of an excess of the anion (**2.7- H)** with dibromo propane, that of the bidentate diborane complex (**3.4**) at 46 ppm and the residual boranophosphide (**2.7 - H**) at 7 ppm. The diboronated diphosphine was isolated in 82 % yield after recrystallisation. These observations indicate that despite its bulky structure the phosphide is more nucleophilic than the fluorinated phosphines and, in the absence of degradation products, the phosphide anion is stable. Chromatography, recrystallisation and storage of the diboranecomplex for 6 months at room temperature did not result in any observable degradation of **3.5**.

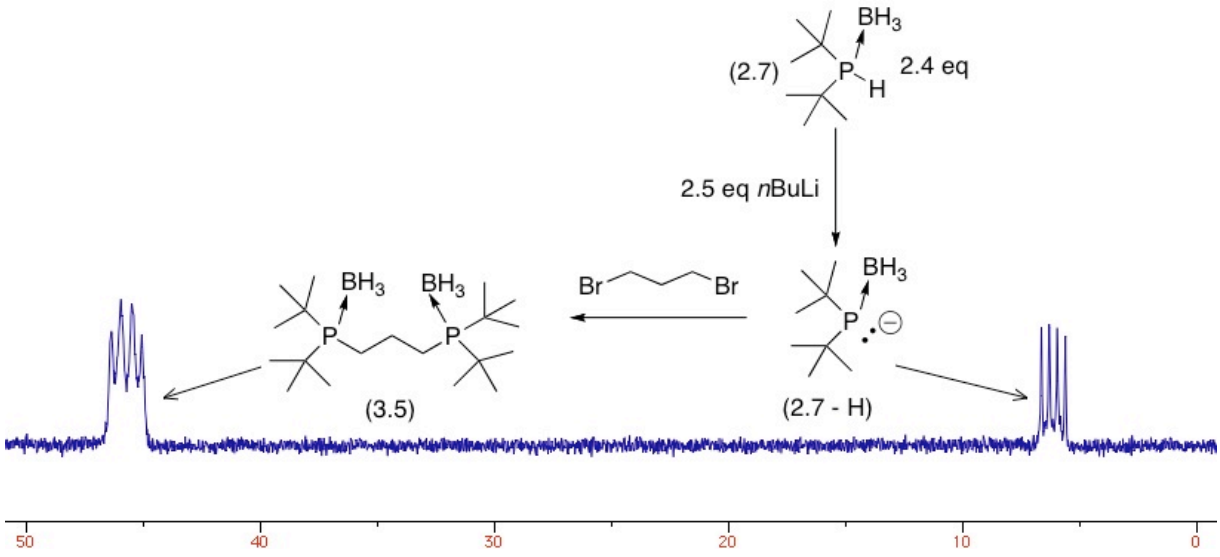
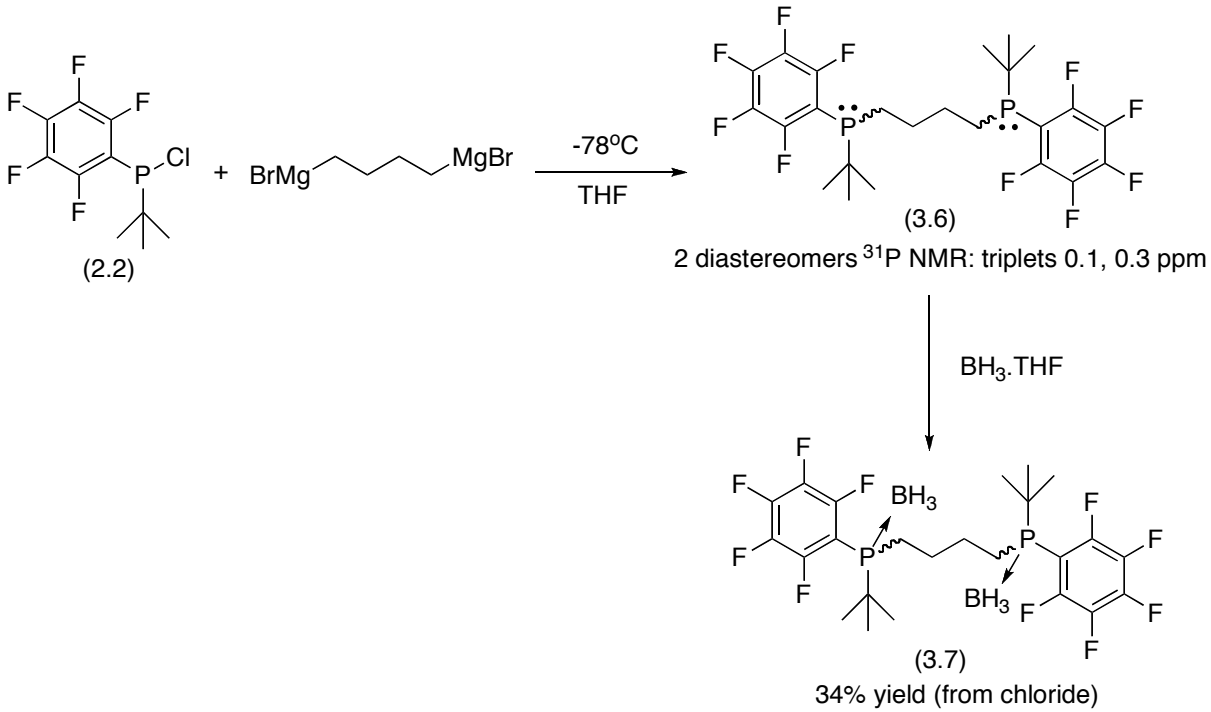


Figure 3 - 7. ^{31}P{H} NMR spectrum of the reaction mixture 16 hours after the addition of excess 2.7 – H to dibromopropane.

3.2.5. Synthesis of a diphosphine using Grignard chemistry (3.6).

As it has been reported that it is possible to synthesise 1,4-bis(bromomagnesio)butane in high yield,[141] it was decided to generate this material and react it with (pentafluorophenyl)(*tert*-butyl)phosphinochloride (**2.2) (**Scheme 3 – 8) . Following a preliminary reaction in which DPPB was successfully synthesised though not isolated, **3.6** was synthesised and the ^{31}P{H} NMR spectrum was recorded. It displays two triplets at 0.1 and 0.3ppm ($^{3}J_{P\text{-}F}$ = 38.6 Hz), corresponding to the presence of the two expected diastereomers in a 1:1 ratio. Addition of

BH_3.THF to the free ligand resulted in the formation of the borane complex **3.7,** which, was found to be suitable for aqueous workup and isolation by column chromatography. The product shows a characteristic broad multiplet at 44.2 ppm in the $^{31}P\{H\}$ NMR spectrum. The ^{19}F spectra is similar to that reported for pentafluorophenyl compounds.[55] However at -125.5 ppm the signal for the *ortho*-fluorine is a broad multiplet due to coupling to boron. No deprotection of the phosphine was detected during chromatography and only limited degradation was observed in a sample after 3 years in storage. The high stability of this borane complex contrasts with that of the parent secondary phosphineborane (**2.2**) and the *ortho*-CF_3phenyl substituted phosphineboranes studied in this work.

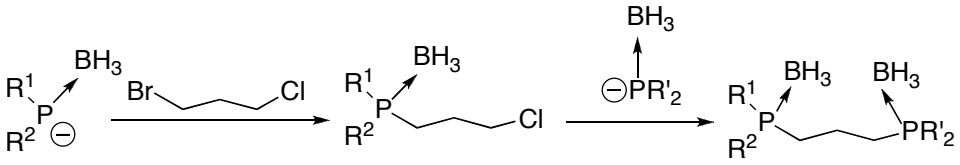


Scheme 3 - 8. Synthesis of a diphosphine (3.6) using Grignard chemistry, and its diborane adduct (3.7).

This result confirmed that bidentate phosphine synthesis using this approach is feasible. However, this method of generating diphosphines was not repeated as the primary interest of this project is the synthesis of propyl bridged phosphines, and 1,3-bis(bromomagnesio)propane is known to be an extremely difficult reagent to prepare successfully due to competing polymerisation and elimination reactions.[142]

3.3. Synthesis of unsymmetrical ligands.

The synthesis of unsymmetrical ligands is a difficult challenge due to the tendency of bis-nucleophiles to become more activated to a second substitution once the first occurs. To overcome this and synthesise propyl bridged ligands it was decided that the use of 1-bromo-3-chloro-propane would make it possible to mono-substitute at the bromine position with a secondary phosphide borane and then a subsequent reaction with a second phosphide to displace the chloride would yield an unsymmetrical diphosphine (Scheme 3 – 9).

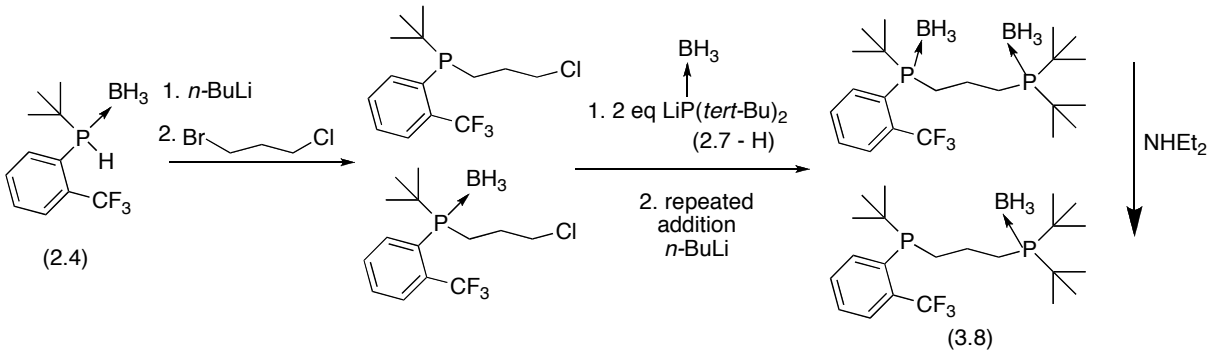


Scheme 3 - 9. General strategy for the synthesis of unsymmetrical diphosphines.

3.3.1. Synthesis of 3.8.

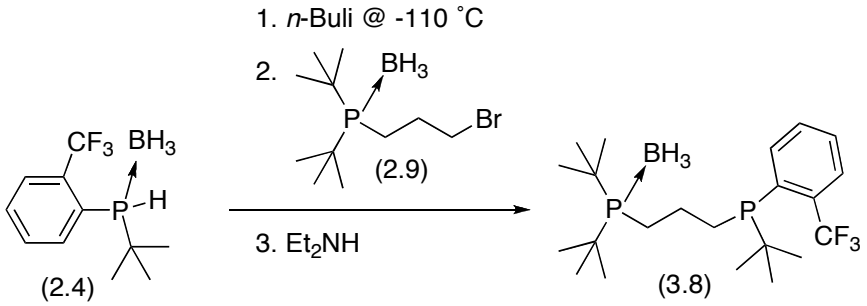
In an exploratory reaction **2.4 - H** was generated and half an equivalent of 1-bromo-3-chloro-propane was then added. ^{31}P NMR spectra obtained shortly afterwards showed only partial reaction, indicating that the anion is insufficiently nucleophilic to displace chloride and form a bidentate phosphine. It was therefore decided that the best route to an unsymmetrical diphosphine was to first react the **2.4 - H** with 1-bromo-3-chloro-propane, displacing the more labile bromide, and then use the more nucleophilic anion **2.7 - H** to displace the chloride.

During the first stage of the reaction the use of optimised conditions allowed for a satisfactory conversion to a mixture of the boronated and unboronated monophosphines. As with the symmetric bidentate phosphines some deprotection occurred during the deprotonation reaction, and further spontaneous decomplexation occurred on standing. Addition of **2.7 - H** gave only small amounts of the desired diphosphine, instead reprotonation of the anion back to **2.7** occurred within hours. The use of additional excess **2.7 - H** did lead to some increased formation of the bidentate phosphine, however conversion remained unsatisfactory with most of the anion reprotonating. The source of the protons is thought to be linked to the formation of species formed by the decomplexation of borane by base (Scheme 3 – 3), as **2.7 – H** does not form **2.7** in the presence of BH_3 alone.



Scheme 3 - 10. Two stage synthesis of 3.8.

The addition of *n*-butyllithium to the reaction mixture had the effect of regenerating the **2.7 - H** and led to better conversion to the bidentate product than the addition of large amounts of **2.7 - H**. An optimised procedure was developed where 2 equivalents of **2.7 - H** were added to the monophosphine mixture, followed by regular addition of *n*-butyllithium to regenerate the **2.7 - H** when it was deemed necessary as judged by ^{31}P NMR (Scheme 3 – 10). This resulted in over 90% conversion to bidentate products over the course of a week during which time the aryl substituted phosphine moiety continued to decomplex. Once satisfactory conversion to bidentate products had been attained, the addition of a small amount of amine and stirring at room temperature completed the decomplexation of the aryl substituted phosphine moiety (without any decomplexation of the dialkyl moiety being evident in the ^{31}P NMR spectrum) resulting in the formation of **3.8**. This behaviour clearly illustrates the differences in the stability of the phosphine borane bond of the two phosphorus moieties.

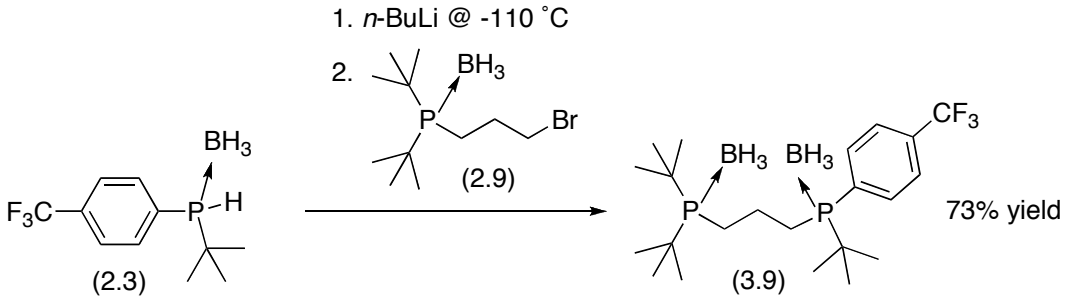


Scheme 3 - 11. Single stage synthesis of 3.8 using 2.9.

The synthesis of **3.8** described in the previous paragraph is inelegant and time consuming. With the later synthesis of **2.9** it was possible to access this bidentate phosphine by a far more convenient route. The anion (**2.4 – H**) was generated and added to a cooled solution of **2.9** and the reaction was allowed to warm to room temperature and stirred overnight (Scheme 3 – 11). The following morning full decomplexation of the *ortho*-trifluoro substituted moiety was

achieved by the addition of amine. No solid material formed during attempts to recrystallise diphosphine. As **3.8** is not enormously air-sensitive it was decided to isolate the material by column chromatography using degassed solvents and collecting fractions under a stream of argon. Using this method it was possible to isolate the **3.8** with only slight contamination with 1-2% oxide (as judged by ^{31}P NMR).

3.3.2. Synthesis of 3.9.



Scheme 3 - 12. Synthesis of 3.9.

3.9 was synthesised by the deprotonation of **2.3** followed by reaction with **2.9** in 73 % yield (Scheme 3 – 12). This material was purified by aqueous workup followed by flash chromatography. The material obtained was an air-stable crystalline solid.

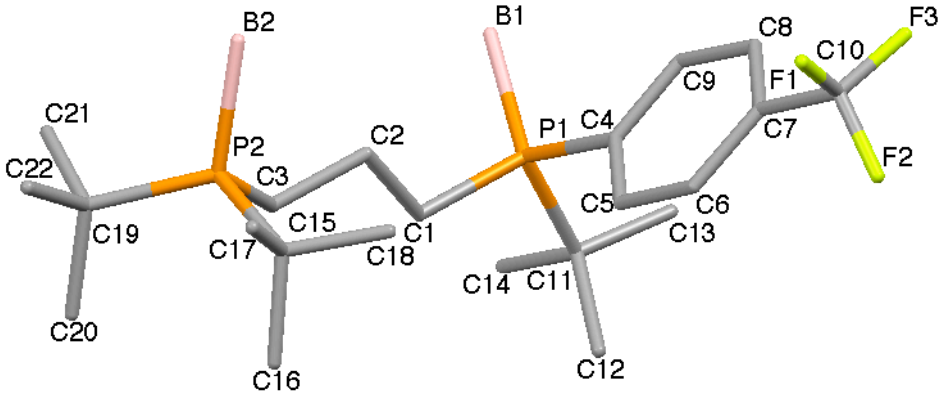


Figure 3 - 8. X-ray crystal structures of 3.9. All hydrogen atoms have been omitted for clarity.

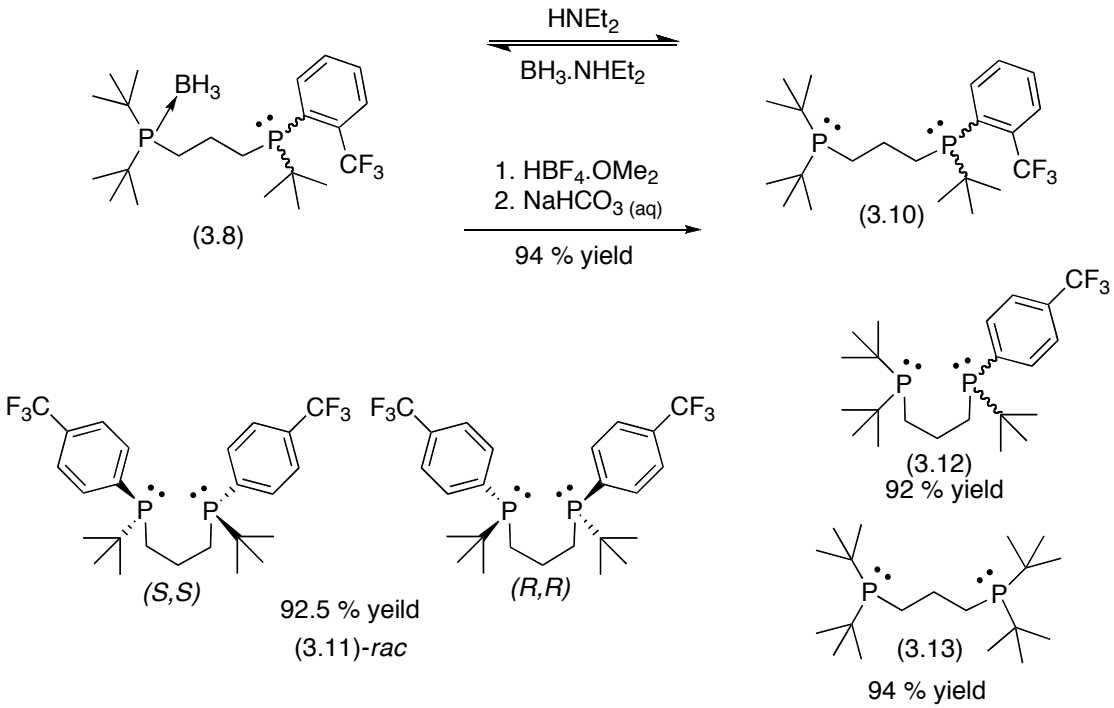
Table 3 - 5. Selected bond lengths (Å) and angles (°) for 3.9, with estimated standard deviations in parentheses.

P1		P2	
P(1)-C(1)	1.821(7)	P(2)-C(3)	1.820(7)
P(1)-C(4)	1.823(7)	P(2)-C(15)	1.824(10)
P(1)-C(11)	1.867(8)	P(2)-C(19)	1.861(9)
P(1)-B(1)	1.924(10)	P(2)-B(2)	1.892(12)
C(1)-P(1)-B(1)	112.0(4)	C(3)-P(2)-B(2)	112.2(5)
C(4)-P(1)-B(1)	111.7(4)	C(15)-P(2)-B(2)	108.6(5)
C(11)-P(1)-B(1)	115.4(4)	C(19)-P(2)-B(2)	112.4(6)

The solid state structure of **3.9** shows that the trialkyl substituted phosphine **P2** has a somewhat smaller P-B bond length than that of the aryl substituted phosphine **P1**. Both of these lengths fall within the usual range of P-B bond lengths for phosphines of this type.[137] The B-P-C bond angles around **P1** are on average more obtuse than those around **P2,** as may be expected due to the increased steric hindrance.

3.4. Decomplexation of diphosphine borane complexes.

In contrast to the facile decomplexation of the *ortho*-trifluoromethylphenyl substituted moiety, the di(*tert*-butyl)phosphine borane moiety required a twenty fold excess of diethylamine and days of refluxing in order to produce the free diphosphine. Others have reported that amines are effective reagents for the decomplexation alkylphosphineboranes.[127] On one attempt diethyl amine allowed the isolation of the free bidentate phosphine **3.10**, however this result proved difficult to replicate on a larger scale. The use of this and other amines often resulted in incomplete decomplexation of the borane accompanied by by-product formation. Unfortunately, the decomplexation reaction is reversible (Scheme 3 -13, upper reaction). It relies on a having a large excess of amine present to push the equilibrium to the left. When the solvent is removed, the excess amine is also removed, the equilibrium returns to the right, and the electron rich phosphine moiety can reboronate.



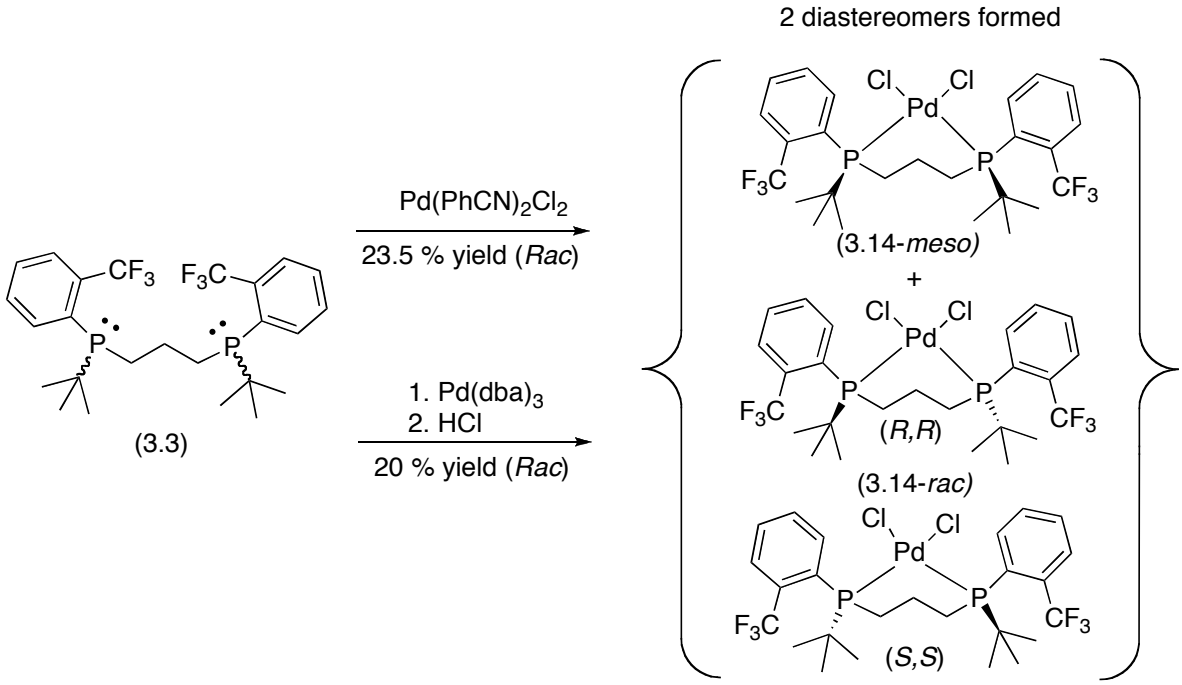
Scheme 3 - 13. The decomplexation of phosphine boranes with yields achieved using the Livinghouse methodology.

Frustration with this method led to its abandonment in favour of the method utilised by Livinghouse, which has been found to be particularly well suited to the decomplexation of electron rich phosphine boranes.[43, 125] This method allowed the successful isolation of the free phosphine ligands **3.10**, **3.11-*rac***, **3.12** and **3.13**, in 94, 92.5, 92 and 94 % yield respectively (Scheme 3 – 13).

3.5. Synthesis of Symmetric bidentate complexes.

3.5.1. Synthesis of 3.14-*rac.*

The reaction of the **3.2** with $[Pd(PhCN)_2Cl_2]$ (Scheme 3 – 14) resulted in a three signals being present in the ^{31}P NMR spectrum. Two sharp peaks were observed, one at 33.7 ppm which corresponds to the *rac* isomer of the dichloride complex (which has been fully characterised). The other sharp peak at 45.4 ppm is assumed to be the *meso* isomer. The third signal between 50 and 60 ppm is the type of broad resonance which is often indicative of the formation of fluxional species. Many tedious recrystallisation steps were required for the successful isolation of the *rac* isomer from this material. The resulting yield of 23.5 % was rather less than desirable.



Scheme 3 - 14. Palladium dichloride complex formation using ligand 3.3.

To improve on this an alternative method involving the reaction of the ligand with $Pd_2(dba)_3$ followed by addition of HCl was employed (Scheme 3 – 13). This had previously been found to give better results in the preparation of bulky diphosphine complexes. This procedure resulted in a slightly lower yield of the *rac* isomer than the previous procedure. However, the purification procedure was greatly simplified as only the two diastereomers were observed in the ^{31}P NMR spectrum. The solid-state structure for this complex was successfully obtained and is shown in (Figure 3 – 9).

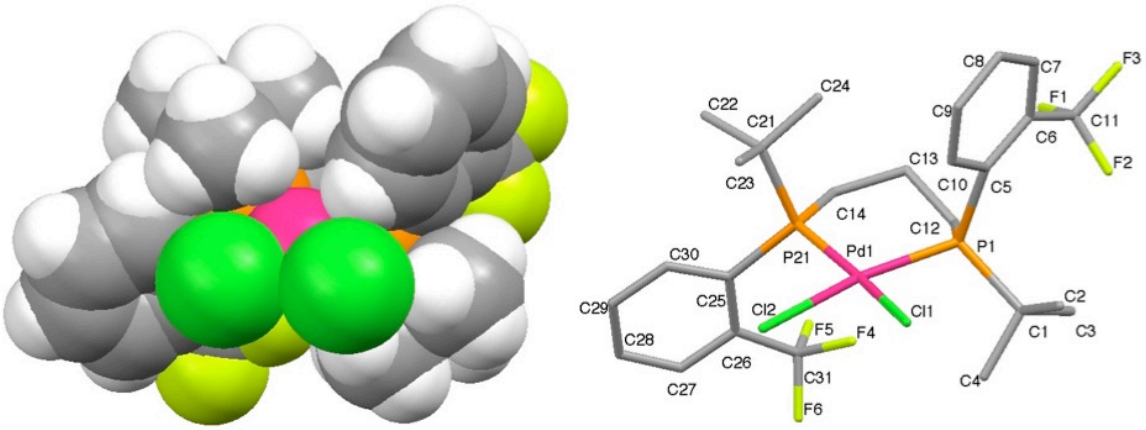


Figure 3 - 9. X-ray crystal structures of 3.14-*rac* showing space filling view and capped sticks view. All hydrogen atoms have been omitted from capped sticks view for clarity.

Table 3 - 6. Selected bond lengths (Å) and angles (°) for 3.14-*rac*, with estimated standard deviations in parentheses.

P(1)		P(21)	
Pd(1)-P(1)	2.3005(9)	Pd(1)-P(21)	2.2729(9)
P(1)-C(1)	1.908(4)	P(21)-C(14)	1.831(3)
P(1)-C(5)	1.870(3)	P(21)-C(21)	1.899(3)
P(1)-C(12)	1.821(3)	P(21)-C(25)	1.851(3)
Pd(1)-Cl(1)	2.3789(9)	Pd(1)-Cl(2)	2.3352(8)
P(1)-Pd(1)-P(21)	96.00(3)	Cl(1)-Pd(1)-Cl(2)	85.47(3)
P(1)-Pd(1)-Cl(1)	93.62(3)	P(21)-Pd(1)-Cl(1)	166.25(3)
P(1)-Pd(1)-Cl(2)	171.16(3)	P(21)-Pd(1)-Cl(2)	86.49(3)

3.14-*rac* has many structural features with measurements which lie between those of [Pd(dppp)Cl_2] and **3.15** as may be expected for this hybrid alky-aryl substituted molecule. The geometry of the ligand around Pd is distorted. One of the aromatic groups is oriented so the CF_3 group is accommodated below the centre of the six membered ring of the chelate. The other is oriented so the CF_3 group points away from the metal centre. One of the most notable features is the short 2.409Å distance between the H atom attached to **C(10)** and the midpoint of the **Pd-Cl(1)** bond adjacent also, the Pd-Cl bond is the one of longest observed in these studies. In the ^{1}H NMR spectrum the resonance for this proton is found at 9.05 ppm which is considerably further downfield than any of the other aryl protons (Figure 3 – 10). These observations suggest some kind of electrostatic interaction is taking place. In the unsymmetric *ortho*- CF_3 substituted complex **3.17** this effect is seen again but no similar effect can be seen in either of the *para*-CF_3 substituted phosphine complexes (**3.16** and **3.18**). Similar observations have been made for other *ortho*-substituted aryl phosphines which are especially active in carbonylation reactions.[143, 144]

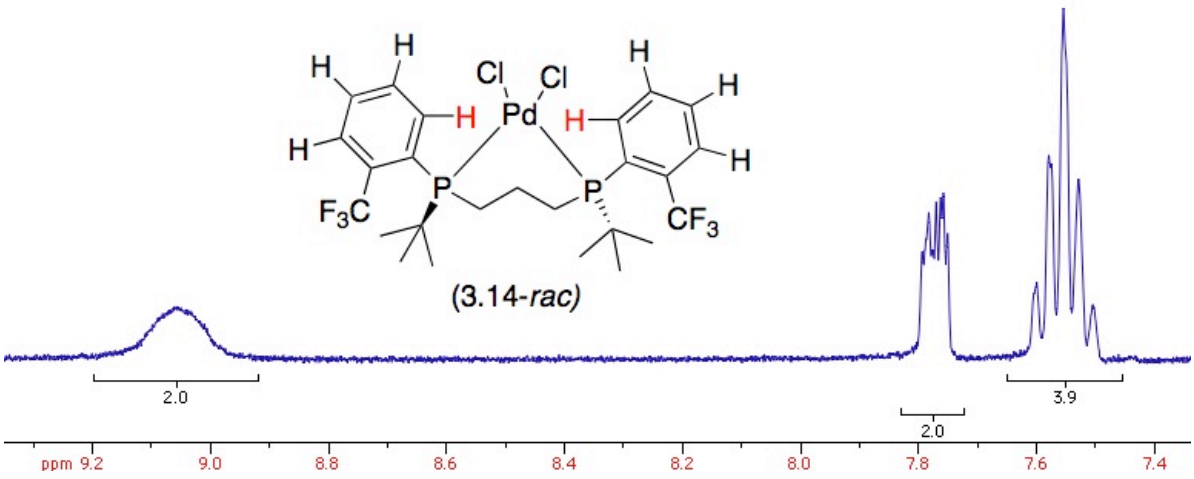
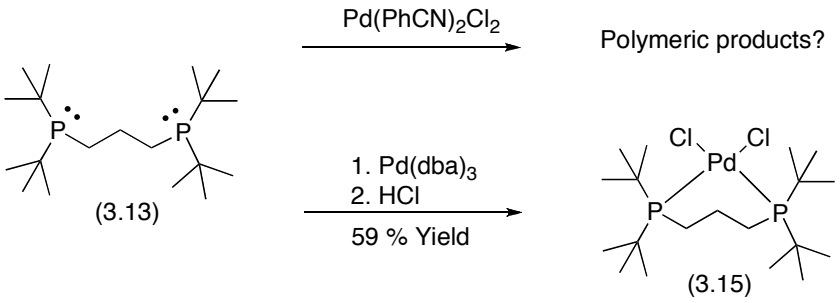


Figure 3 - 10. ^{1}H NMR spectrum showing aryl protons region for 3.14-*rac*. *Ortho* hydrogens give rise to the broad multiplet at 9.5 ppm.

3.5.2. Synthesis of 3.15.

The ^{31}P NMR spectrum taken shortly after the reaction of **3.13** with $Pd(PhCN)_2Cl_2$ did not show the desired product (**3.15**) in any appreciable quantity (Scheme 3 – 15). Instead, two groups of signals are observed around 45 ppm and 75 ppm. This may be the result of the formation of polymeric products in which the ligand bridges between palladium atoms, as similar reactions have been reported previously for this compound.[5]



Scheme 3 - 15. Synthesis of 3.15.

The use of the alternative method discussed above using Pd_2dba gave far more satisfactory results, with **3.15** being isolated in 59 % yield. The ^{31}P{H} NMR spectrum shows a sharp peak at 41.0 ppm. Though this complex is believed to have been prepared previously, somewhat surprisingly this is the first time it has been reported and fully characterised in the open literature. The crystal structure of the analogous platinum dichloride complex has been reported by Harada[96] and a series of platinum complexes based on this ligand have also been reported by Carr.[145]

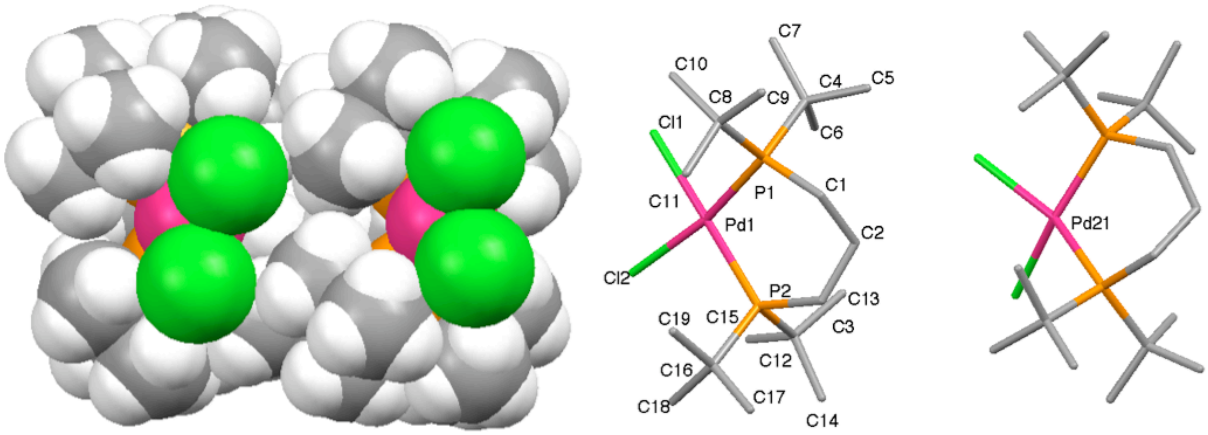


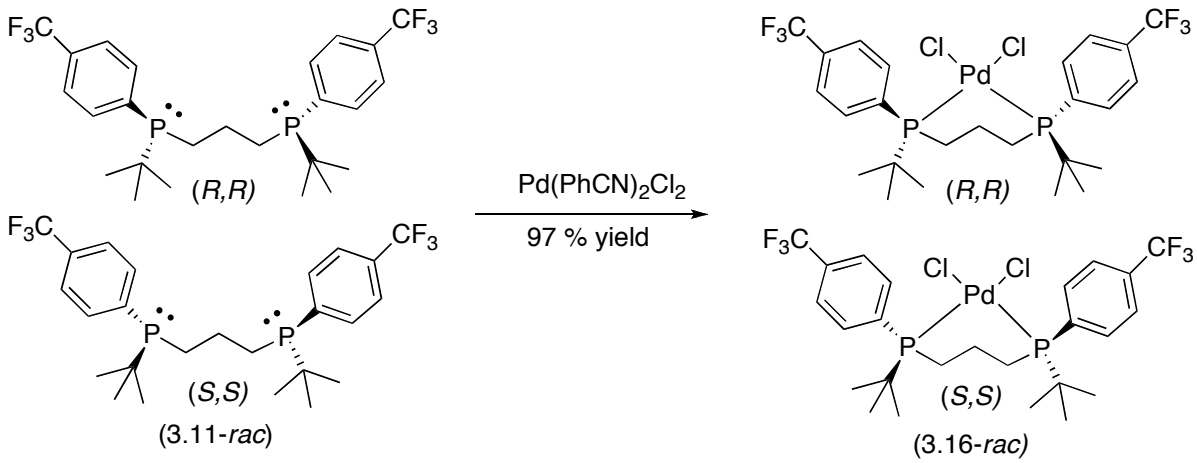
Figure 3 - 11. X-ray crystal structures of 3.15 showing space filling view (left) and capped sticks view (right). All hydrogen atoms have been omitted from capped sticks view for clarity.

Table 3 - 7. Selected bond lengths (Å) and angles (°) for 3.15 (one molecule of two), with estimated standard deviations in parentheses.

Pd(1)			
Pd(1)-P(1)	2.302(2)	Pd(1)-Cl(1)	2.370(2)
Pd(1)-P(2)	2.315(2)	Pd(1)-Cl(2)	2.362(2)
P(1)-C(1)	1.829(7)	P(2)-C(3)	1.821(7)
P(1)-C(4)	1.898(8)	P(2)-C(16)	1.893(8)
P(1)-C(8)	1.907(8)	P(2)-C(12)	1.903(8)
P(1)-Pd(1)-P(2)	97.91(8)	Cl(1)-Pd(1)-Cl(2)	85.46(7)
P(1)-Pd(1)-Cl(1)	87.29(8)	P(2)-Pd(1)-Cl(1)	171.88(8)
P(1)-Pd(1)-Cl(2)	169.49(8)	P(2)-Pd(1)-Cl(2)	90.16(8)

The unit cell contains two distinct molecules. The arrangement of ligands around **Pd(1)** is slightly distorted from planar. The other molecule, containing **Pd(21)**, is severely distorted from planar into an unusual more tetrahedral arrangement. The bite angles are almost identical for both molecules and are wide compared to [Pd(dppp)Cl_2] (90.79°). The Cl-Pd-Cl angles are significantly smaller than that found in the dppp analogue (90.58°), which is likely to be an effect of the more sterically demanding substituents.

3.5.3. Synthesis of 3.16-*rac.*



Scheme 3 - 16. Synthesis of 3.15-*rac.*

In contrast to the reaction of its *ortho* substituted analogue, **3.11 -*rac*** reacted with [Pd(PhCN)$_2$Cl] resulting in a pronounced colour change within seconds (Scheme 3 -16). The bright yellow crystalline powder was easily isolated in almost 100 % yield (**3.16-*rac***). The difference in coordination behaviour between the two ligands is almost certainly due to the increased steric influence of the *ortho*-CF_3 substituent. The ^{13}C spectrum is consistent with the structure although the central carbon atom of the propyl bridge does not show any ^{2}J coupling

to phosphorus. The solid state structure of **3.16-*rac***, which crystallised as its chloroform solvate, reveals that environment around Pd is almost planar. The average P-Pd distance in this molecule is shorter than that of **3.15**, lying between those of **3.14-*rac*** and [dpppPdCl2]. The average Pd-Cl distance however, is shorter than that of **3.15** but larger than that of **3.14-*rac*** and [dpppPdCl2].

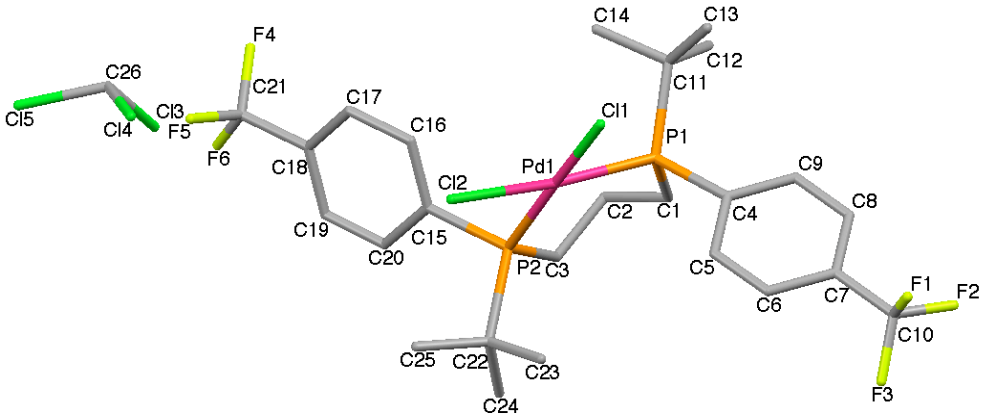


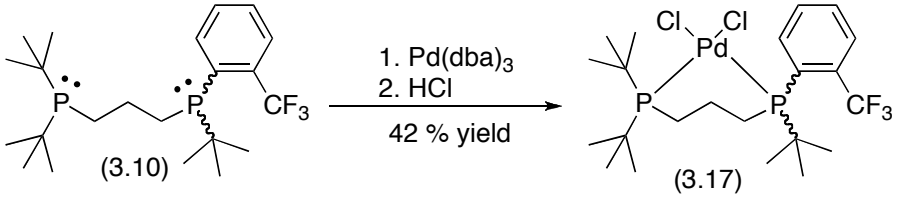
Figure 3 - 12. X-ray crystal structures of 3.16-*rac* All hydrogen atoms have been omitted for clarity.

Table 3 - 8 Selected bond lengths (Å) and angles (°) for 3.16-*rac*, with estimated standard deviations in parentheses.

P1		P2	
Pd(1)-P(1)	2.258(3)	Pd(1)-Cl(2)	2.363(3)
Pd(1)-Cl(1)	2.367(3)	Pd(1)-P(2)	2.281(3)
P(1)-C(1)	1.824(11)	P(2)-C(3)	1.845(11)
P(1)-C(4)	1.832(11)	P(2)-C(15)	1.831(11)
P(1)-C(11)	1.895(13)	P(2)-C(22)	1.919(11)
P(1)-Pd(1)-P(2)	96.61(10)	Cl(2)-Pd(1)-Cl(1)	88.63(9)
P(1)-Pd(1)-Cl(1)	87.18(10)	P(2)-Pd(1)-Cl(1)	174.62(11)
P(1)-Pd(1)-Cl(2)	174.77(10)	P(2)-Pd(1)-Cl(2)	87.78(10)

3.6. Unsymmetrical Complexes.

3.6.1. Synthesis of 3.17.



Scheme 3 - 17. Synthesis of 3.17.

The synthesis of **3.17** was again performed by reaction with Pd_2dba followed by conversion to the dichloride with HCl (Scheme 3 - 17). Although the material was successfully obtained in this way, several recrystallisation steps were required to allow the isolation of the pure material, resulting in a moderate yield of 42 %. It is an interesting feature of this complex and **3.17** that no observable P-P coupling is observed in the ^{31}P NMR spectrum despite the unsymmetrical structure. The solid state structure of **3.16** shows three unique molecules in the unit cell, one in which the geometry around Pd is approximately planar and two which exhibit more distortion.

Table 3 - 9. Selected bond lengths (Å) and angles (°) for 3.17 (one of the three unique molecules as shown in Figure 3 – 13, right), with estimated standard deviations in parentheses.

P1		P2	
Pd(1)-P(1)	2.279(2)	Pd(1)-P(2)	2.241(2)
Pd(1)-Cl(1)	2.339(2)	Pd(1)-Cl(2)	2.302(2)
P(1)-C(1)	1.792(8)	P(2)-C(3)	1.806(8)
P(1)-C(4)	1.835(8)	P(2)-C(19)	1.859(8)
P(1)-C(11)	1.860(9)	P(2)-C(15)	1.872(8)
P(1)-Pd(1)-P(1)	92.98(8)	Cl(1)-Pd(1)-Cl(2)	86.65(7)
P(1)-Pd(1)-Cl(1)	96.79(7)	P(2)-Pd(1)-Cl(2)	88.86(7)
P(1)-Pd(1)-Cl(2)	163.38(8)	P(2)-Pd(1)-Cl(1)	160.27(8)

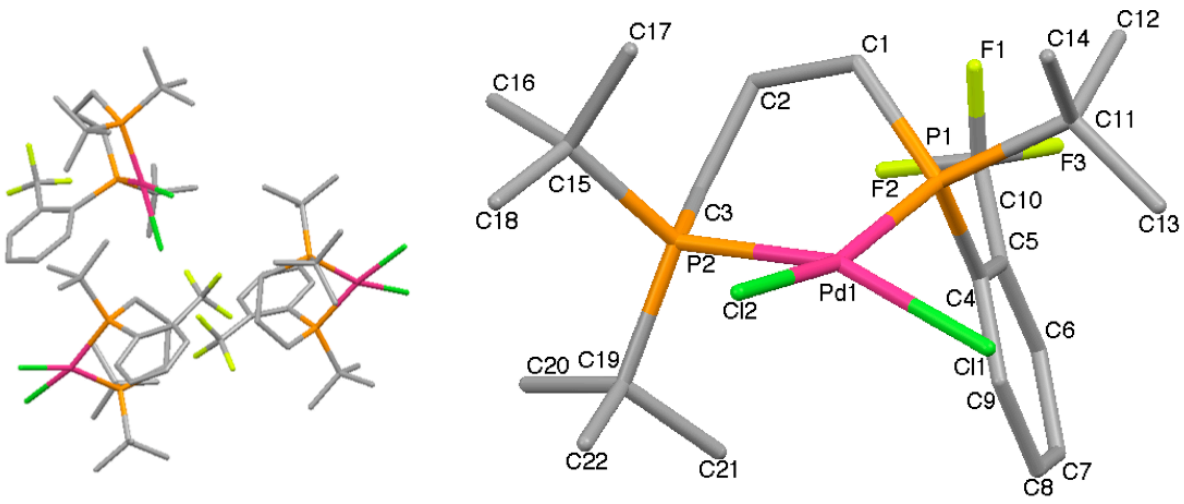
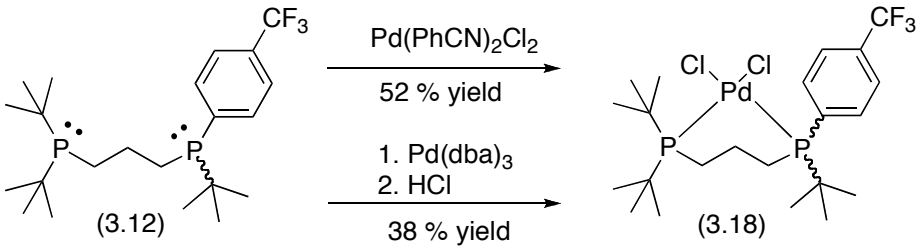


Figure 3 - 13. X-ray crystal structures of 3.17 showing the three unique molecules in the unit cell (left) and a close up of one of the three unique molecules (right). All hydrogen atoms have been omitted for clarity.

3.6.2. Synthesis of 3.18.



Scheme 3 - 18. Synthesis of 3.18 using two methods.

3.18 was synthesised directly using $[Pd(PhCN)_2Cl_2]$, resulting in a moderate yield of 52 % (Scheme 3 -18). An alternative attempt using Pd_2dba_3 followed by HCl resulted in a disappointingly low yield of 38%.

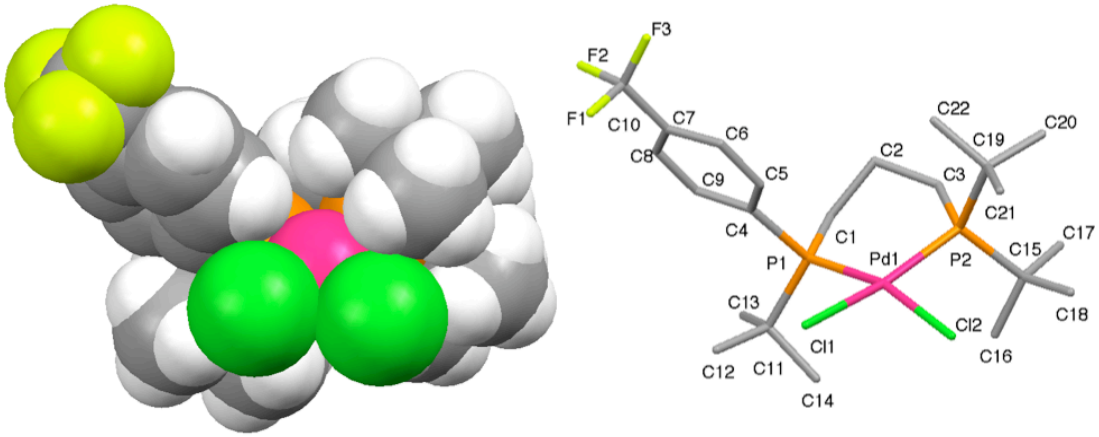


Figure 3 - 14. X-ray crystal structures of 3.18 showing space filling view and capped sticks view. All hydrogen atoms have been omitted from capped sticks view for clarity.

Table 3 - 10. Selected bond lengths (Å) and angles (°) for 3.18, with estimated standard deviations in parentheses.

P1		P2	
Pd(1)-P(1)	2.280(4)	Pd(1)-P(2)	2.306(5)
Pd(1)-Cl(1)	2.376(5)	Pd(1)-Cl(2)	2.367(4)
P(1)-C(1)	1.784(18)	P(2)-C(3)	1.851(17)
P(1)-C(4)	1.826(17)	P(2)-C(15)	1.896(18)
P(1)-C(11)	1.89(2)	P(2)-C(19)	1.90(2)
P(1)-Pd(1)-P(2)	96.68(17)	Cl(2)-Pd(1)-Cl(1)	85.60(16)
P(1)-Pd(1)-Cl(1)	86.38(17)	P(2)-Pd(1)-Cl(2)	93.65(16)
P(1)-Pd(1)-Cl(2)	164.91(16)	P(2)-Pd(1)-Cl(1)	168.74(15)

3.7. Coordination chemical shifts.

The coordination chemical shifts are shown below and it can be seen that those for the aryl substituted ligand moieties are larger than those seen for di-*tert*butyl substituted moieties. Additionally, the values for unsymmetrical ligands are slightly larger than those seen for the symmetrical molecules.

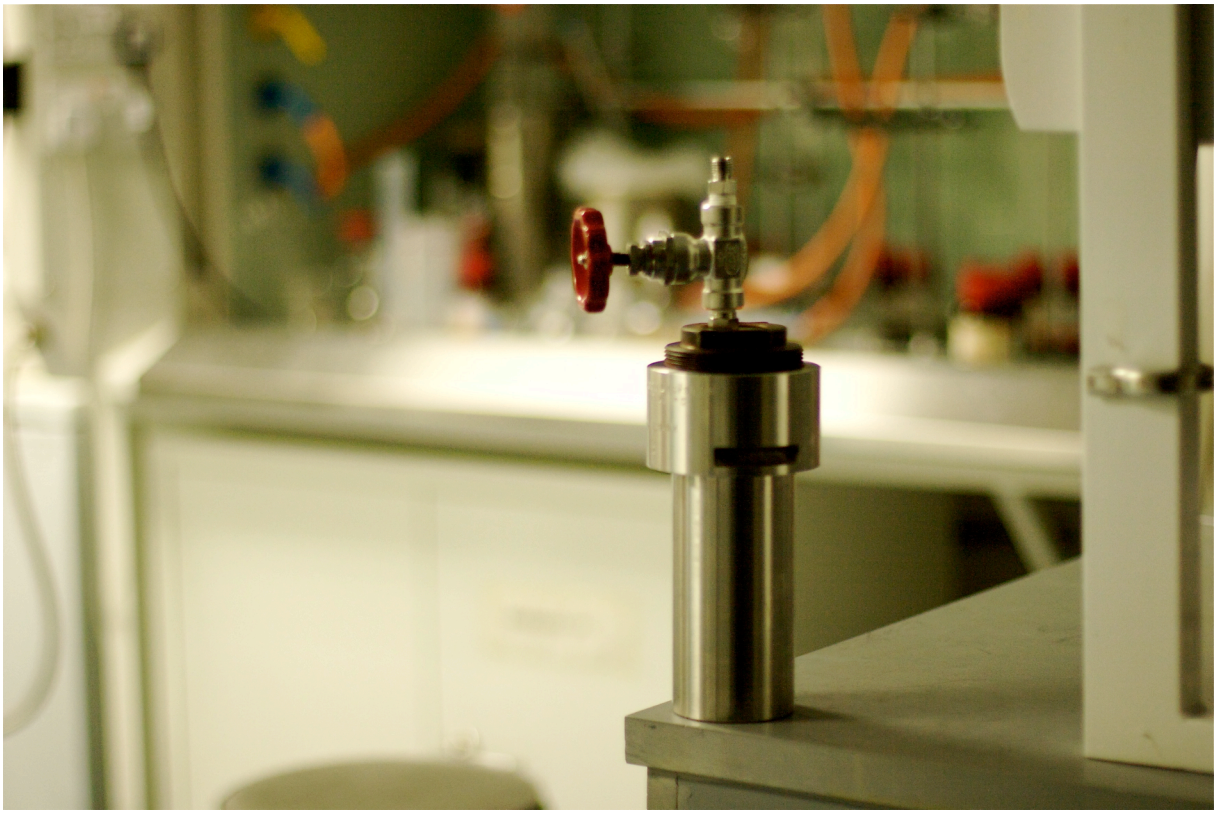
Table 3 - 11. Coordination chemical shifts for diphosphines synthesised in this project

Complex	Free Ligand δP ppm		$PdCl_2$ Complex δP ppm		Coordination Chemical Shift Δ ppm	
3.14-*rac*	-8.2		33.7		41.9	
3.15	26.8		41.0		14.2	
3.16-*rac*	2.0		28.1		26.1	
	R_2P	**ArRP**	**R_2P**	**ArRP**	**R_2P**	**ArRP**
3.17	27.4,	-10.0	43.8,	33.5	16.4	43.5
3.18	24.8,	2.2	41.4	31.2	16.6	29.0

3.8. Summary.

A range of bulky fluorinated diphosphines has successfully been synthesised and palladium complexes of these ligands have been formed and isolated, with the exception of **3.2** which did not form a complex with palladium. The use of phosphine boranes during this study, in some cases allowed the easy synthesis of otherwise sensitive materials such as **3.13**. However, when the deprotonation of the secondary phosphine boranes was attempted (in some cases), decomplexation complicated the reactions. In isolation procedures stable borane complexes were easily purified. However, the bulky *ortho*-CF_3phenyl substituted diphosphines spontaneously decomplexed and laborious isolation procedures were required. Decomplexation of unstable boranes with amines was found to be convenient. However, this method gave poor results for more electron rich phosphines, and the decomplexation of boranes using $HBF_4.OMe_2$ was found to be far superior. The synthesis of unsymmetrical ligands from **2.9** was found to be straightforward compared to the alternative two-step procedure. In palladium complexation reactions the use of Pd_2dba_3 followed by HCl was generally a more reliable route to dichloride complexes of bulky ligands than the use of $Pd(PhCN)_2Cl_2$.

4. Catalysis with Palladium Complexes of Novel Bulky Fluorinated Phosphine Ligands.

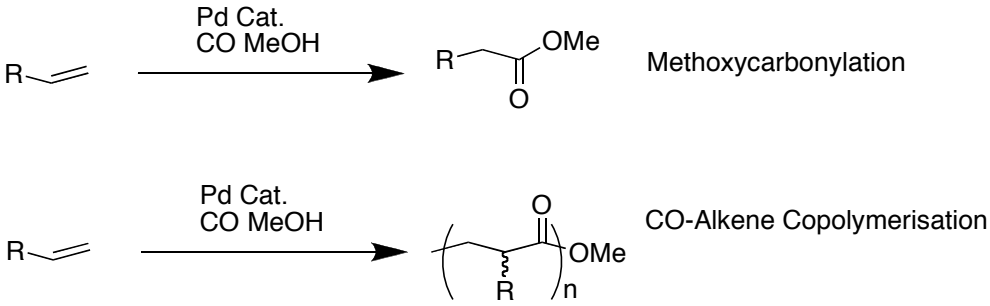


sasol
reaching new frontiers

4.1. Alkoxycarbonylation of Alkenes.

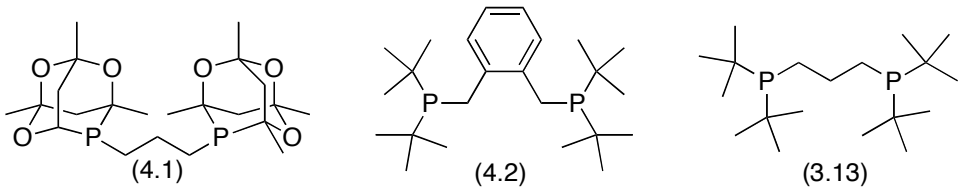
4.1.1. Background.

In the drive towards the selective formation of terminal oxygenates, the palladium catalysed methoxycarbonylation of alkenes is of growing industrial importance.[146, 147] This reaction is used to produce carboxylic acid esters from a range of alkenes. The methoxycarbonylation of ethylene yields methyl propionate (Scheme 4 – 1),[5, 148] a potential intermediate in the synthesis of acrylic polymers, whilst higher alkenes can give longer chain linear esters which are used industrially as a source of linear alcohols and acids, for use in paints, detergents and other bulk chemicals.

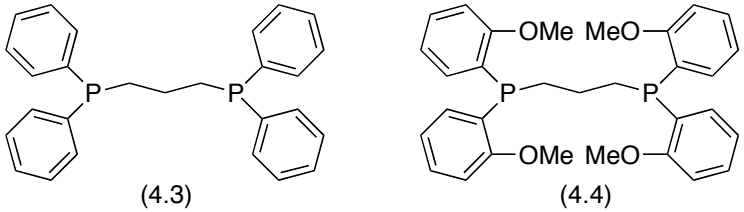


Scheme 4 - 1. Carbonylation reactions of alkenes in methanol.

This reaction is very closely related to CO/alkene copolymerisation process, which produces a high molecular weight alternating polyketone (Scheme 4 – 1). This material is of considerable interest as it is a high strength thermoplastic, produced from inexpensive monomers. It is illustrative of the importance of the stereoelectronic character of the diphosphine ligand in deciding selectivity that when **3.13** is used as a ligand methyl propionate produced,[7] yet when **4.3** is used a perfectly alternating olefin/CO polymer is produced.[149]



Ligands which produce methoxycarbonylation products.



Ligands which produce alternating copolymers.

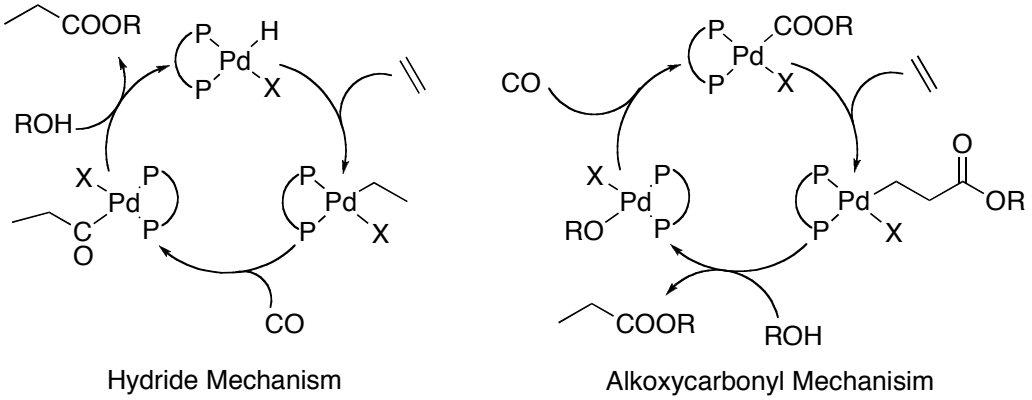
Figure 4 - 1. Ligands which show activity in palladium catalysed carbonylation reactions.

Increasing steric bulk around phosphorus has been found to increase productivity in the copolymerisation reaction.[9, 144] However, this relationship only holds to a point, beyond which the alkoxycarbonylation reaction predominates. The high activity of bulky ligands in these reactions has been attributed to factors such as the destabilisation of catalyst resting states and the diminished tendency toward the formation of catalytically inactive bis-chelates. With ligands such as **4.1**,[6] **4.2**[5, 26] and **3.13**,[7] it has been postulated that the steric bulk is so great that it hampers the copolymerization process and only allows monomeric products to form.[9] Indeed, it has been found that when a less bulky isopropyl substituted analogues of **4.2** and **3.13** are used in the reaction the selectivity reverts back towards the production of oligomers.[127]

4.1.2. Mechanism in the Alkoxycarbonylation of Alkenes.

Two mechanisms have been proposed for the palladium catalysed methoxycarbonylation of alkenes, the "hydride mechanism" and the "alkoxycarbonyl mechanism" (Scheme 4 – 2). In the hydride mechanism the reaction begins with the insertion of an alkene into a palladium hydride bond to produce an alkyl palladium species, followed by coordination and migratory insertion of CO into the Pd alkyl bond to form an acyl palladium species. Alcoholysis of the metal acyl bond produces the ester product and regenerates the palladium hydride. The alkoxycarbonyl mechanism, by contrast, begins by alkene insertion into the palladium alkoxycarbonyl bond, resulting in the formation of a metal alkyl species. Alcoholysis in this case results in the formation of the ester and an alkoxymetal complex. Subsequent CO

coordination followed by migratory insertion leads to the regeneration of the alkoxycarbonyl species.

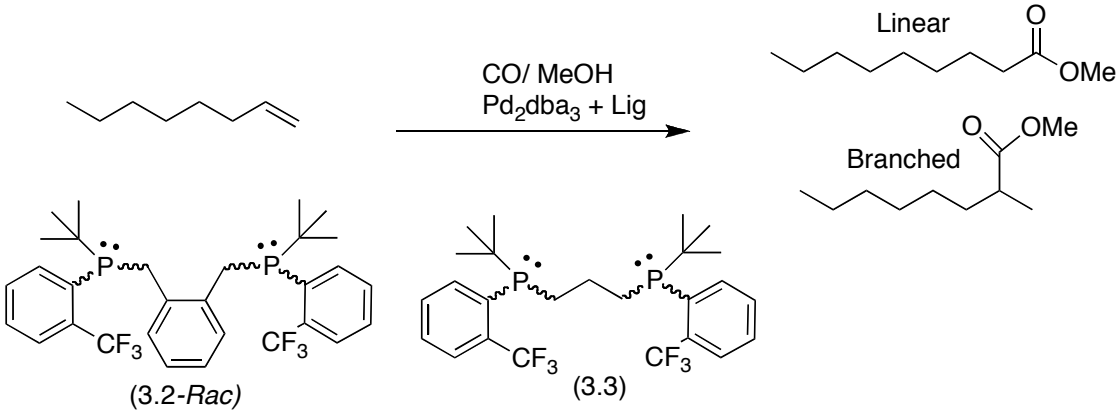


Scheme 4 - 2. Simplified mechanisms for the Alkoxycarbonylation of ethene.

Supporting evidence has been found for both mechanisms,[26, 148, 150-152] though it is generally accepted that the hydride mechanism is more common in the palladium catalysed alkoxycarbonylation of alkenes. However, the mechanism which operates is dependent on the choice of ligand, conditions and substrate.

4.1.3. Methoxycarbonylation of 1-octene.

In view of the importance of bulky ligands in alkoxycarbonylation, the novel ligands **3.2-*rac*** and **4.12**, with their unusual mix of sterically bulky yet electronically very different substituents, were selected as candidates to further probe the factors which decide the selectivity and activity of the ligands used in this reaction.



Scheme 4 - 3 Methoxycarbonylation of 1-octene. Pd conc. 1 mM, ligand conc. 3mM, MsOH conc. 6 mM, MeOH 20 ml, 1-octene 10 ml, polyvinylpyrrolidone 25 mgs.

3.2-*rac* was submitted for testing as a ligand in the Pd catalysed methoxycarbonylation of 1-octene (Scheme 4 – 3), to Dr Hendrick van Rensburg of Sasol who tested the ligand for activity under their standard conditions. However, there was no observable reaction, as observed by CO uptake. The reaction mixture was visually examined after the reaction and was found to contain a black powder, assumed to be metallic Pd. This suggests that this ligand does not bind to the metal under these conditions, which are commonly used for *in situ* catalyst formation, and therefore the ligand has no potential for catalytic application in alkoxycarbonylation. In contrast to other ligands studied in this work there was no observable reaction when **3.2-*rac*** was added to various Pd(0) and Pd(II) precursors (Chapter 3).

3.3 was also tested as a ligand in the methoxycarbonylation of 1-octene under the same conditions as **3.2-*rac***, and did show some catalytic activity toward the production of methylnonanoate. However, the selectivity toward the production of the linear product, of 5.6:1, and the rate are very low when compared with the very high linear selectivity and rate of reaction which is achievable with ligands **4.1**, **4.2 and 3.13**. Although the reaction rate was low, the fact that some catalysis was observed was considered encouraging as most ligands tested in this reaction afforded no carbonylation whatsoever. These findings are further evidence that any reduction in the steric bulk of the ligands used in this reaction is detrimental to linear selectivity and rate.

4.2. Hydroxycarbonylation

4.2.1.1. Background

One of the most important applications of the hydroxycarbonylation of alkenes is to convert vinylarenes into branched carboxylic acids such as 2-aryl-propanoic acids (Figure 4 - 1). These compounds are useful synthetic building blocks, but also form an important class of anti-inflammatory agents (with annual revenue from anti-inflammatories estimated at over $16 billion in 2006[153]). There is a huge variety of routes by which these compounds can be accessed,[154] but a regioselective hydroxycarbonylation followed by a classical resolution to separate the two enantiomers has been found to be commercially viable, and is used in the production of (S)-Naproxen.

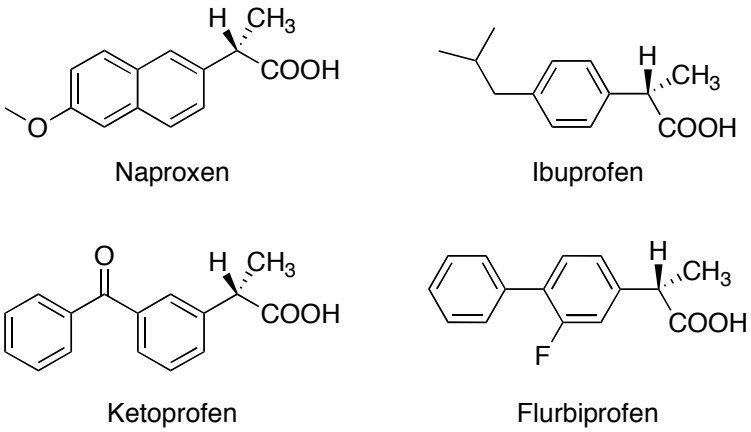
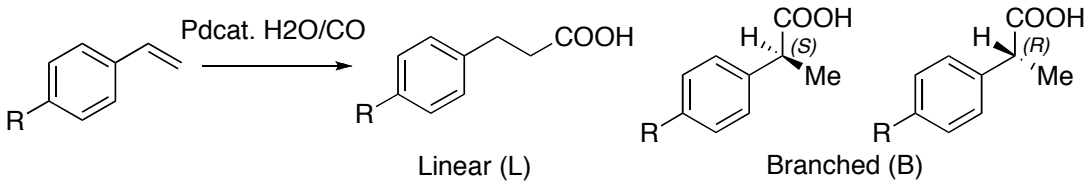


Figure 4 - 2. Examples of non-steroidal anti-inflammatory drugs accessible through hydroxycarbonylation.

There is therefore considerable interest in further developing this process to perform the transformation of vinylarenes to carboxylic acids in a way that is both regio- and stereoselective (Scheme 4 – 4).[155] Several studies have however found that in this reaction and the closely related methoxycarbonylation of styrene, only monodentate phosphines favour the production of the branched isomer[156-158] whereas the linear isomer is favoured by *cis* chelates,[69, 150, 157] with few exceptions.[67, 68, 159]

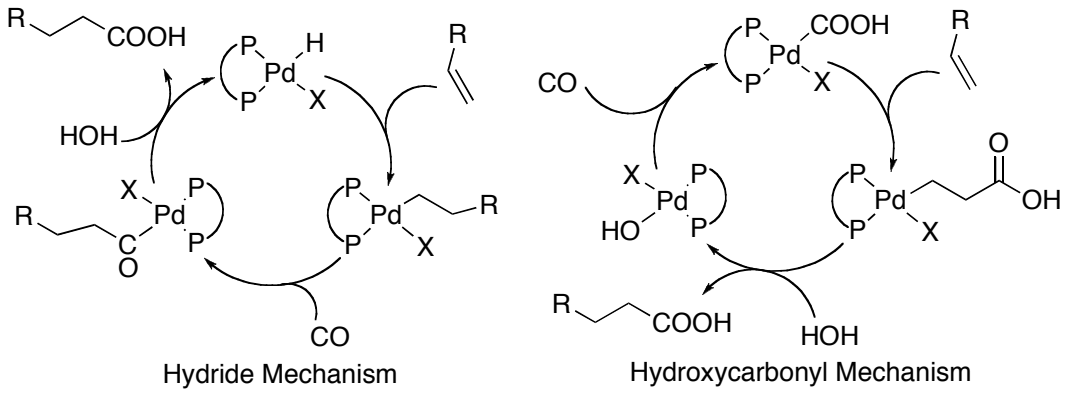


Scheme 4 - 4. General hydroxycarbonylation reaction showing the three possible stereoisomers.

This poses a major challenge for monodentate ligands as there is less control of the steric environment around the site of catalysis and therefore the transfer of chiral information to the substrate is less efficient.[106]

4.2.1.1. Mechanism in hydroxycarbonylation.

Similarly to the previously mentioned methoxycarbonylation reaction there are two reaction mechanisms which are commonly invoked in the literature (Scheme 4 – 5). The one which starts with alkene insertion into a palladium hydride bond, and ends with hydrolysis to yield the acid, is named the hydride mechanism. The alternative mechanism begins with alkene insertion into the palladium hydroxycarbonyl bond before hydrolysis followed by CO insertion into the palladium hydroxyl bond to regenerate the active species.



Scheme 4 - 5. Simplified mechanisms for the hydroxycarbonylation reaction.

Del Rio *et al* have extensively studied and reviewed the hydroxycarbonylation mechanism and concluded that the hydride mechanism is most probably operating in the hydroxycarbonylation reaction using PPh_3,[69, 150, 160] though other catalyst systems may favour alternative pathways. In Del Rio's studies high selectivity towards the branched isomer was observed in hydroxycarbonylation reactions where monodentate complexes were used as catalysts.

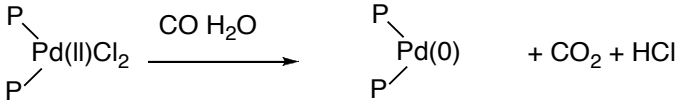
4.2.1.2. General Conditions.

As high activity and selectivity for the branched isomer had previously been attained by Seayad and co-workers[157] using a combination of LiCl and *para*-toluenesulphonic acid (TsOH), the same promoters were employed in the reactions performed in the current study. The use of methylethylketone as the solvent allowed the reactants, catalyst and promoters to be solubilised in a single phase. In previous reports the combination of high catalytic activity and selectivity towards the desired branched isomer has been achieved by the use of CO high pressures[161] with the rate found to be low under moderate conditions. The CO pressures (50 bar or lower) and temperatures (130 °C or lower) used in this study are mild by comparison.

4.2.1.3. Catalyst Precursors.

It was desirable to use palladium dichloride catalyst precursors in this study as these materials are typically solids, which are stable to the atmosphere and conveniently isolated in high purity by recrystallisation. This means it is far easier to measure the milligram quantities used in catalysis using these compounds rather than free ligands which are often gums or oils, and also, palladium dichloride complexes can also be more fully characterised using X-ray crystallography. Del Rio *et al*[69] have compared the use of palladium dichloride and palladium(0) precursors for *in situ* catalyst formation with monodentate and bidentate

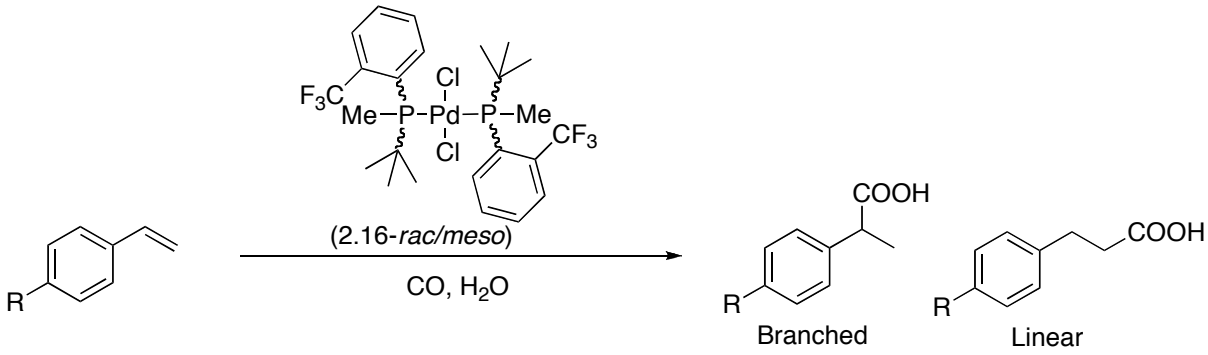
catalysts. In general it has been found that palladium dichorides perform just as well, if not better than other precursors used in the hydroxycarbonylation reaction, both in terms of conversion and selectivity toward the branched isomer.



Scheme 4 - 6. Reduction of palladium dichloride complexes under hydroxycarbonylation conditions.

It has been shown previously that palladium dichloride complexes can be reduced in the presence of CO and water to provide Pd(O) species (Scheme 4 - 6).[158] It seems likely that similar reactions can occur for the complexes used in this study, leading to the catalytically active species.

4.3. Hydroxycarbonylation using Monodentate phosphine complex 2.16-*rac/meso*.



Scheme 4 - 7 Hydroxycarbonylation of vinyl arenes using 2.16-*rac/meso*.

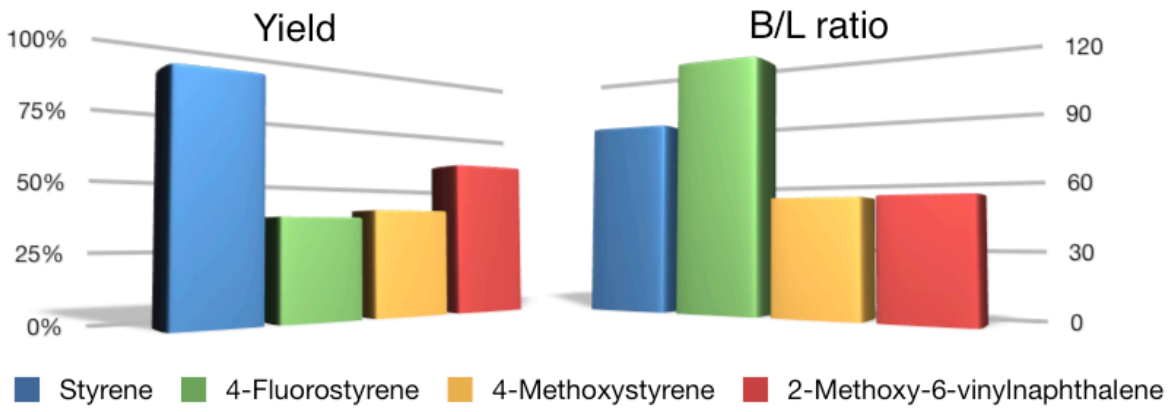


Figure 4 - 3. Reactions carried out in butan-2-one at 50 bar CO pressure, 120 °C, 20 mol% LiCl, 20 mol% TsOH, 2.5 equivalents water relative to substrate and 1 mol % 2.16-*rac/meso* for 2 hours.

To evaluate the effectiveness of phosphines with a bulky fluorine containing architecture as ligands in the hydroxycarbonylation reaction the bismonophosphine complex **2.16-*rac/meso*** was tested with four substrates with contrasting electronic characters (Figure 4 -2). The complex successfully performed the transformation, giving the highest activity for styrene (88% yield), and 2-methoxy-6-vinylnapthalene (60% yield), whilst low yields were attained for the electron rich 4-methoxystyrene and the electron poor 4-fluorostyrene. In general the B/L ratios for these products are high compared to some previous reports in which PPh_3 was the ligand,[69, 162] but lower than those reported by Seayad.[157] In accordance with Seayad's work, the B/L ratio observed in the current study is greatest for 4-fluorostyrene and the lowest selectivities are obtained for the electron rich methoxy substituted substrates.

4.4. Hydroxycarbonylation with novel bidentate ligand complexes.

As **2.16-*rac/meso*** had been found to be an effective catalyst, reactions were performed to evaluate the suitability of the novel bidentate phosphines synthesised in this study as ligands for the hydroxycarbonylation reaction. All the symmetrical bidentate phosphines tested in this study were the chiral but racemic isomers (with the exception of **3.3**), which may be relevant for the long term goal of developing an enantioselective version of this reaction, as the majority of enantioselective catalysts are also based on *C*2 symmetric chiral bidentate ligands.

4.4.1. Comparison with known ligands.

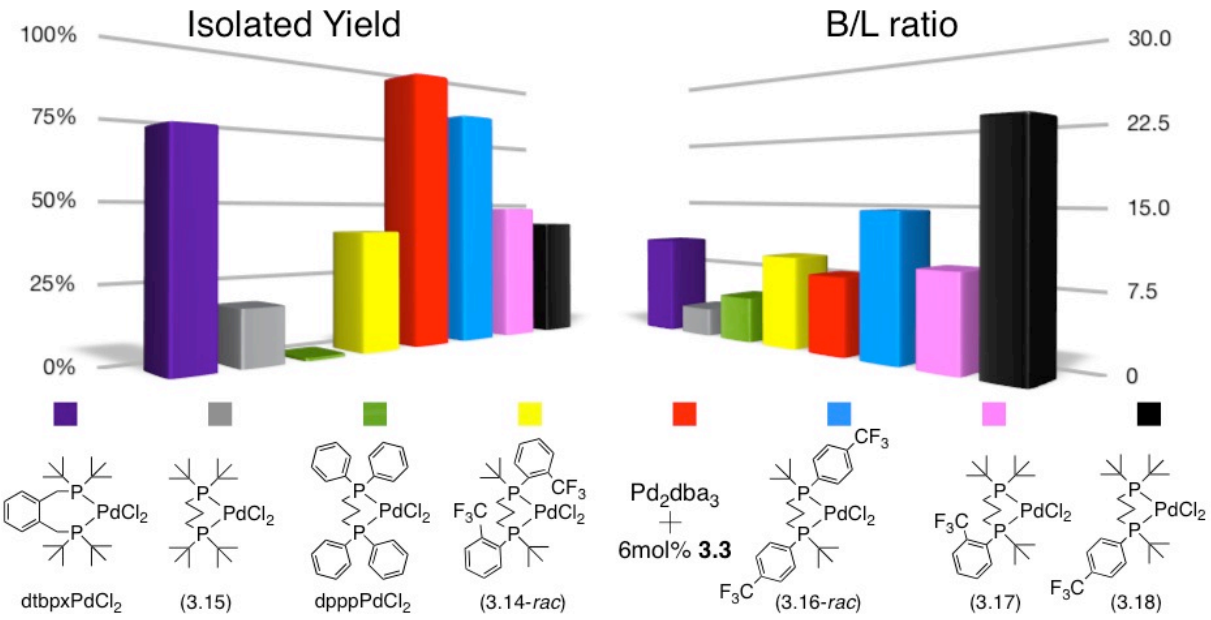


Figure 4 - 4. Reactions carried out in butan-2-one at 50 bar CO pressure, 130 °C, 20 mol% LiCl, 20 mol% TsOH, 2.5 equivalents water relative to styrene and 2 mol % Pd complex for 2 hours.

A series of experiments was performed to compare the catalytic performance of the complexes synthesised in this project with known complexes. The results show that complexes based on the novel ligands synthesised in this study give superior branched selectivity and yields when compared to the analogous complex of dppp. Good branched selectivity and yield was also observed for the xylyl bridged ligand dtbpx, which has previously been reported to be selective for the branched isomer in the related methoxycarbonylation of styrene.[68] The B/L ratio for complex **3.15** is 3.0. This is unexpected as this ligand has previously been reported to be selective for the linear isomer in the methoxycarbonylation of styrene.[68] The yield for complex **3.14-*rac*** was quite poor at 40%, however it was found that the if the catalyst was formed *in situ* from $Pd_2.dba_3$ and a 3 fold excess of ligand **3.3** a much higher yield of 95% could be obtained, though the selectivity decreased slightly. Complex **3.16-*rac*** showed a higher activity and selectivity for the branched acid, without the requirement for excess ligand to be present. The highest selectivity observed under these conditions was for the unsymmetrical phosphine complex **3.18**. The reactions in Figure 4 – 3 were stopped prematurely to aid comparison of the ligands. Other experiments over 16 hours gave higher yields using the novel ligands reported here.

4.4.2. Effect of additional ligand.

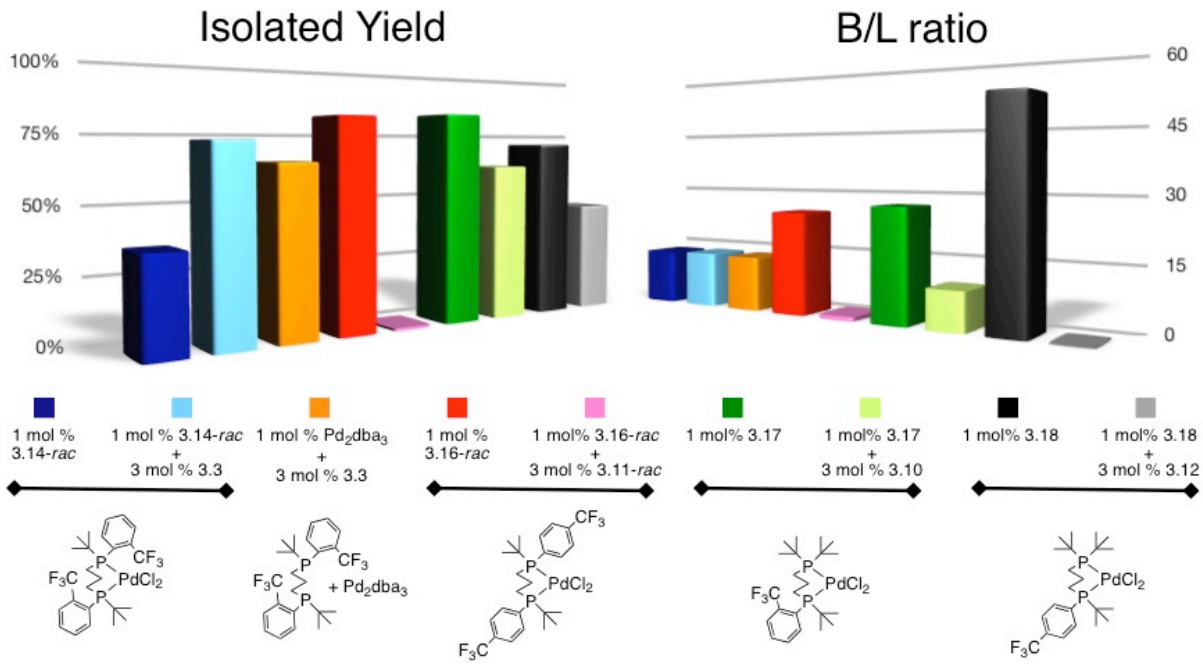


Figure 4 - 5 Reactions carried out in butan-2-one at 50 bar CO pressure, 120 °C, 20 mol% LiCl, 20 mol% TsOH, 2.5 equivalents water relative to styrene for 16 hours.

A series of experiments were run in which additional diphosphine ligand was added to the Pd complex. It can be seen that when additional ligand is used in combination with complex **3.14-*rac*** the yield is approximately double whilst the B/L ratio is unaffected. It is also evident that *in situ* catalyst formation from Pd_2dba_3 and 3 mol% of ligand **3.3** does not give a significantly different result under these conditions. In contrast with complex **3.14-*rac*,** the introduction of additional ligand **3.11** to complex **3.16-*rac*** results in almost total collapse of the hydroxycarbonylation activity and selectivity. This may be due to the formation of catalytically inactive bischelates, which are presumably more readily formed by ligands which are less bulky. Similarly, the yields for catalytic runs for both unsymmetrical ligand complexes (**3.17** and **3.18**) are negatively influenced by additional ligand, as are the B/L ratios.

4.4.3. Variation of substrate.

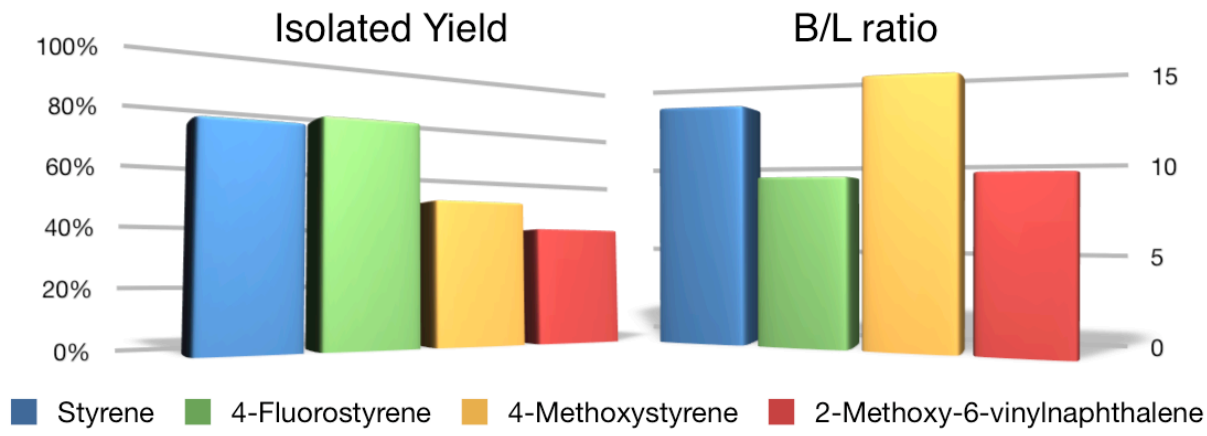


Figure 4 - 6 Reactions carried out in butan-2-one at 50 bar CO pressure, 120 °C, 20 mol% LiCl, 20 mol% TsOH, 2.5 equivalents water relative to substrate for 16 hours with 1 mol% complex 3.14-*rac* and 3 mol% ligand 3.3.

To test the generality of the 1 mol% complex **3.14-*rac*** / 3 mol% ligand **3.3** catalyst system, the hydroxycarbonylation of the four substrates of varying electronic character mentioned above was performed. The yield of product from 4-fluorostyrene is a little greater than that for styrene with the methoxy substituted substrates giving substantially lower yields. In contrast to the monodentate complex **2.16-*rac/meso***, the hydroxycarbonylation of 4-fluorostyrene is less selective for the branched isomer than styrene, and the electron rich 4-methoxystyrene shows the highest selectivity for the branched acid.

4.4.4. Effect of pressure.

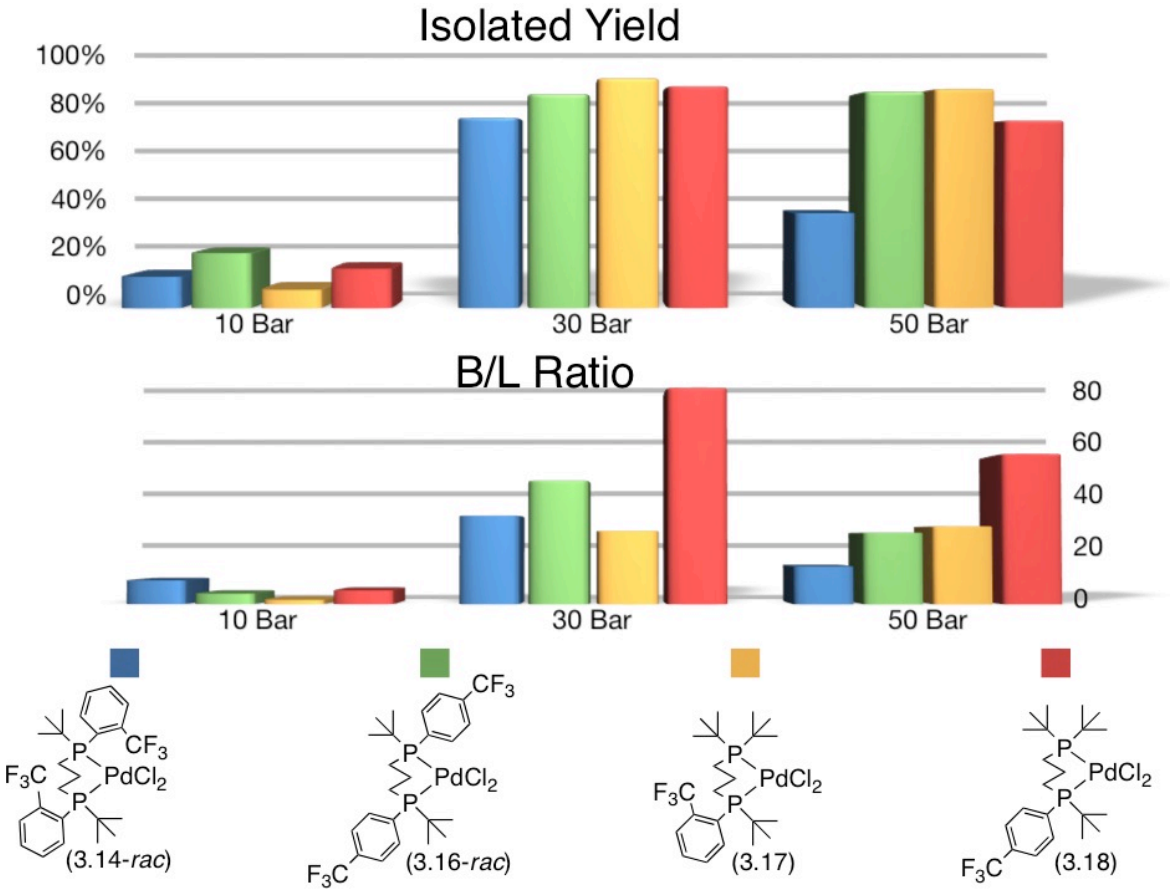


Figure 4 - 7. Reactions carried out in butan-2-one at 120 °C, 20 mol% LiCl, 20 mol% TsOH, 2.5 equivalents water relative to styrene for 16 hours with 1 mole% Pd complex.

Catalytic runs were performed for four novel bidentate complexes at varying pressures. The results show that catalytic activity is dramatically affected by CO pressure and collapses at lower pressures. Also, the branched selectivity is negatively affected by low pressures. At 30 bar all complexes produced good yields and good (for complex **3.18**, excellent) selectivity for the branched isomer. At 50 bar the yields are similar or slightly lower for most complexes, except **3.14-*rac*** which was exactly half as active as it had been at 30 bar. Branched selectivity was also negatively affected by higher pressure with the exception of **3.17** which shows a very slight increase. There do not appear to be any clear patterns as to which structural features influence catalytic behaviour though it could be argued that in these experiments the *para*-CF_3 substituted phosphines are more selective. The excellent selectivity (B/L = 75.5, 98.7 % branched) obtained with the unsymmetrical complex **3.18** at 120 °C and 30 bar is remarkable. This, to the best of our knowledge, is the highest branched selectivity that has ever been achieved in the hydroxycarbonylation of any vinylarene with a complex based on a diphosphine ligand.

4.4.5. Effect of temperature.

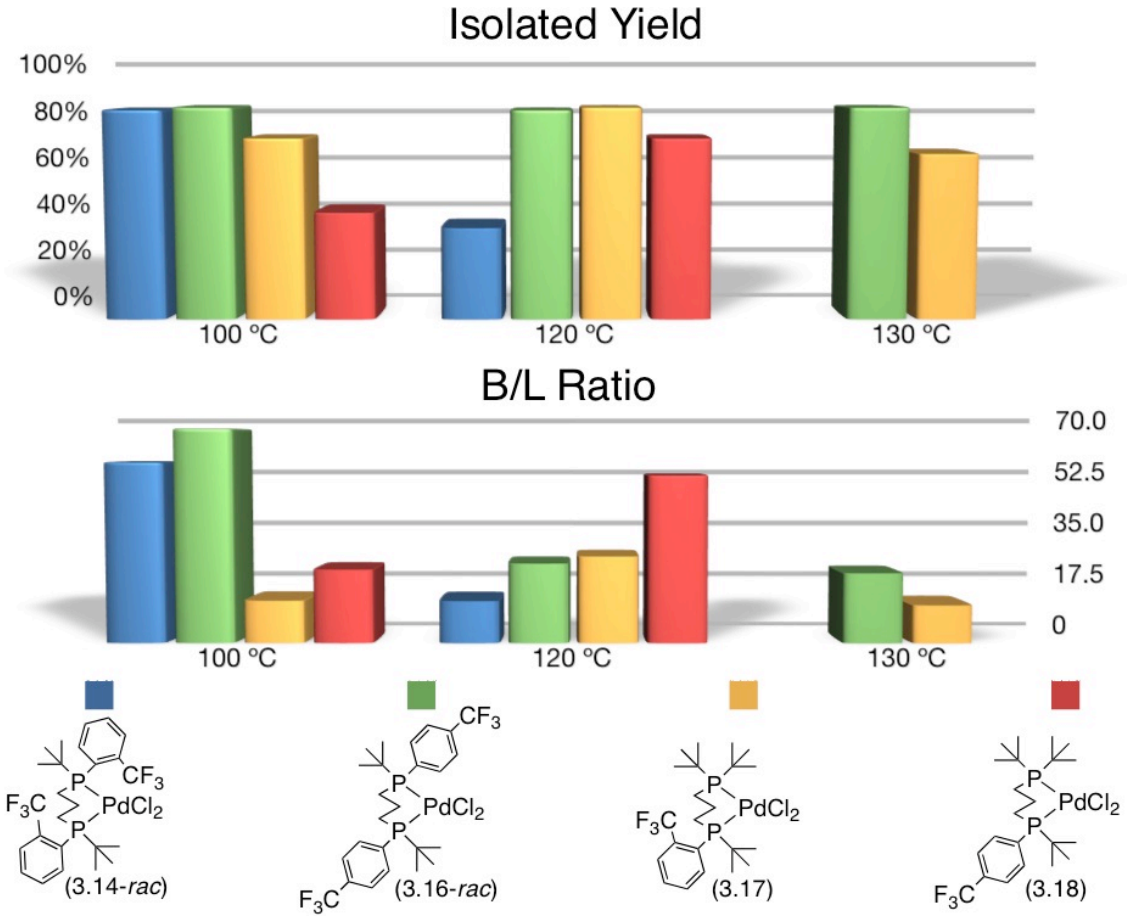


Figure 4 - 8 Reactions carried out in butan-2-one at 50 bar CO pressure, 20 mol% LiCl, 20 mol% TsOH, 2.5 equivalents water relative to substrate for 16 hours.

The effects of temperature are shown in Figure 4 – 7. Yields of acid produced by the complexes at 100 °C are good, with the exception of **3.18** which gives only a 42 % yield of the acid, however the yield with this complex is increased at 120 °C. This behaviour contrasts with that shown by complex **3.14-*rac*** which gives a substantially lower yield at the higher temperature. It has been shown above that yields with this complex can be increased by the use of additional ligand. These observations suggest that with this complex, ligand degradation is a problem and this degradation is faster at higher temperatures. The B/L ratio obtained from these complexes also shows a marked dependence on temperature. The symmetrical ligands are highly selective for the branched isomer at lower temperatures but the selectivity is substantially diminished upon an increase in temperature. However, the unsymmetrical ligand based catalysts become more selective on an increase in temperature from 100 to 120 °C.

4.4.6. Effect of Promoters.

The high selectivity towards linear acids shown by the ligands in this study is in contradiction with the often quoted paradigm for the carbonylation of styrene: "monophosphines as ligands give 2-phenylpropanoic products as the major products and the 3-phenyl propanoic products are obtained when diphosphines are used."[9, 69] It should be especially noted that in the present study B/L ratios of >1 have been observed for all ligands, not just the novel ligands synthesised in this study. It was therefore decided, as the other conditions used in this reaction are similar to those used previously, that the role of the promoters TsOH and LiCl, which have not to our knowledge ever been used with bidentate phosphines, should be investigated.

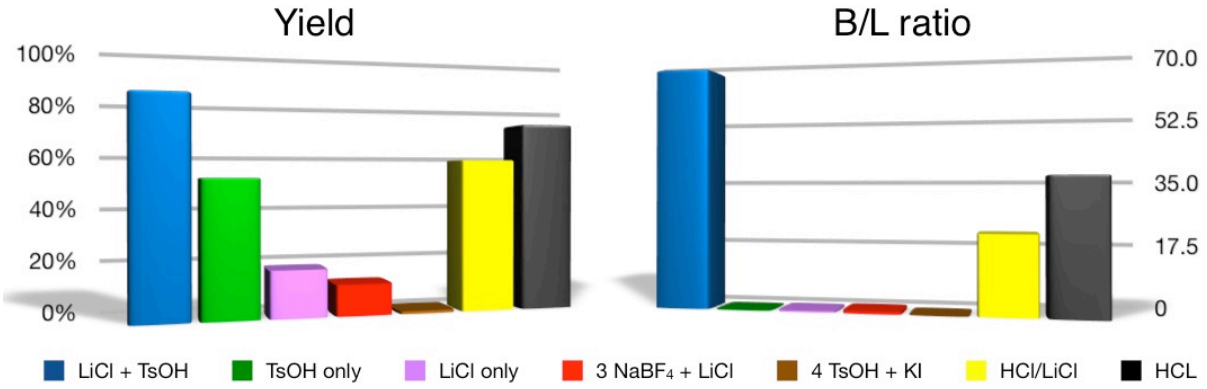


Figure 4 - 9. Styrene hydroxycarbonylation in butan-2-one at 50 bar CO pressure, 100 °C, 1 mol% 3.16-*rac*, 2.5 equivalents H_2O relative to substrate for 16 hours, 20 mol% of each promoter stated was added.

The results (Figure 4 – 8) show that catalyst activity is significantly affected by the promoters. The yield achieved in the lithium chloride/TsOH promoted reaction is almost double that with TsOH only, and over four times that in the presence of LiCl alone, whereas the TsOH/KI promoted reaction gives no activity at all. The most dramatic effects are seen in the selectivity with B/L ratios of less than one for promoter combinations other than those in which H^+ and Cl^- are present. The highest selectivity is achieved with the LiCl/TsOH system, which gives a very high B/L ratio of 67. It is clear from these results that the effect that this promoter system has on the activity and selectivity of the hydroxycarbonylation of styrene is "greater than the sum of its parts."

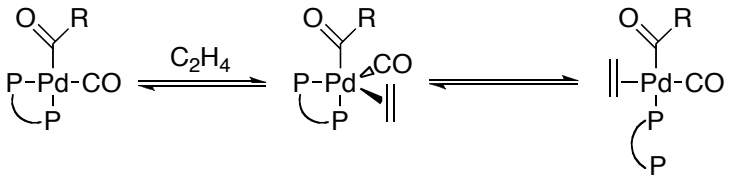
4.5. Analysis of results.

The following discussion includes information which may be relevant to understanding the processes that lead to the outstanding selectivity seen here, and how these may be relevant to the development of enantioselective hydroxycarbonylation of vinylarenes with diphosphines.

4.5.1. Influence of *ortho*-CF_3 substitution in for catalytic activity.

The solid state structures of the complexes shown in this study show that it is possible for the *ortho*-CF_3 substituted phenyl groups of the ligands **3.3 (**Figure 3 - 9**)** and **3.10 (**Figure 3 -13**),** which it was hoped would exert a strong steric influence, to take up positions were they are remote from the site of catalysis. In general, the results show that the hydroxycarbonylation is more selective for the branched acid when the CF_3 substitution is in the *para*-position for both the symmetrical and unsymmetrical ligands. However, the differences in selectivity are relatively small if expressed in percentages of the total yields. This may be an indication that the presence of the bulky *ortho*-CF_3 groups exerts little steric influence. An exception to this is, when additional ligand is present, a profound difference is clearly seen between the activity of the two complexes **3.14** and **3.16 (**Figure 4 -4**)**. A plausible explanation for this difference in activity is that *ortho*-CF_3 groups hinder the formation of stable catalytically inactive bis chelate species.

4.5.2. Coordination mode of Bisphosphine ligands.



Scheme 4 - 8. An example of an "arm off" unidentate diphosphine complex.

It has previously been shown that in bisphosphine catalyst systems similar to those in this study, the ligand can adopt unidentate coordination modes[5] and these types of complexes have been proposed as catalytic species in carbonylation reactions (Scheme 4 – 7).[163] Unidentate coordination of the ligands used in this study would not be inconsistent with the observed high branched selectivity. However, it has been found that *cis* coordination of bidentate ligands is crucial for the alcoholysis of acyl palladium species,[9, 164] which is closely related to the hydrolysis step required for hydroxycarbonylation. The question of whether the ligand

adopts a monodentate coordination mode during catalysis is of key importance for the development of an enantioselective version of this reaction as bidentate chelates are more adept at enforcing the constrained steric environment necessary for effective enantiocontrol.

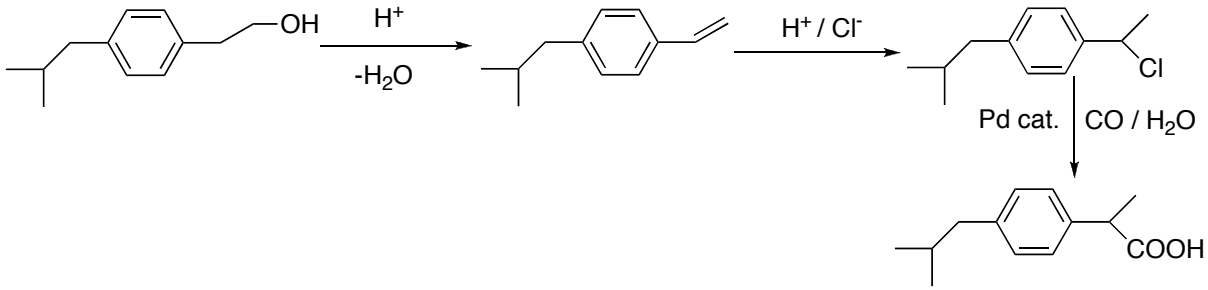
4.5.3. Previous studies on the use of promoters.

The reaction conditions were initially chosen, as in previous in reports with monophosphine ligands, they had given high activities and selectivity for the branched isomer.[156, 157, 165] However, a deeper search of the literature reveals that these conditions play a fundamental role in dictating the outstanding branched selectivity seen in these reactions. The use of promoters such LiCl and various acids in carbonylation reactions for the production of arylpropionic acids has been the subject of several studies[158, 160, 162] and these promoters have been found to significantly influence catalyst activity and selectivity. The use of acids with strongly coordinating counter-ions such as HI has been found to be detrimental to catalytic activity.[166] This is probably due to the fact that they block reaction sites on palladium, inhibiting coordination of reactants. Weakly coordinating counter-ions by contrast have been found to be beneficial.[159] In the carbonylation of phenylethanol in CH_2Cl_2, Bonnet found that the concentration of tetrafluoroboric acid had a pronounced effect on chemoselectivity towards arylpropionic acids, yet had little effect on regioselectivity. In the aqueous hydroxycarbonylation of propene using a trisulfonated triphenylphosphine catalyst, a high concentration of *para*-toluenesulfonic acid has been found to enhance catalytic activity and also inhibit the formation of palladium black.[166]

4.5.4. Comments on the importance of chloride ions.

Whilst it is difficult to make direct comparisons due to the sparse amount of data concerning bidentate phosphines, the unusually high selectivity towards the branched isomer that is observed in this study for all catalysts is explained by the action of the promoters in this reaction. Chloride ions play an important role in governing the regioselectivity in these reactions, given that in the closely related Pd catalysed alkoxycarbonylation of styrene a catalyst based on **3.13** gave a contrasting 10:1 selectivity in favour of the linear isomer in the absence of chloride.[68] Jayasree[156] has reported an active and selective biphasic phosphine, N-O ligand system for the carbonylation of styrene, which uses the same combination of LiCl and TsOH promoters as was used in this study. This report is particularly interesting as it provides evidence that during the reaction styrene forms 1-(phenyl)ethyl chloride which is proposed as the active substrate (Scheme 4 – 8). These reactions produce the branched acid

with over 10:1 selectivity, but in the absence of LiCl the linear product predominates. It is also reported that the carbonylation of 1-(4-isobutylphenyl)ethanol, 4-isobutylstyrene and 1-(4-isobutylphenyl)ethyl chloride provide identical results, and the following mechanism has been proposed to explain this (Scheme 4 – 9). The formation of 1-(phenyl)ethyl chloride has been confirmed in the current study by ^{1}H NMR analysis of the crude reaction mixtures.

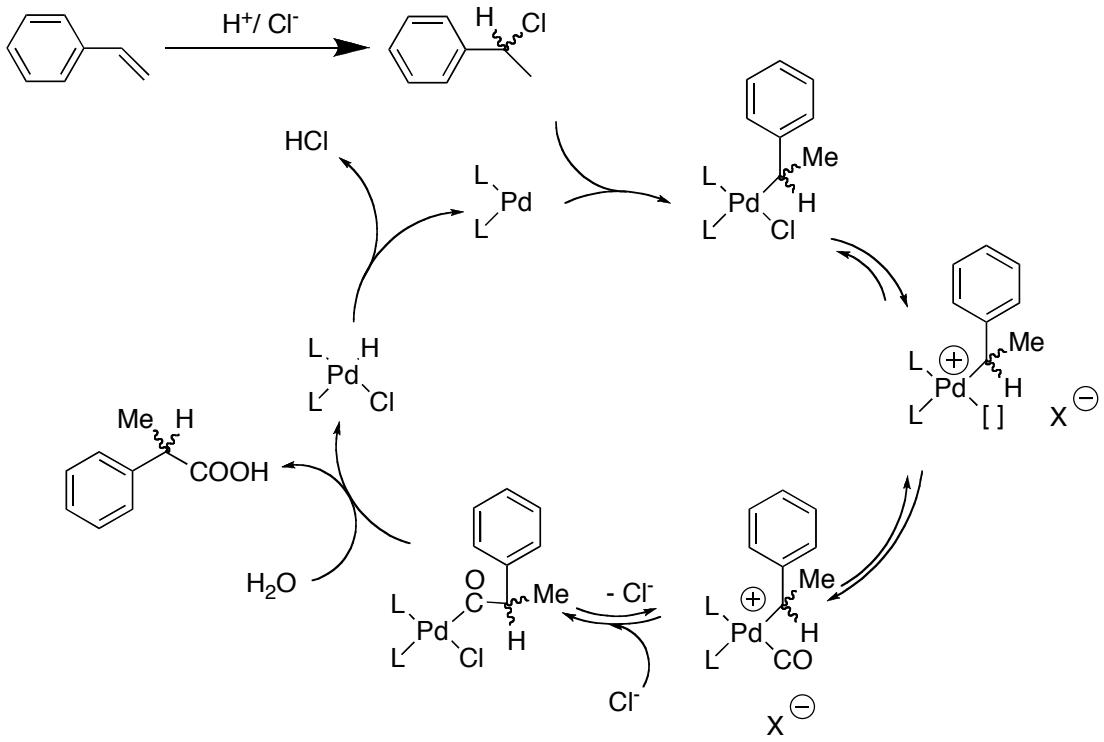


Scheme 4 - 9. Formation of 1-(4-isobutylphenyl)ethyl chloride from 1-(4-isobutylphenyl)ethanol under hyroxycarbonylation conditions and subsequent branched acid formation.

Similar examples of high branched selectivity in the presence of chloride ions are reported for a variety of triphenylphosphine systems in the carbonylations of styrene and phenylethanol in organic solvents.[156, 157, 160, 162]

4.5.5. Suggested mechanism for hydroxycarbonylation in this study.

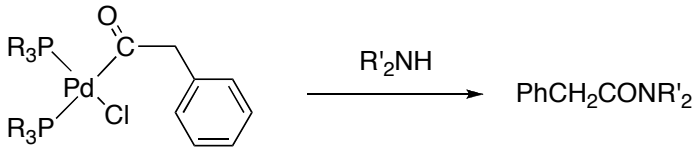
If the formation of the aryl chloride is operating in the reactions in the current study, it would mean that the high selectivity for the branched isomer observed has its root in the Markovnikov[167] addition of HCl across the alkene double bond, before any carbonylation activity by the catalyst takes place. It would then seem reasonable to suppose that the first stage of the catalytic cycle is oxidative addition to a Pd(0) species. Previously, similar species, formed by the reductive elimination of acid from the palladium hydride, have been proposed as intermediates in the hydride cycle of the hydroxycarbonylation reaction.[150] The presence of the non-coordinating anion TsO^{-} allows for the charge to be balanced, and may be more effective than chloride at maintaining a site where CO can more effectively compete for coordination.



Scheme 4 - 10. Suggested mechanism for the branched selective hydroxycarbonylation observed in this study using the TsOH and LiCl promoter system.

4.5.6. Theoretical studies.

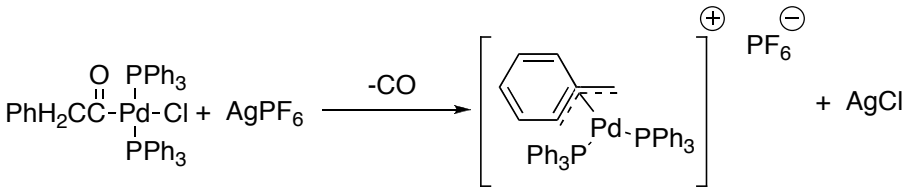
Lin[168] has studied the oxidative addition of benzyl chlorides to palladium(0) diphosphine complexes and the reactions of these compounds with CO to yield phenacetyl palladium(II) complexes. The reaction of these complexes with amine nucleophiles in the absence of CO was found to be influenced by the basicity of the coordinated phosphine, with Me_3P coordinated complexes producing poor yields of the amide compared to the less basic Ph_3P.



Scheme 4 - 11. Reaction of phenacetyl palladium(II) complexes with amine nucleophiles.

In the current study where hydrolysis rather than aminolysis of the acetyl-palladium bond is a key step, it was found that the more basic **3.13** based catalyst gave considerably lower yields than the less basic fluorine containing ligands. Others have also found that electron poor ligands are well suited to the hydroxycarbonylation reaction.[67] Lin's study also shows that n^3-benzylic complexes were formed in the presence of non coordinating anions, and that

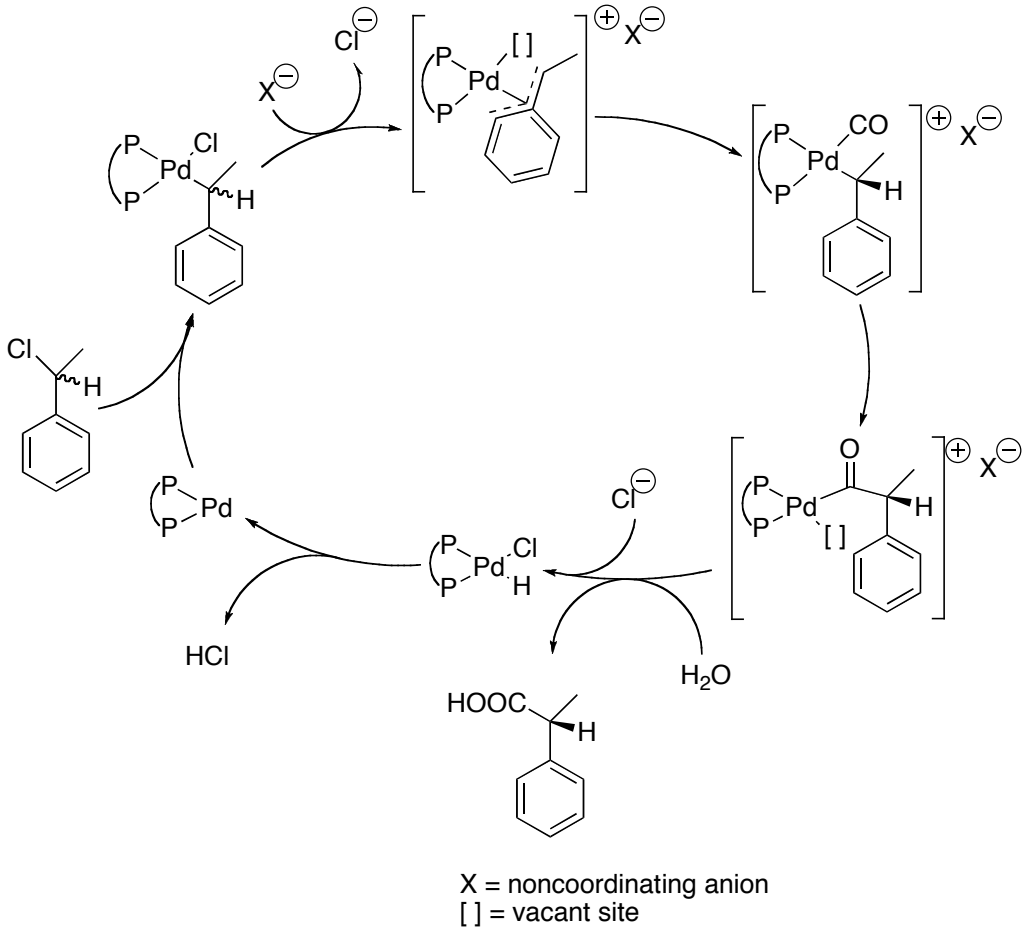
phenylacetyl palladium chloride complexes could be decarbonylated and converted to the n^3-benzylic complex by the addition of $AgPF_6$ (Scheme 4 -12). The promotion of n^3-benzylic complexes may be a factor in the deciding the selectivity observed in the current study given that the non-coordinating TsO^- anion is present in the reaction mixture.



Scheme 4 - 12. The formation palladium of n^3-benylic species, with decarbonylation.

4.6. Prospects for enantioselective hydroxycarbonylation based on the results of the current study.

If the hydroxycarbonylation reactions in this study do proceed through the formation of (1-chloroethyl)benzene, then this has implications for the long term goal of developing an enantioselective version of this reaction based on the results presented here. This would involve the chiral centre of the aryl chloride being formed in the absence of any enantiocontrol before oxidative addition of the substrate to the palladium centre. Therefore, attempts to control enantioselection would most probably rely on the formation of the prochiral n^3-benylic intermediate, and a subsequent enantioselective isomerisation back to the n^1 complex prior to insertion of CO. Incorporating the observations of Lin, the following tentative mechanism is evolved (Scheme 4 – 13).



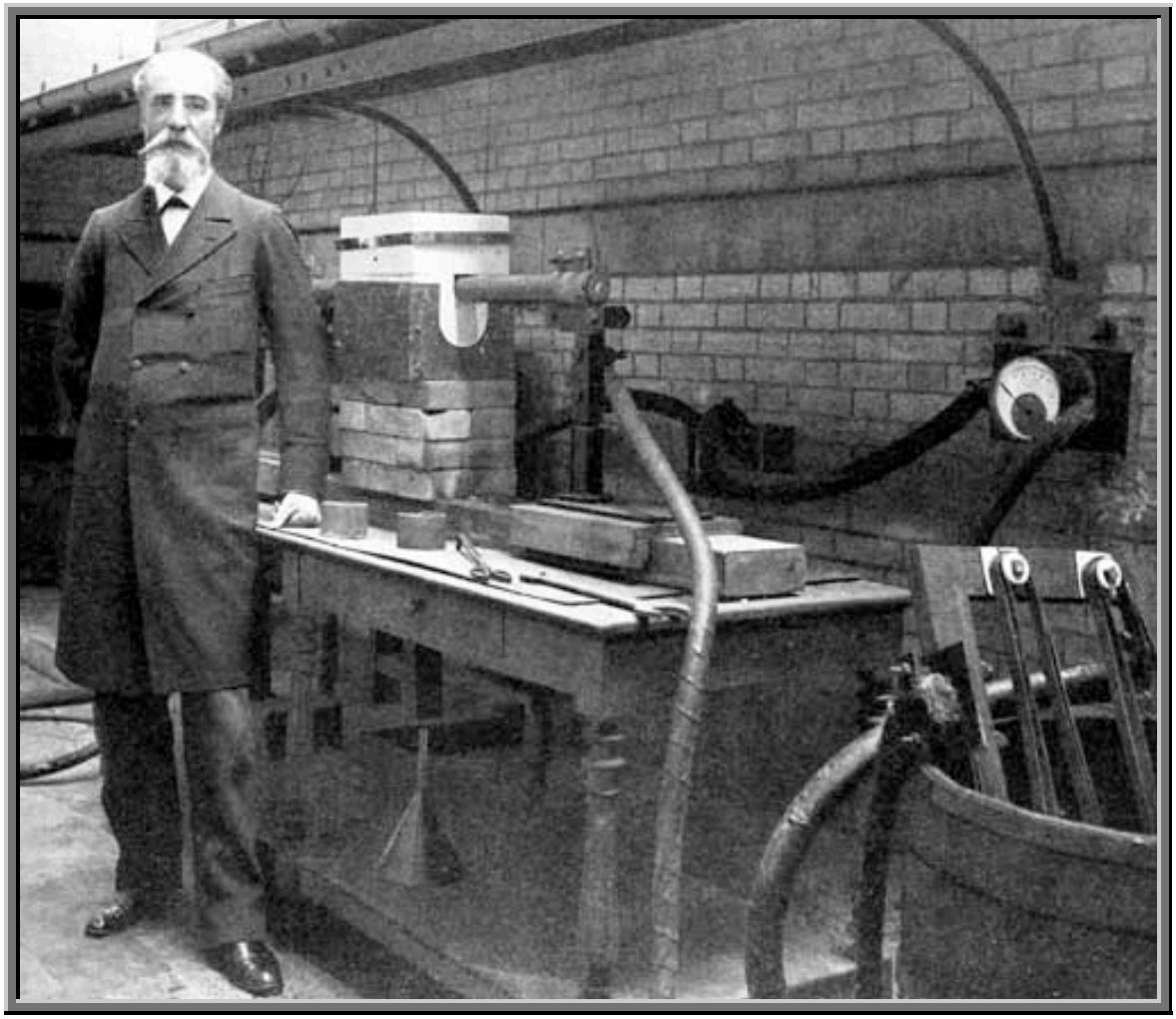
Scheme 4 - 13. A suggested catalytic cycle for the enantioselective hydroxycarbonylation of (1-chloroethyl)benzene with a bidentate ligand and the TsOH and LiCl promoter system.

Other possibilities would also exist for controlling enantioselection, depending on the reversibility of the formation of the palladium substrate complex, the relative rates that the two enantiomers are carbonylated and hydrolysed, and the extent to which β hydride elimination occurs to regenerate prochiral styrene. Work is ongoing by other workers within the group to achieve enantioselective hydroxycarbonylation based on the results presented here.

4.7. Summary.

Novel complexes based on bidentate fluorinated ligands have been tested in carbonylation reactions. Ligands with electron poor subunits have been shown to give superior activity and branched selectivity in the hydroxycarbonylation of styrene under relatively mild conditions. The novel complexes presented here in combination with LiCl and TsOH promoters have shown selectivity for the branched isomer in excess of any reported so far for a catalyst based on a bidentate phosphine ligand. The role of the LiCl and TsOH promoters has been shown to be crucial to the performance of these ligand systems. A tentative mechanism has been suggested to explain these findings.

5. Synthesis of Fluorinated Phosphacycles.



Henri Moissan, who in 1886, was the first to successfully isolate elemental fluorine, at the Faculty of Science in Paris.

5.1.1. Fluorination

Electrophilic fluorination has received much interest in recent years, mainly due to the advent of new fluorination reagents such as Selectfluor,[169, 170] NFSI, DAST[171] and xenon difluoride.[172]

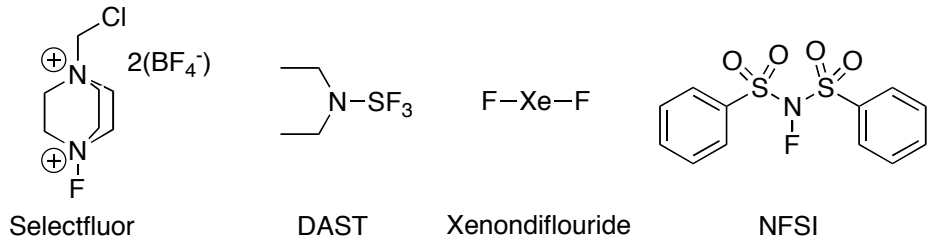


Figure 5 - 1. Electrophilic fluorination reagents which have become popular in recent years.

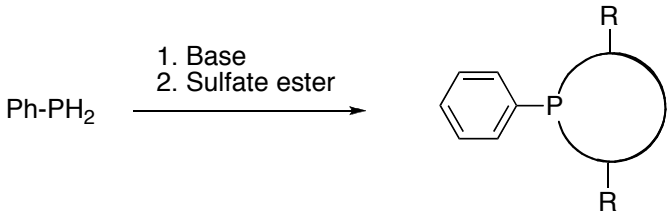
These replace reagents such as perchloryl fluoride and elemental fluorine, the latter of which is notoriously difficult reagent to work with due to the fact it is highly toxic, exhibits little selectivity, has the potential for runaway free radical reactions, and also attacks many of the materials normally used to contain gases. The dangerous nature of elemental fluorine is graphically illustrated in this account by Henri Moissan which was presented at a meeting of the Chemical Society in 1897, in a paper titled *On the Properties of Liquid Fluorine:*[173]

> *Oil of turpentine, in the solid state, is attacked by liquid fluorine. To perform this experiment a little oil of turpentine was placed at the bottom of a glass tube surrounded with boiling liquid air. As soon as a small quantity of fluorine was liquified on the surface of the solid, combination took place with explosive force. After each explosion, the current of fluorine gas was kept up slowly, a fresh quantity of liquid fluorine was formed, and the detonations succeeded each other at intervals of 6-7 minutes. Finally, after a longer interval of about 9 minutes, the quantity of fluorine formed was sufficient to cause, at the moment of the reaction, the complete destruction of the apparatus. In several of these experiments a little liquid fluorine accidently fell on the floor; the wood instantly took fire.*

Selectfluor by contrast has been found to be a mild, stable, reliable and relatively non-toxic reagent which is effective in the fluorination of a vast array of substrates with high selectivity. Due to the ionic nature of Selectfluor, it has been found to be most effective when used in polar solvents such as acetonitrile, DMF and water.

5.1.2. Synthesis of cyclic phosphines.

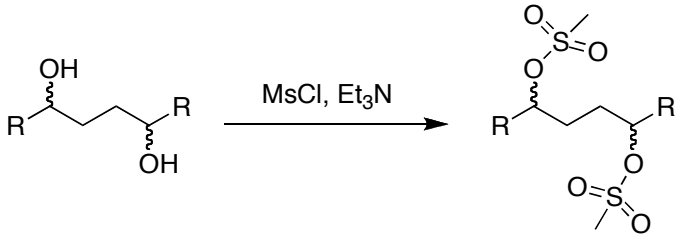
Phosphacycles have been synthesised using dihalides[174], by the reaction of phosphorus chlorides in the presence of $AlCl_3$,[175] and by the use of dilithiated alkanes to dialkoxy phosphines.[109] However, the method most commonly used in recent years is the reaction of phosphides with sulfate esters (Scheme 5 – 1). 4 and 5 membered phosphacycles have been synthesised using dimesylates[100, 176] and cyclic sulfates.[177, 178]



Scheme 5 - 1. General synthesis of phosphacycles using sulfate esters.

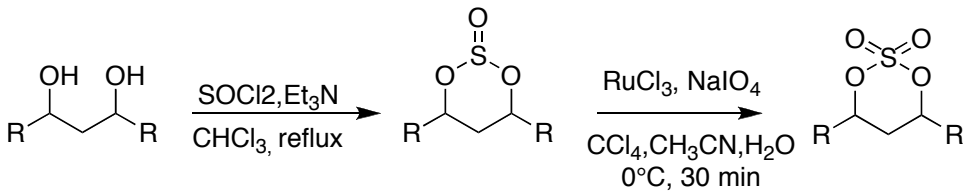
5.1.3. Synthesis of sulfate esters.

The synthesis of mesylates is usually achieved by the reaction of alcohols with mesityl chloride in the presence of base (Scheme 5 – 2).



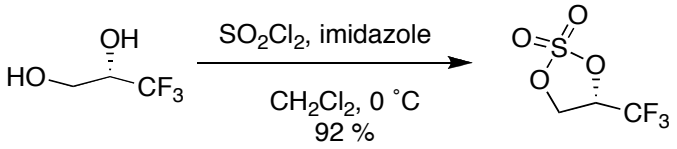
Scheme 5 - 2. General synthesis of mesylates using mesityl chloride.

Sharpless[179, 180] has published a method by which cyclic sulfates can be conveniently accessed in good yield (Scheme 5 - 3), which is often cited in the synthesis of cyclic phosphines.[103, 181, 182] The reaction proceeds first by formation of the cyclic sulphite by reaction with thionyl chloride, followed by a ruthenium catalysed biphasic oxidation to yield the cyclic sulfate.



Scheme 5 - 3. General synthesis of cyclic sulfates using the Sharpless procedure.

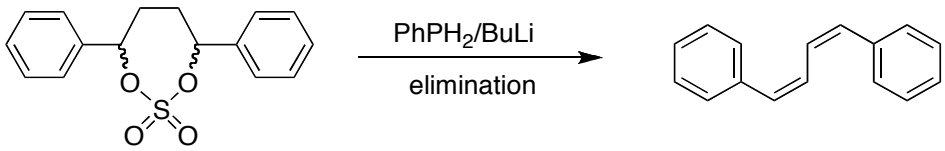
The direct transformation of diols into cyclic sulfates using sulfuryl chloride has been reported (Scheme 5 - 4).[183] This method is not as general as the procedure using thionyl chloride because side product formation is commonly observed.[184] However, this synthesis is reportedly well suited for electron deficient compounds,[185, 186] and this method has the advantage of avoiding the exposure to water that occurs during the Sharpless process, and the subsequent possibility of hydrolysis.



Scheme 5 - 4. Direct synthesis of cyclic sulfates using sulfuryl chloride.[186]

5.2. Synthesis of phosphacycles using fluorinated diols.

The first objective in this route to a fluorinated phosphine was to access a fluorinated diol from which sulfate esters could be prepared. **5.2** was chosen as a desirable target compound as there is no opportunity for elimination under nucleophilic attack, which can be a problem in reactions of this type (Scheme 5 – 5).[187]

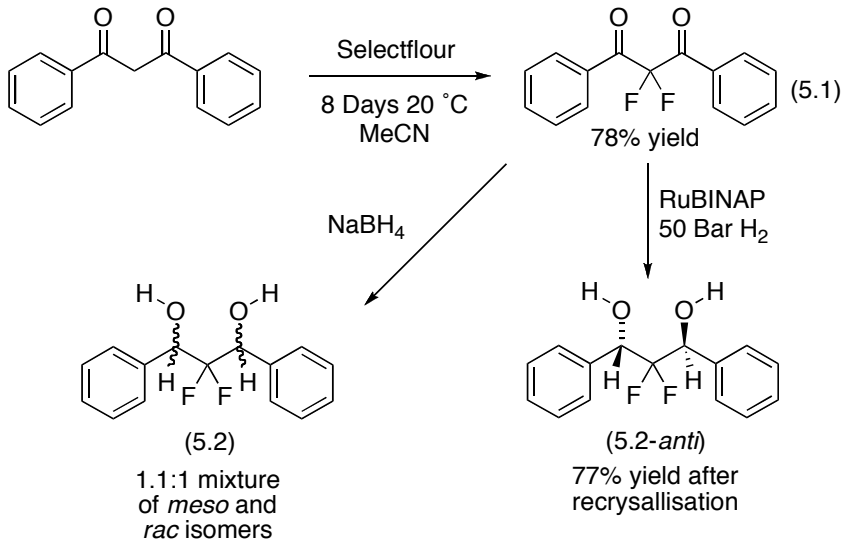


Scheme 5 - 5. An example of an elimination reaction in the attempted synthesis of a phospholane.

The presence of two fluorine atoms within the phosphetane ring would, it was hoped, lead to modified coordination and catalytic behaviour in any phosphine ligand synthesised.

5.2.1. Synthesis of a difluorinated diol (5.2).

The preparation of difluorodione **5.1** was performed by the slow but relatively high yielding procedure previously described by Banks (Scheme 5 – 6).[188]



Scheme 5 - 6. Synthesis of 5.2.

As a ruthenium catalyst based on BINAP has been found to effectively produce the *anti* isomer in the diastereoselective hydrogenation of diketones,[189] the decision was taken to attempt to use a similar system for the transformation of this electron poor substrate (**5.1**) (Scheme 5 - 6). A modified catalyst preparation method was used in which benzeneruthenium chloride dimer and (S)-BINAP were subjected to microwave heating. This allowed quicker and more efficient catalyst formation than traditional methods. Hydrogenation of **5.1** overnight in methanol at 50 bar with this catalyst allowed the selective production of a single diastereomer (**5.2-*anti***), which was isolated after recrystallisation in 77% yield. A solid-state structure of this compound was obtained to confirm the stereochemistry of this compound (Figure 5 – 2). In contrast a 1:1.1 mixture of *meso*:*rac* isomers produced when the same transformation was performed using $NaBH_4$ as the reductant. Further stereoselective reduction of this compound has been investigated by other workers in the group.[190]

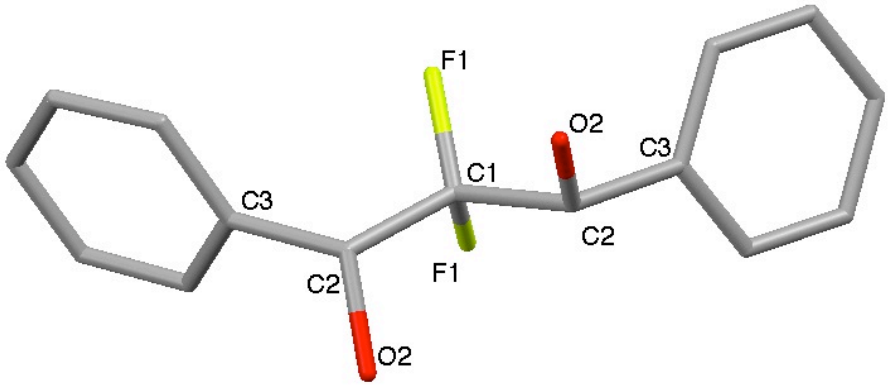
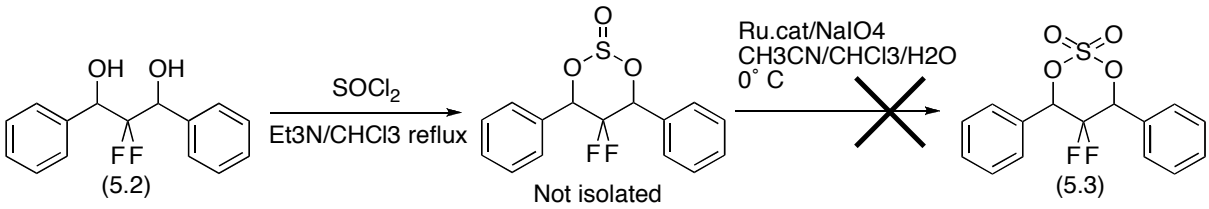


Figure 5 - 2. X-ray structure of 5.2-*anti*. All hydrogens omitted for clarity.

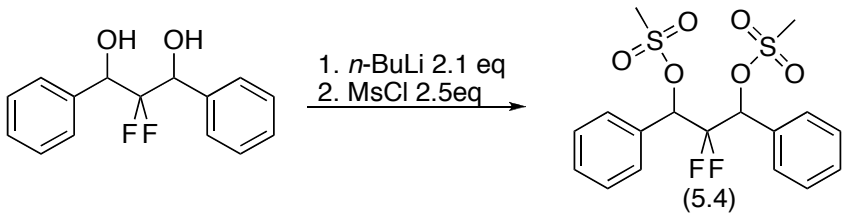
5.2.2. Fluorinated sulfate ester synthesis.

Attempts to generate cyclic sulfate (**5.3**) from **5.2** following the Sharpless procedure were not successful (Scheme 5 -7), instead this yielded complicated mixtures of products in which the cyclic sulfate may have been a minor component although the mass spectrum showed no evidence of this.



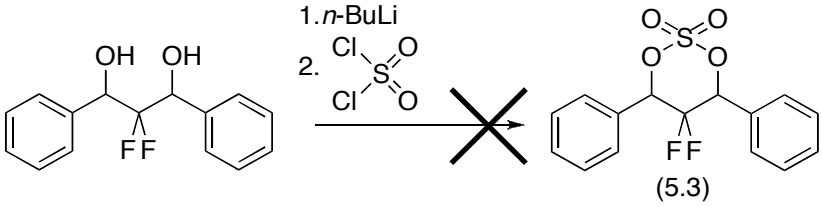
Scheme 5 - 7. Attempted synthesis of a cyclic sulfate (5.3) using the Sharpless procedure.

Attempts were made to generate other leaving groups that would allow reaction with nucleophiles, using mesityl chloride, trifluoromethanesulfonic anhydride, and toluene sulphonic chloride. However, none of these reactions resulted in the desired products. The substitution of the stronger base, *n*-butyllithium for Et_3N eventually led to the successful synthesis of the dimesylate (**5.4**) (Scheme 5 -8). The requirement of a strong base was unexpected as the alcohol protons were expected to be fairly acidic. The dimesylate was synthesised in 63% yield after work up and recrystallisation. However, the cyclic sulfate could not be obtained using this modified deprotonation procedure.



Scheme 5 - 8. Synthesis of 5.4.

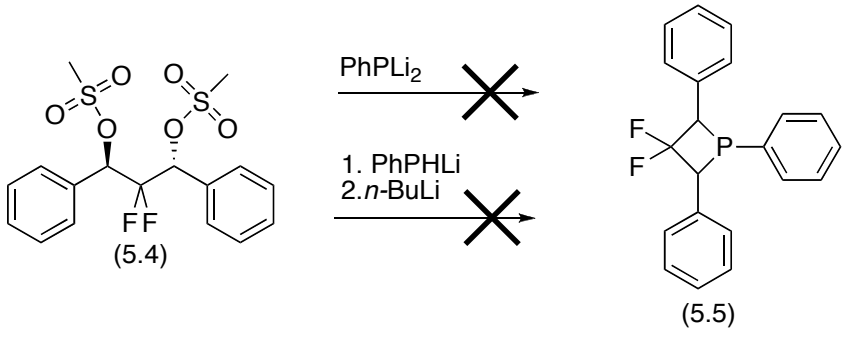
The attempted synthesis of the cyclic sulfate by the use of *n*-butyllithium to deprotonate followed by reaction with sulfuryl chloride (Scheme 5 – 9) also resulted in complicated mixtures in which the desired product could not be positively identified.



Scheme 5 - 9. Attempted direct synthesis of 5.3 using sulfuryl chloride.

5.2.3. Attempted ligand synthesis using 5.4.

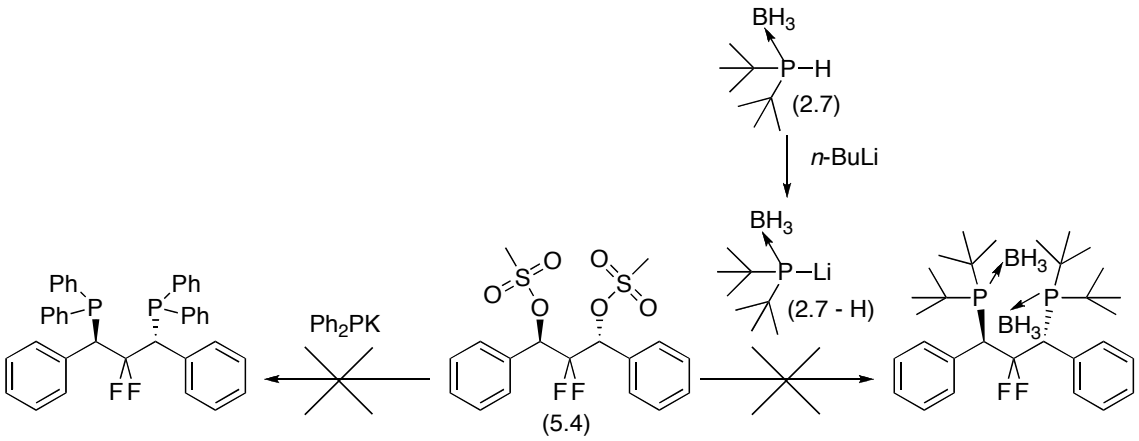
The dimesylate (**5.4**) was used in an attempt to synthesise a phosphetane (**5.5**) by reaction with the mono lithio and dilithio phosphides (Scheme 5 – 10). However, this was judged as unsuccessful due to the lack of any observable P-F coupling in the ^{19}F and ^{31}P NMR spectra.



Scheme 5 - 10. Attempted synthesis of a phosphetane using 5.4.

As the synthesis of phosphetanes is known to be challenging, some simpler reactions were performed to gain some understanding of how the dimesylate (**5.4**) reacts with nucleophiles (Scheme 5 - 11). Additionally, if these reactions were successful they would generate novel

bidentate ligands with difluoro substitution in the propyl bridge, which would fulfil the project aim of synthesising bulky fluorinated diphosphines.

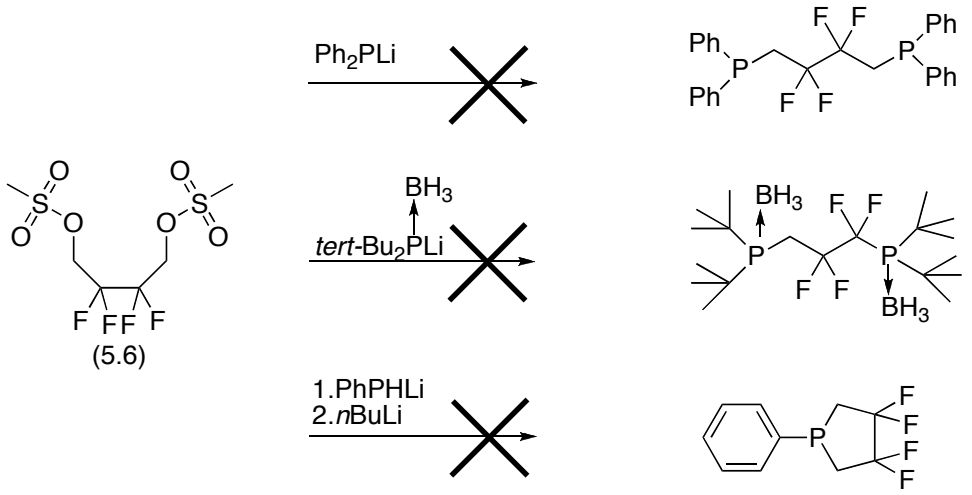


Scheme 5 - 11. Efforts toward the synthesis of bidentate phosphines from 5.4.

The reaction of Ph_2PLi with the mesylate failed to produce any species for which a P-F coupling could be observed in NMR spectra, and the mass spectra showed no peak that could reasonably be assigned to the bis-substituted or even mono-substituted product. Similarly the reaction of the dimesylate with *tert*-Bu_2PLi borane showed no sign of the desired product instead the result was the reprotonation to yield the phosphine borane (**2.7**). This observation indicates that the dimesylate may be prone to abstraction of protons.

5.2.4. Attempted ligand synthesis using 2,2,3,3-tetrafluorobutane-1,4-diol.

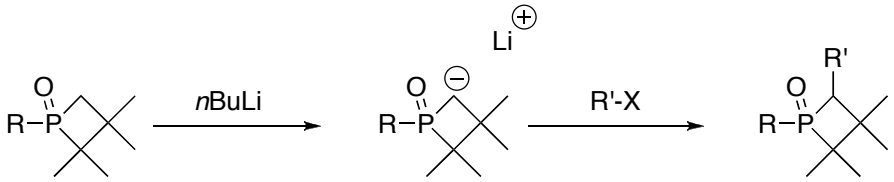
Similar experiments to those detailed above were attempted using commercially available 2,2,3,3-tetraflourobutane-1,4-diol. The dimesylate (**5.6**) was successfully synthesised in 87% yield after recrystallisation but attempts to synthesise the cyclic sulfate did not prove fruitful. The reaction of *tert*-Bu_2PLi borane with the dimesylate resulted in reprotonation of the phosphide anion, and reaction with Ph_2PK similarly resulted in no product in which P-F coupling could be seen (Scheme 5 - 12). Indeed the main product was diphenylphosphine. An attempt at phospholane synthesis with this material yielded the type of complex mixture often indicative of polymer formation. However, no P-F coupling was discernable. Surprisingly, **5.6** was found to be stable, surviving several months of storage under atmospheric conditions with no sign of degradation in contrast to other sulfate esters which readily hydrolyse.



Scheme 5 - 12. The attempted synthesis of ligands based on 5.6

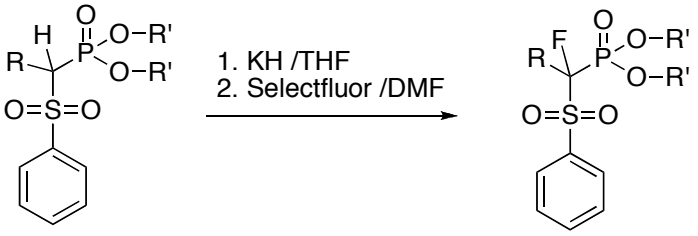
5.3. Fluorinated phosphacycles by fluorination of known phosphacycles.

In view of the difficulties experienced in the attempts to form fluorinated phosphacycles discussed above, it was decided to synthesise some literature phosphacycles to gain some experience with the methodology. These compounds would in themselves be potential precursors for fluorinated phosphacycles. The modification of phosphacycle structures has been performed by Marinetti, allowing the introduction of additional functional groups at the α-carbon. Reactions of this type have been performed using phosphine oxides (Scheme 5 – 13),[191] and sulfur adducts,[174] and may also be possible with borane adducts. These reactions have involved deprotonation of the α-carbon with various bases, followed by reaction with various electrophiles.



Scheme 5 - 13. Elaboration of a phosphetane.

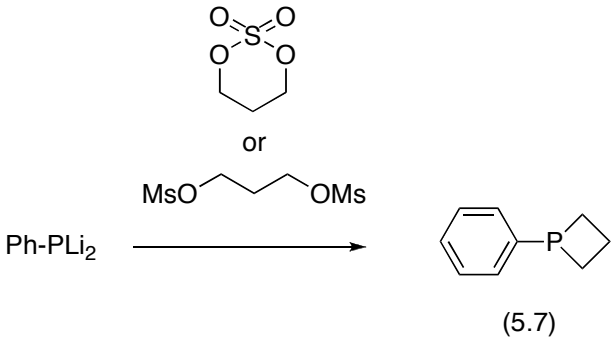
As the metallation reaction appears to be quite general it was planned to use this method to generate a nucleophile and react this with a source of electrophilic fluorine such as Selectfluor. Reactions of this type have been performed previously to allow the fluorination of β-ketophosphonates and sulfonylalkylphosphonates (Scheme 5 – 14).[170, 192]



Scheme 5 - 14. Fluorination of sulfonylalkylphosphonates.

5.3.1. Phenyl Phosphetane.

Several attempts were made to synthesise phenyl phosphetane (**5.7**) using both the dimesylate and the cyclic sulfates, which were synthesised using the methods mentioned above, in reactions with $PhPLi_2$ as detailed by Marinetti (Scheme 5 – 15).[126] However, these reactions resulted in complex mixtures containing the polymeric products that are often produced in reactions of this type.[177, 193]

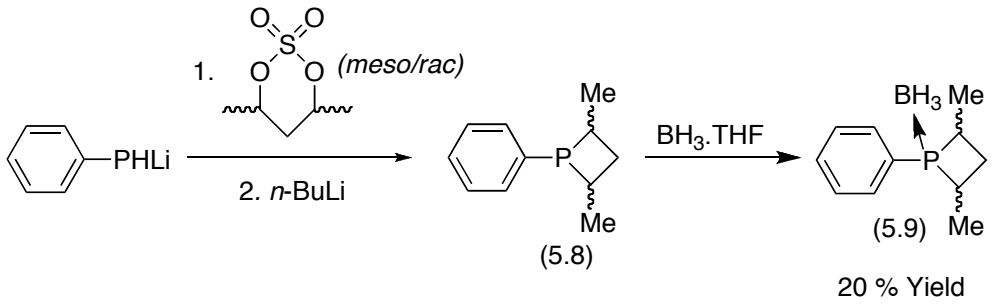


Scheme 5 - 15. Synthesis of phenyl phosphetane using $PhPLi_2$.

The alternative two step procedure where the formation of the phosphacycle is accomplished by reacting the monophosphide with the cyclic sulfate, followed by a second addition of *n*-butyllithium to effect ring closure, produced similar results.

5.3.2. Synthesis of 2,4-dimethylphenylphosphetane (5.8).

The synthesis of 2,4-dimethylphenylphosphetane by the two step procedure outlined by Berens[177] (cheaper *rac*/*meso* mixtures of 2,4-pentane diol were employed to form the cyclic sulfate) was more successful (Scheme 5 – 16). The subsequent addition of BH_3.THF allowed successful isolation of the target compound as the borane adduct, by means of aqueous work up followed by flash chromatography under atmospheric conditions.



Scheme 5 - 16. Synthesis of 2,4-dimethylphenylphosphetaneborane.

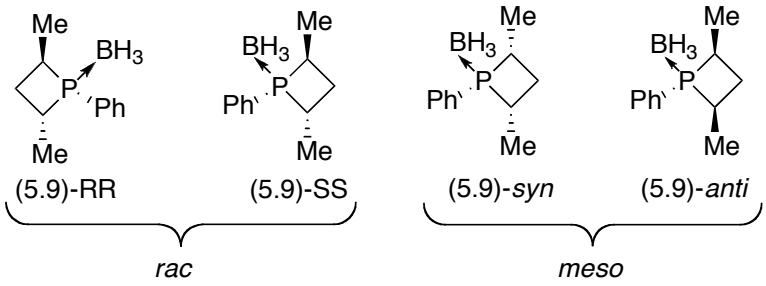
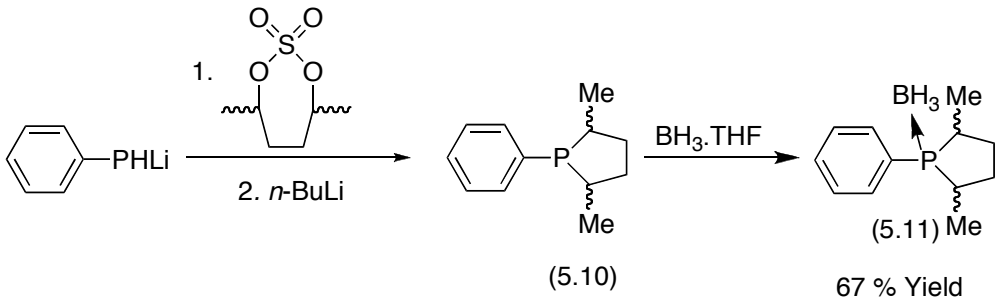


Figure 5 - 3. The four possible stereoisomers of 2,4-dimethylphenylphosphetaneborane (5.9).

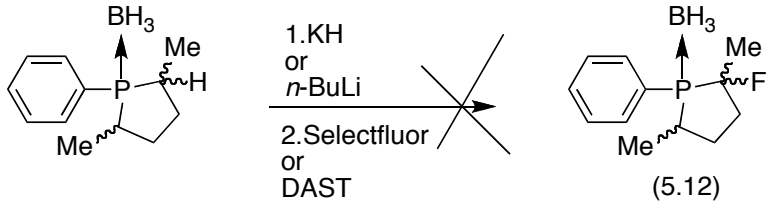
The yield of 20% is consistent with that reported by Berens, however an attempt to replicate this result on a larger scale gave disappointing low yield of 7.5%. The ^{31}P NMR spectrum shows the presence of two isomers. The signal at δ 52.2 ppm is assigned as the two *rac* enantiomers in accordance with previous reports,[126] and the signal at 48.9 ppm is assigned as one of either *meso* isomers **5.9-*syn*** or **5.9-*anti*** (Figure 5 – 3). Traces of the third possible isomer may also be present but it is not obvious owing to the characteristically weak signals of phosphine borane complexes. The question as to which of the two possible *meso* isomers is visible is still open, though steric arguments would suggest that **5.9-*anti*** would be more readily formed. In the $^{1}H\{P\}$ NMR spectrum the three sets of doublets are seen, which is accordance with three unique methyl environments arising from the existence of the two main isomers. Traces of the second *meso* isomer also appear to be present. In the ^{1}H NMR spectrum these signals are present as doublets of doublets, δ1.36 and 0.93 are assigned as the *rac* isomers[126] whilst the signal at 1.00 (dd, $^{3}J_{P-H}$ = 17.2 Hz, $^{3}J_{H-H}$ = 7.0 Hz) and the trace signal at 1.12 (dd, $^{3}J_{P-H}$ = 19.3 Hz, $^{3}J_{H-H}$ = 6.6 Hz) are tentatively assigned as isomers **5.9-*anti*** and **5.9-*syn*** respectively.

5.3.3. Fluorination of 2,4-Dimethylphenylphospholane derivatives.



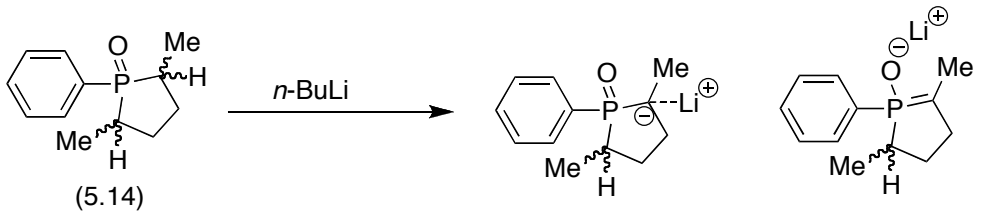
Scheme 5 - 17. Synthesis of 2,4-dimethylphenylphospholaneborane.

The difficulties experienced whilst seeking to synthesise an amount of phosphetane sufficient for further exploratory experiments led to the decision to pursue the synthesis of phospholanes, which are known to be more easily synthesised than their four membered counterparts. The synthesis of 2,5 dimethyl-1-phenylphospholane was performed as per the procedure described in the patent by Boerner[194] (but again using a *rac*/*meso* diol mixture) (Scheme 5 – 18). In contrast to the attempts to synthesise phosphetanes, **5.10** was produced cleanly with virtually no side product formation. On one occasion, the reaction product was distilled to purify the free phosphine. Three signals are seen in the ^{31}P NMR spectrum, indicating the presence of the *meso* and *rac* isomers. The signal at 11.5ppm is assigned as the *rac* isomers in accordance with the procedure. The small signal at 15.0 ppm and the larger 20.5 ppm are tentatively assigned as the *syn* and *anti* isomers respectively on the basis of steric arguments. In the proton spectrum the predicted 4 dd signals are present in ratios corresponding to those seen for the signals in the ^{31}P spectrum. Addition of BH_3.THF to the reaction mixture resulted in formation of the borane complexes (**5.11)**, which allowed for isolation of the product by aqueous work up followed by flash chromatography, resulting in a satisfactory 67% yield.

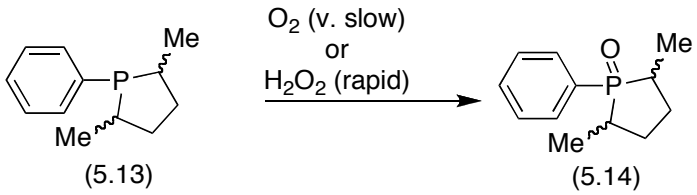


Scheme 5 - 18. Attempted fluorination of 2,4-dimethylphenylphosphetaneborane.

Several attempts were made to fluorinate the phospholane borane by deprotonation followed by the addition of Selectfluor (Scheme 5 – 18), however no evidence of P-F coupling could be discerned in any of the spectra of the resulting mixtures. Similar reactions with DAST and NFSI gave similar results. As fluorination is reportedly possible at saturated sites in carbonyl compounds[188] and alkanes[195] using Selectfluor, a base-free transformation was attempted. However, no evidence of the desired product was observed. The deprotonation-alkylation reactions had previously been reported using phosphacycle oxides, therefore a decision was taken to pursue this alternative and more established approach. It was reasoned that phospholane oxides may be more effective in stabilising the negative charge on the α-carbon leading to the formation of more stable anions than is possible with phosphine boranes.

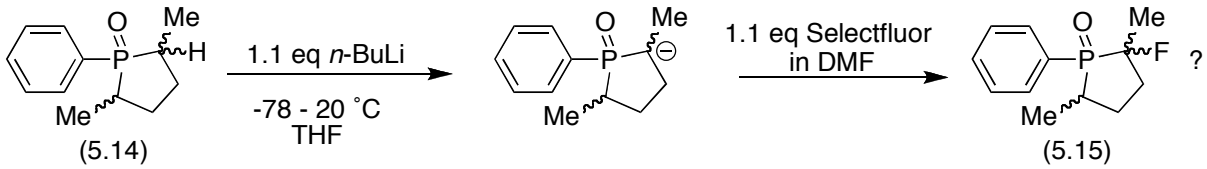


Scheme 5 - 19. Deprotonation of 5.14 with *n*-butyllithium, with resonance structures that may be responsible for stabilisation of the anion.



Scheme 5 - 20. Oxidation of 2,4-dimethylphenylphospholane.

Oxidation of the dimethyl phosphacycles proved to be non trivial. Previously, 2, 5-Dimethyl-l-phenylphospholane has been reported to be moderately stable to oxidation, however during attempts to prepare the oxide it was found that this compound is remarkably resistant to oxidation. Bubbling oxygen through a CH_2Cl_2 solution of the phospholane for 4 hours resulted in less than 2% conversion to the oxide as judged by ^{31}P NMR. The addition of an excess of hydrogen peroxide to a THF solution of the phospholane however, resulted in the rapid conversion to **5.14** which was isolated by flash chromatography. Again three isomers were observed.



Scheme 5 - 21. Fluorination of 2,4-Dimethylphenylphospholane oxide.

Several attempts were made to form a fluorinated phospholane oxide (**5.15**) from this material using a variety of bases and conditions. The most promising result was observed when after addition of *n*-butyllithium to a THF solution of the phospholane oxide which resulted in an orange solution on warming to room temperature. A DMF solution of Selectfluor was added to this and after work up, three doublets were observed in the ^{19}F NMR spectrum with coupling constants of between 65 and 67 Hz (Figure 5 – 4). The ^{31}P spectrum shows a complex mixture of products complicated by many signals. However, three small doublets were present which have corresponding coupling constants to those seen in the ^{19}F spectrum (Figure 5 – 5). The values of these coupling constants and the chemical shifts of these signals do not seem unreasonable when compared to the value of $^{2}J_{P\text{-}F}$ for an α-fluorinated phosphine oxide which has been prepared previously.[196] These results are tentatively ascribed to the formation of the desired fluorinated phospholane oxide. However, it should be noted that these products were minor components in a complex mixture. Therefore, it was decided that no further investigation of this synthesis would be performed.

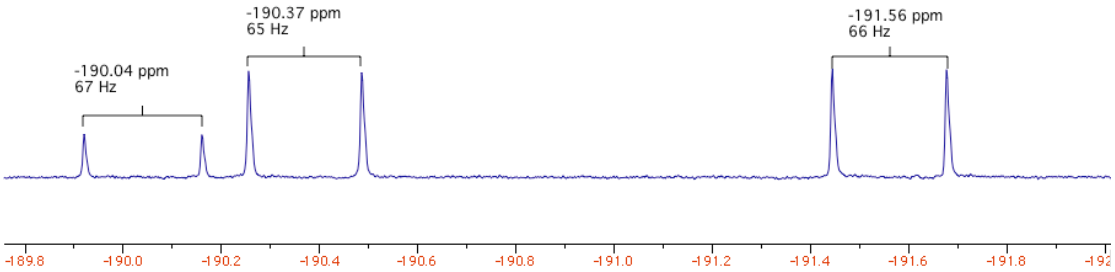


Figure 5 - 4. Signals observed in the $^{19}F\{H\}$ spectrum after the attempted fluorination of 5.14.

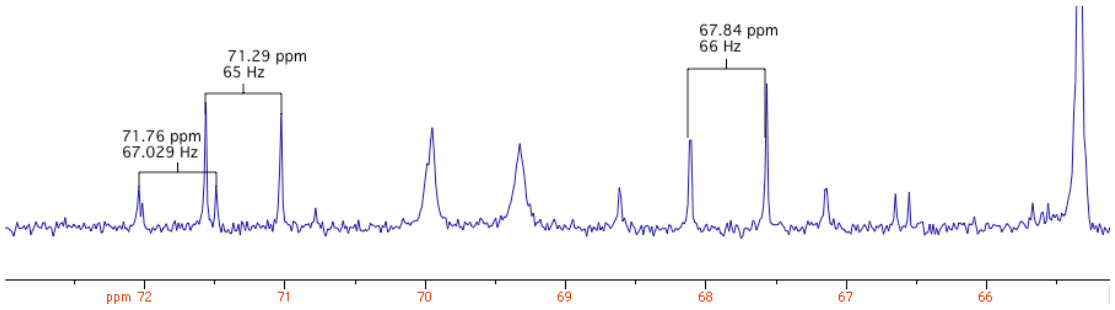
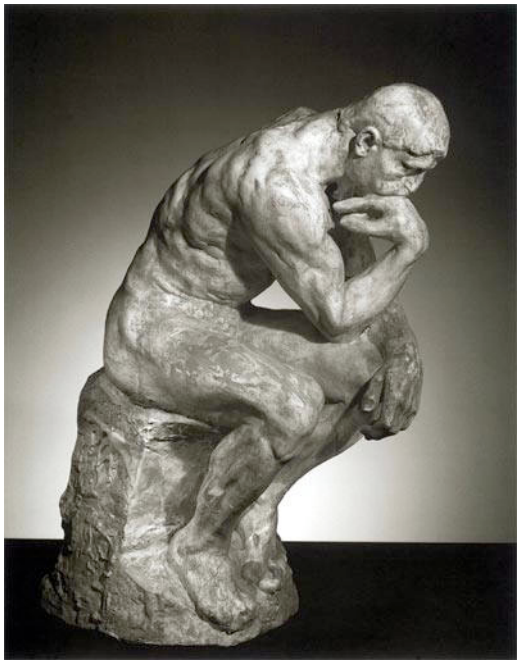


Figure 5 - 5. Minor products in the $^{31}P\{H\}$ spectrum after the attempted fluorination of 5.14.

5.4. Summary.

Phosphacycle synthesis is a difficult task (even with conventional reagents) and the synthesis of phosphacycles from fluorinated subunits showed no signs of success. It may be that the inclusion of fluorine leads to significant differences in the formation of sulfate esters and the subsequent reactions of these compounds with nucleophiles which may make phosphacycle synthesis using this strategy unachievable. There are some indications that the fluorination of ready made phosphacycle oxide compounds may be possible, though further research is required to confirm this and optimise these reactions. In view of the limited progress towards fluorinated phosphacycles a decision was taken to concentrate on the development of bulky fluorinated phosphines which proved to be more fruitful (chapters 2 – 4). Fluorinated phosphacycles remain elusive.

6. Conclusions and further work.



6.1. Synthesis.

Many of the phosphine boranes synthesised in this study were found to be unstable due to the combination of their high steric demand and the lower basicity of phosphorus in compounds when a fluorinated aryl substituent is present. The use of borane protection (which has proved to be a powerful technique for the synthesis of alkyl phosphines) considerably complicated the synthesis in many cases. It is now realised that the use of borane protection must be carefully considered along with possible alternatives. Tailored approaches must be developed as there is currently no "one size fits all" strategy for the synthesis of bulky fluoroaryl substituted phosphines.

6.1.1. Unsymmetrical diphosphine synthesis.

The synthesis of the 1,halo-3-(Di(*tert*-butyl)phospine)propaneboranes (**2.8** and **2.9**), which were robust, easily handleable crystalline solids, confirmed how useful of this method of protection when the borane complexes are stable. It should be possible to synthesise further analogues of these compounds using electron rich phosphine boranes and different bridging halides, which could in turn be used to provide easy access to libraries of unsymmetric diphosphine compounds.

6.1.2. Use of borane methods for the synthesis of bulky fluorinated phosphines.

The use of secondary phosphine boranes in the synthesis of bidentate phosphines based on the *ortho*-trifluoromethylphenyl substituted phosphines (**3.2**, **3.3** and **3.10**), proved particularly troublesome. However, this was pursued despite the difficulties because of the perceived benefits (Chapter 2). It is now apparent that although these benefits apply to alkyl phosphines they do not necessarily apply to bulky fluorinated phosphines of the type synthesised in this project, and that the benefits are often outweighed by the disadvantages.

6.1.3. Reduced nucleophilicity of phosphines with fluorine containing aryl groups.

The elimination of the possibility of quaternisation reactions was one of the primary reasons that phosphine borane methods were pursued. However, in reactions performed since most of this work has been completed it has been found that quaternisation is not a significant risk for the *ortho*-trifluoromethylphenyl substituted phosphines.[197] It is now thought that the presence of a fluorine containing substituent makes compounds of this type far less susceptible to the quaternisation reactions that electron rich dialkyl substituted phosphines readily undergo. It is

also likely that phosphides of the type derived by deprotonation of bulky secondary phosphines containing fluorinated aryl groups are significantly less basic than dialkyl substituted phosphides and therefore the tendency toward elimination reactions is also reduced. If this is so, phosphines of this type might be far more conveniently synthesised without the formation of borane complexes prior to bisphosphine formation.

6.1.4. Reduced tendency toward oxidation.

Protection from oxidation during isolation is another often cited benefit for the use of borane protection. However, several of the compounds in this study spontaneously decomplexed and the resulting free phosphines had to be isolated. Great care was taken in the isolation of the decomplexed bisphosphine compounds (**3.3** and **3.8**) by chromatography. However, the equipment used was makeshift and the solvent removal took place under atmospheric conditions resulting in some limited oxidation. The isolation of these compounds by this method was only possible due to the fact they are not hugely oxidation sensitive. However, with the advent of centrifugal chromatography systems,[198] which are purpose built to allow separation and isolation of fractions under an inert atmosphere, it may be somewhat easier to isolate of free phosphines in the future.

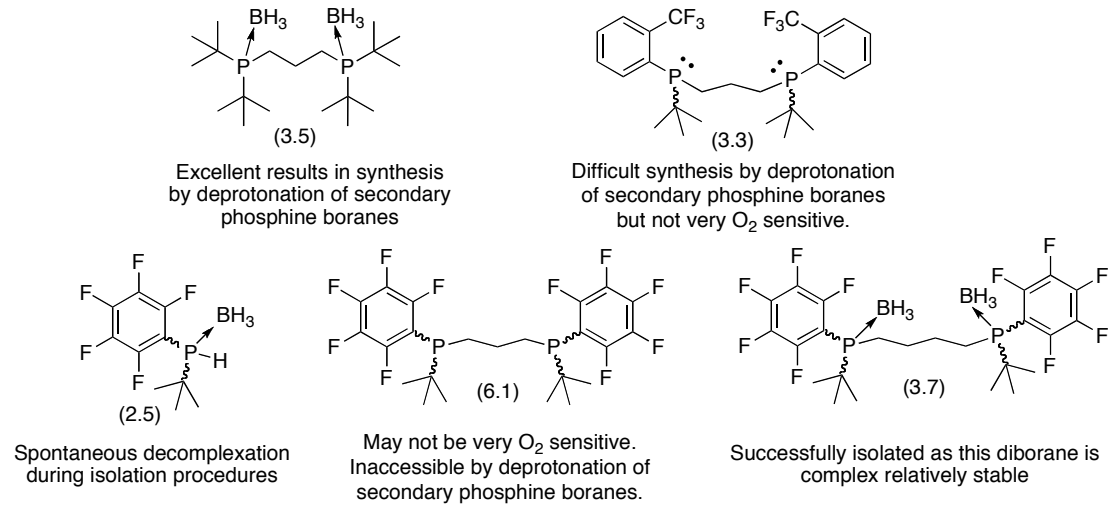


Figure 6 - 1. Examples of ligands and comments on the suitability of borane synthesis methods.

6.1.5. Future synthesis of bulky fluorinated ligands.

The synthesis of **3.6** from the phosphine chloride followed by the formation of its borane complex **3.7**, which was relatively stable, illustrates that, the choice of which stage in the synthetic sequence borane protection is applied can be critical to the success of the synthesis and purification of bulky fluorinated bisphosphine compounds. It should be noted that due to the instability of the secondary phosphine borane complex (**2.5**) we were unable to synthesise the propyl bridged pentafluorophenyl substituted analogue (**6.1**) using the same strategy which is so powerful for the synthesis of **3.5**. It is therefore clear that alternative strategies are required for the synthesis and handling of this attractive ligand.

6.1.6. Phosphonium salts as alternatives to phosphine boranes.

The storage and handling of phosphines can be extremely challenging which is one reason why phosphine boranes have become popular. However, phosphonium salts have been shown to be air stable and easily handleable, without requiring the sometimes troublesome decomplexation step involved with boranes. Fu[199] and Beller[3] have both reported the successful use of electron-rich phosphonium salts for *in-situ* catalyst formation. It may well be worth investigating the use of phosphonium salts for the synthesis of bulky fluorinated ligands which do not form robust borane complexes. Also, it may be possible to purify these compounds by recrystallisation.

6.2. Catalysis.

6.2.1. Bulky *ortho*-trifluoromethylphenyl substituted ligands in catalysis.

The degree to which a large amount of steric hinderance effects catalysis in these reactions is unclear as trifluoromethyl moieties in the *ortho* position may orientate away from palladium where its steric effect is negligible during catalysis. The development of ligands where the fluorinated groups are restricted so they are forced to project more into the region around the metal increasing the effective cone angle may lead to more pronounced differences in catalytic behaviour which may be worthy of investigation.

6.2.2. Enantioselective catalysis.

The excellent selectivity for the production of branch propionic acids seen in the reactions performed in this project results from a combination of the action of the promoting (LiCl/TsOH) additives used, and the stereoelectronic character of the bulky fluorinated ligands synthesised in this project. Further studies are required to probe the mechanism of the

observed catalysis. If the proposed mechanism (Scheme 4 – 10) is indeed operating, it is not clear whether it would be possible to perform an enantioselective version of this reaction using this system. The screening of known stereoselective ligands such as BINAP with the LiCl/TsOH promoter system may provide direct evidence of the potential for the development of such a reaction. However, the current evidence suggests that electron poor ligands are especially well suited to this reaction, so it may be that success will only be attained through the development of novel fluorinated enantiopure ligands. Compounds containing chiral bridging units have been prepared previously[200] and shown good enantioselectivity in the hydroformylation of styrene, and using similar synthesis methods it may be possible to prepare fluorinated analogues.

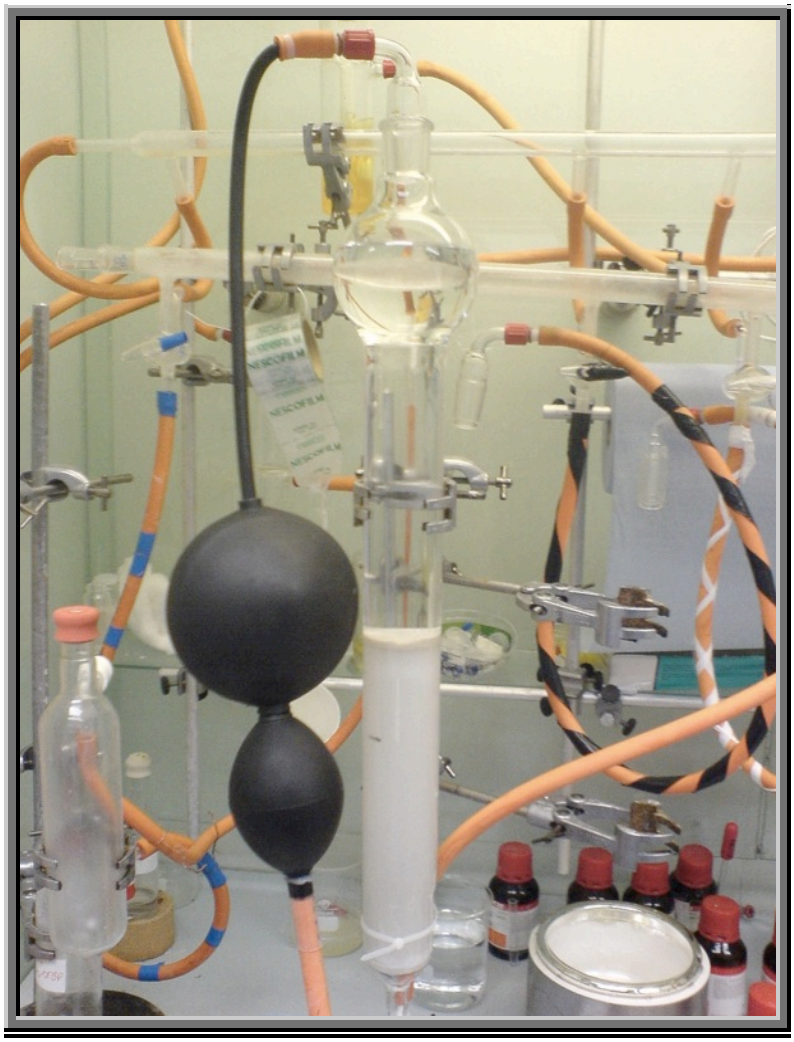
6.2.3. Increasing catalyst stability.

The degradation of the catalyst was identified as a potential problem in reactions using **3.14** and reactions with other complexes did not go to completion. An unusual Pd –H interaction was identified in the ^{1}H NMR spectrum of this compound for the *ortho* hydrogens (figure 3 – 10). These two facts may be linked. It should be noted that ligand **6.1** would be a bulky fluorinated ligand which possesses only fluorine in the *ortho* positions and hence may be more stable to degradation reactions due to the high strength of the P-F bond (if the causes of the ligand degradation are indeed linked to the Pd-H interaction).

6.3. Summary.

Palladium complexes based on novel bulky fluorinated ligands have been prepared and these have given the highest recorded regioselectivity for the branched isomer in the hydroxycarbonylation of styrene. The promoters used in this reaction have been found to be crucial to achieving this selectivity. Further development of this work may yield an enantioselective variant of this industrially important reaction.

7. Experimental.



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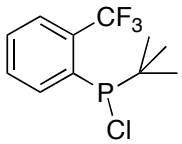
7.1. General Experimental procedures and instrumentation.

Routine NMR data was recorded either on a Bruker Avance 300 (^{1}H at 300 MHz, ^{13}C at 75 MHz, ^{19}F at 282 MHz, ^{31}P at 121 MHz) or a Bruker Avance II 400 (^{1}H at 400 MHz, ^{13}C at 100 MHz, ^{19}F at 376 MHz, ^{31}P at 161 MHz). ^{1}H and ^{13}C spectra were referenced to external tetramethylsilane, ^{19}F spectra were referenced to external trichlorofluoromethane, and ^{31}P spectra were referenced to external phosphoric acid. Chemical shifts are expressed in parts per million. Chemical ionisation mass spectroscopy and electron ionisation mass spectroscopy were performed on a Micromass GCT spectrometer. Electrospray mass spectroscopy was performed on a Micromass LCT spectrometer. All were operated by Mrs Caroline Horsburgh. Microanalysis was carried out for C and H using an EA 1110 CHNS CE Instruments elemental analyser by Mrs. S. Williamson. Infra-red absorbsion spectra were recorded on a Perkin Elmer GX-FTIR System spectrometer. Thin layer chromatography was performed using 0.20mm layers of silica gel supported on plastic sheets (Macherey-Nagel, Polygram Sil G/UV$_{254}$) or using 0.20mm layers of aluminium oxide supported on plastic sheets (Merck Aluminium oxide F$_{254}$). Preparative chromatography was performed using Davasil silica gel 35-70u. Dry degassed diethyl ether, petroleum ether, THF and toluene were obtained from an Innovative Technologies Puresolve 400 solvent still. Other solvents were bought and used as received without further purification other than degassing by either purging with nitrogen or repeated freeze/thaw cycles under vacuum. Organic solutions were dried by standing over anhydrous sodium sulphate and evaporated either under reduced pressure on a rotary evaporator or under reduced pressure whilst agitating manually. *Tert*-butyldichlorophosphine was obtained from the Aldrich Chemical Company and used as received. All manipulations were carried out under an atmosphere of nitrogen unless otherwise stated.

7.2. Mono-phosphine Compounds

7.2.1. (*Ortho*-trifluoromethylphenyl)(*tert*-butyl)chlorophosphine (2.1).

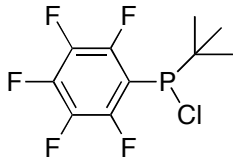


Ortho-bromobenzotrifluoride (9.17 g, 6.23 cm^3, 40.75 mmol) was dissolved in 20 ml of diethyl ether in a dry schlenk tube and cooled to -78 °C. *N*-butyllithium (16.30 cm^3, 40.75 mmol as a 2.5 M solution in hexanes) was added to this dropwise whilst stirring and the

solution was then allowed to warm to room temperature. *Tert*-butyldichlorophosphine (6.480 g, 40.75 mmol) was dissolved in diethyl ether, and the stirred solution was cooled to -78 °C. The aryl-lithium solution was then added dropwise to the phosphine solution and after this, the reaction was allowed to gradually warm to room temperature. The solvent was then removed under vacuum and the 30 ml of hexane was added to precipitate the lithium chloride. The solution was then filtered as it was transferred by cannula to a schlenk tube and the solvent removed under vacuum to give a brown oil which was distilled under vacuum (85-105 °C) to give the title compound (7.64 g, 28.5 mmol) in 70% yield as a colourless air and moisture sensitive liquid. In the syntheses described here, a one-pot method to prepare the borane was devised, which is also reproduced below.

^{1}H-NMR (300 MHz; C_6D_6): δ_H 1.45 (9 H, d, $^{3}J_{H-P}$ = 13.7 Hz, 3(C**H**$_3$), 6.95 (1 H, t, $^{3}J_{H-H}$ = 8 Hz, Ar**H**), 7.1 (1 H, t, $^{3}J_{H-H}$ = 8 Hz, Ar**H**), 7.45 (1 H, dd, $^{3}J_{H-H}$ = 10.5 Hz, $^{3}J_{H-P}$ = 3.8 Hz Ar**H** *o*-P), 8.05 (1 H, dm, $^{3}J_{H-H}$ = 8.8 Hz, Ar**H** *o*-CF_3). ^{19}F-NMR (282 MHz; C_6D_6): δ_F 71.9 (d, J_{F-P} = 72.9 Hz). ^{31}P{^{1}H}-NMR (121.5 MHz; C_6D_6): δ_P 100.6 (q, J_{P-F} = 72.5 Hz).

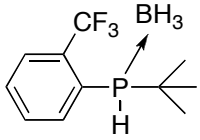
7.2.2. (Pentafluorophenyl)(*tert*-butyl)chlorophosphine (2.2).



This compound has previously been prepared by Mayer and Clarke. In a glove box resinous *tert*-butyldichlorophosphine (5.089 g, 32 mmol) was weighed into a schlenk tube. Magnesium cuttings (0.745g, 32mmol) were stirred dry in a separate schlenk with a catalytic amount of iodine. THF (40ml) was then added and the suspension cooled to -10°C prior to the addition of C_6F_5Cl (4.133 cm^3, 32 mmol). After 1 hour the reaction was allowed to warm to room temperature. Once all the magnesium was consumed the resulting brown solution was transferred to a dropping funnel and added dropwise to a cold (-78 °C) solution of the phosphine in THF (20ml). After complete addition of the Grignard the solution was allowed to gradually warm to room temperature. After 16 hours the solvent was removed and toluene was added to precipitate the magnesium chloride. The solution was transferred by cannula filtration to another vessel where the solvent was removed yielding (Pentafluorophenyl)(*t*-butyl)phosphinechloride (3.9 5g, 13.6 mmol) in 42.5 % yield.

^{1}H-NMR (300 MHz; C_6D_6): δ_H 1.02 (9 H, d t, $^{3}J_{H-P}$ = 15.2 Hz, $^{5}J_{H-F}$ = 1 Hz, 3C**H**$_3$). ^{31}P{^{1}H}-NMR (121.5 MHz; C_6D_6): δ_P 94.2 (t, $^{3}J_{P-F}$ = 55.6 Hz). ^{19}F-NMR (282 MHz; C_6D_6): δ_F -128.1 (2 F, d m, *o*-F), -149.2 (F, m, *p*-F), -161.3 (F, m, *m*-F).

7.2.3.1. (*Ortho*-trifluoromethylphenyl)(*tert*-butyl)phosphinoborane (from (*ortho*-trifluoromethylphenyl)(*tert*-butyl)chlorophosphine) (2.4).



(*Ortho*-trifluoromethylphenyl)(*tert*-butyl)chlorophosphine (1.171 g, 4.37 mmol) was dissolved in THF (20 ml) and the solution was cooled to 0 °C prior to the addition of $NaBH_4$ (0.495 g, 13.08 mmol). The reaction mixture was allowed to warm to room temperature gradually and was stirred until the chloride was completely converted to the secondary borane as judged by ^{31}P NMR. The solvent was removed under vacuum and (under atmospheric conditions) the residue redissolved in dichloromethane and transferred to a separating funnel for work up (water/dichloromethane). The organic layer was retained, dried over Na_2SO_4 and the solvent removed under vacuum to give 1.002 g of crude product. Flash chromatography (1-10 % diethyl ether in hexane,) gave two fractions. (*Ortho*-trifluoromethylphenyl)(*t*-butyl)phosphinoborane (0.6025 g, 2.42 mmol, 55.6 % yield) was obtained in the second fraction, as a colourless white solid after the removal of the solvent. An analytical sample was prepared by recrystallisation from hexane at low temperature (-78 °C).

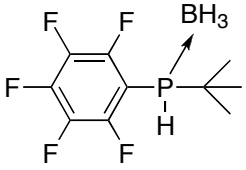
Anal. Calc'd for $C_{11}H_{17}F_3PB$: C, 53.27; H, 6.91 % found: C, 53.05; H, 6.95 %. ^{1}H-NMR (300 MHz; $CDCl_3$): δ_H 0.50 (3 H, m, B**H**$_3$), 1.05 (9 H, d, $^{3}J_{H-P}$ = 15.3 Hz, C(C**H**$_3$)$_3$), 5.45 (1 H, dm, $^{1}J_{H-P}$ = 384.8 Hz, P-**H**), 7.45 (1 H, t, $^{3}J_{H-H}$ = 7.5 Hz, Ar**H**), 7.55 (1 H, t, $^{3}J_{H-H}$ = 7.5 Hz, Ar**H**,) 7.65 (1 H, dm, $^{3}J_{H-H}$ = 7.6 Hz, Ar**H** *o*-CF_3), 7.8 (1 H, dd, $^{3}J_{H-P}$ = 12.2 Hz, $^{3}J_{H-H}$ = 7.4 Hz, Ar**H** *o*-P). ^{1}H{^{31}P}-NMR (300 MHz; $CDCl_3$): δ_H 0.50 (3 H, m, B**H**$_3$), 1.05 (9 H, s, C(C**H**$_3$)$_3$), 5.45 (1 H, m, P-**H**), 7.45 (1 H, t, $^{3}J_{H-H}$ = 7.5 Hz, Ar**H**), 7.55 (1 H, t, $^{3}J_{H-H}$ = 7.5 Hz, Ar**H**) 7.65 (1 H, dm, $^{3}J_{H-H}$ = 7.6 Hz, Ar**H** *o*-CF_3), 7.8 (1 H, d, $^{3}J_{H-H}$ = 7.4 Hz, Ar**H** *o*-P). ^{13}C{H}-NMR (75.5 MHz; $CDCl_3$): δ_c 25.8 (d, $^{3}J_{C-P}$ = 3 Hz, **C**H_3), 28.4 (d, $^{1}J_{C-P}$ = 31.1 Hz, P-**C**(CH_3)), 122.5 (qd, $^{1}J_{C-F}$ = 276 Hz, $^{4}J_{C-P}$ = 2.2 Hz, **C**F_3), 124.5 (dq, $^{1}J_{C-P}$ = 40.5 Hz, J_{C-F} = 1.7 Hz, Ar**C**-P), 125.6 (dq, $^{2}J_{C-F}$ = 6.6 Hz, $^{2}J_{C-P}$ = 4.3 Hz, Ar**C** *o*-CF_3), 130.3 (d, $^{4}J_{C-P}$ = 2.2 Hz, Ar**C**

p-P), 130.7 (dq, $^{2}J_{C-P}$ = 11.5 Hz, $^{4}J_{C-F}$ = 0.9 Hz Ar**C** *o*-P), 131.2 (qd, $^{2}J_{C-F}$ = 28.8 Hz, $^{2}J_{C-P}$ = 2.1 Hz, Ar**C**-CF_3), 134.1 (d, $^{3}J_{C-P}$ = 13.4 Hz, Ar**C** *m*-P). $^{19}F\{^{1}H\}$-NMR (282 MHz; $CDCl_3$): δ_F 57.1 (d, $^{4}J_{F-P}$ = 2 Hz). ^{31}P-NMR (121.5 MHz; $CDCl_3$): δ_P 17.3 (br,m). $^{31}P\{^{1}H\}$-NMR (121.5 MHz; $CDCl_3$): δ_P 17.3 (dm br, $^{1}J_{P-H}$ = 390 Hz). IR (cm^{-1}), KBr, 3050, 2950, 2350, 2200, 1300, 1150. M.S. ES-: *m/z* 247.12 ([M- H]$^-$ requires 247.10). M.S. ES+: *m/z* 271.04 ([M + Na]$^+$ requires 271.10).

7.2.3.2. (*Ortho*-trifluoromethylphenyl)(*tert*-butyl)phosphinoborane (2.4). (Direct from (*tert*-butyl) dichlorophosphine without isolation of chlorophosphine).

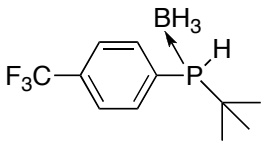
Bromobenzotrifluoride (1.03 cm^3, 7.58 mmol) was dissolved in 20 cm^3 of diethyl ether in a dry schlenk tube and cooled to -78 °C. *N*-butyllithium (3.1 cm^3, 7.75 mmol as a 2.5 M solution in hexanes) was added to this dropwise whilst stirring and then the solution allowed to warm to room temperature. *Tert*-butyldichlorophosphine (1.198 g, 7.58 mmol) was dissolved in diethyl ether, and the stirred solution was cooled to -78 °C. The solution of the lithated compound was then added dropwise and the solution allowed to warm to room temperature. The solvent was then removed under vacuum to give an oil. This was redissolved in 100 cm^3 THF and cooled to 0 °C before $NaBH_4$ (1.2 g, 30 mmol) was added. The reaction was allowed to warm to room temperature and the reaction allowed to continue until it was judged complete by ^{31}P NMR. The solvent was then removed and the residue re-suspended in dichloromethane. After work up (dichloromethane/water) the organic layers were combined, dried over $MgSO_4$, filtered and the solvent removed to provide a clear oil which solidified on standing. This was then recrystallised from hexane at -78 °C to yield the title compound as colourless crystals (1.720 g, 0.693 mmol, 91.5 % yield). Data identical to previous preparation.

7.2.4. Attempted synthesis of (Pentafluorophenyl)(*tert*-butyl)phosphinoborane (2.5).



(Pentafluorophenyl)(*tert*-butyl)chlorophosphine was dissolved in THF (40 ml) and cooled to 0 °C before $NaBH_4$ was added with good stirring. The reaction was allowed to gradually warm to room temperature and the reaction allowed to continue overnight. ^{31}P-NMR showed the chloride had been completely converted to what is assumed to be the secondary phosphineborane (δ 18.0, br, m) however attempts at work up, recrystallisation and column chromatography resulted in decomposition of the product.

7.2.5. *Tert*-butyl(*para*-(trifluoromethyl)phenyl)phosphinoborane (2.6).

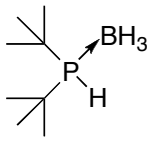


Magnesium cuttings (0.5 g, 20.5 mmol) were activated by being stirred dry with a catalytic amount of iodine in an inert atmosphere, to this was added a diethyl ether solution of 1-bromo-4-(trifluoromethyl)benzene (2.5 cm^3, 18.0 mmol) which reacted vigorously to form the Gringard. This solution was added dropwise to a cooled (-78 °C) solution of *tert*-butylphosphinodichloride (2.85 g, 17.9 mmol). The solution was maintained at low temperature until the dry-ice was exhausted to allow a very gradual warming to room temperature (approximately 6 hours) at which point the reaction progress was monitored by ^{31}P NMR and additional Gringard added (as above) as necessary for satisfactory conversion of the dichloride. The resulting mixture of *tert*-butyl(4-(trifluoromethyl)phenyl)phosphinochloride/bromide was then cooled to 0 °C, $NaBH_4$ (2.0 g, 60 mmol) added, and the reaction mixture stirred for several days until satisfactory conversion to the secondary phosphinoborane had been achieved as judged by ^{31}P NMR. At this point, the solvent was removed under vacuum and (under atmospheric conditions) the residue

partitioned between dichloromethane/water and organic layer washed twice. The organic layer was retained, dried over $MgSO_4$ and filtered before the solvent was removed. Flash chromatography (20 % diethyl ether in hexane) yielded the product in the second fraction as a clear viscous oil (2.78 g, 11.2 mmol, 62.5% yield). The material obtained in this way always contained a small amount (>2 % by ^{31}P-NMR) of impurity (thought to be the phosphine oxide, ^{31}P-NMR: δ 47.57 (d, $^{1}J_{P-H}$ = 453 Hz), ^{31}P{H}-NMR: δ 47.57 (s)), it was however pure enough for further synthesis.

^{1}H-NMR (300 MHz; C_6D_6): δ_H 0.6 (3 H, m br w, B**H$_3$**), 1.1 (9 H, d, $^{3}J_{H-P}$ = 11 Hz, 3(C**H$_3$**)), 5.1 (1 H, dq, $^{1}J_{H-P}$ = 387 Hz, $^{3}J_{H-H}$ = 7 Hz, P-**H**), 7.7 (4 H, m, 4Ar**H**). ^{1}H{^{31}P}-NMR (300 MHz; C_6D_6): δ_H 0.6 (3 H, m br w, B**H$_3$**), 1.1 (9 H, s, 3(C**H$_3$**)), 5.1 (1 H, m, P-**H**), 7.7 (4 H, m, 4Ar**H**). ^{13}C{H}-NMR (75 MHz; $CDCl_3$): δ_c 25.5 (d, $^{3}J_{C-P}$ = 3 Hz, **C**H$_3$), 27.6 (d, $^{1}J_{C-P}$ = 32 Hz, P-**C**(CH$_3$)$_3$), 122.6 (q, $^{1}J_{C-F}$ = 272 Hz, **C**F$_3$), 124.4 (d q, $^{3}J_{C-P}$ = 9.5 Hz, $^{3}J_{C-F}$ = 4 Hz, Ar**C** *o*-CF$_3$), 128.9 (dq, $^{1}J_{C-P}$ = 50 Hz, $^{5}J_{C-F}$ = 1 Hz, Ar**C**-P), 132.5 (qd, $^{2}J_{C-F}$ = 33 Hz, $^{4}J_{C-P}$ = 2.5 Hz, Ar**C**-CF$_3$), 133.4 (M, $^{2}J_{C-P}$ = 8 Hz, Ar**C** *o*-P). ^{19}F-NMR (282 MHz; $CDCl_3$): δ_F 63.7 (s). ^{31}P-NMR (121 MHz; $CDCl_3$): δ_P 32.0 (dm, $^{1}J_{P-H}$ = 368 Hz). ^{31}P{^{1}H}-NMR (121 MHz; $CDCl_3$): δ_P 32.0 (m). IR (cm^{-1}), KBr, 3050, 2950, 2350, 2200, 1300, 1150. Single Mass Analysis MS ES-: *m/z* 247.1027 ([M - H]$^+$ $C_{11}H_{16}BF_3P$ requires 247.103).

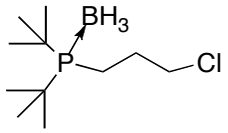
7.2.6. Di-*tert*-butylphosphinoborane (2.7).



Di-*tert*-butylchlorophosphine (5.00 g, 31.25 mmol) was dissolved in 80 ml THF and cooled to 0°C and $NaBH_4$ (4.7 g, 151 mmol) was added and the reaction was allowed to continue for 48 hours at which point the reaction was judged (^{31}P NMR) to be complete. The solvent was then removed under vacuum and the residue partitioned between CH_2Cl_2/water in air, at this point there was considerable evolution of hydrogen from unreacted $NaBH_4$. The organic layer was retained and washed twice with water before being dried over $MgSO_4$, filtered and the solvent removed under vacuum to give the a clear oil that solidified on standing. This was then purified by recrystallisation from hexane at low temperature (-78 °C) to yield the title compound (4.30 g) as a white crystalline solid.

^{1}H-NMR (400 MHz; $CDCl_3$): δ_H 0.4 (3 H, m br w, B**H**$_3$), 1.2 (18 H, d, $^{3}J_{H-P}$ = 13.5 Hz, 6(C**H**$_3$)), 3.9 (1 H, d q, $^{1}J_{H-P}$ = 345 Hz, $^{3}J_{H-H}$ = 6 Hz, P-**H**).^{1}H{^{31}P}-NMR (400 MHz; $CDCl_3$): δ_H 0.4 (3 H, m br w, B**H**$_3$), 1.2 (18 H, 6(C**H**$_3$)), 3.9 (1 H, q, $^{3}J_{H-H}$ = 6 Hz, P-**H**). ^{13}C{H}-NMR (100 MHz; $CDCl_3$): δ_c 28.9 (d, $^{2}J_{C-P}$ = 1.5 Hz, **C**H$_3$), 30.5 (d, $^{1}J_{C-P}$ = 29 Hz, P-**C**). ^{31}P{^{1}H}-NMR (121.5 MHz; $CDCl_3$): δ_P 49.5 (m),^{31}P-NMR (121.5 MHz; $CDCl_3$): δ_P 49.5 (d m, $^{1}J_{P-H}$ = 345 Hz). Ms ES+: *m/z* 183.12 ([M+Na]$^{+}$ requires 183.14).

7.2.7. Di-*tert*-butyl(3-chloropropyl)phosphinoborane (2.8).

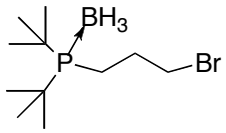


Di-*tert*-butylphosphinoborane (0.310 g, 1.93 mmol) was dissolved in THF (10 ml) and cooled to -78 °C with good stirring. *N*-butyllithium (0.775 cm^3, 1.93 mmol as a 2.5 M solution in hexane) was added to this dropwise and then the solution was allowed to warm to room temperature for complete conversion to the anion. The solution was again cooled to -78 °C and 1-bromo-3-chloropropane (192 μl, 1.93 mmol) was added rapidly, to avoid disubstitution. The temperature was maintained overnight until the dry ice was exhausted, at which point the solvent was removed under vacuum. The residue was partitioned between CH_2Cl_2/water and the organic phase washed twice with water before being dried over $MgSO_4$, filtered and the solvent removed under vacuum. Flash chromatography (10 % diethyl ether in hexane) yielded the product in the second fraction as a white crystalline solid (0.265 g, 1.12 mmol, 58% yield). An analytical sample was prepared by recrystallisation from hexane at low temperature (-78 °C).

Anal. Calcd for $C_{11}H_{27}BClP$: C, 55.85; H, 11.50 % found: C, 56.25; H, 12.15 %. ^{1}H-NMR (300 MHz; $CDCl_3$): δ_H 1.2 (18 H, d, $^{3}J_{H-P}$ = 12.5 Hz, 6(CH_3)), 1.7 (2 H, m, C**H**$_2$-P), 2.07 (2 H, m, C-C**H**$_2$-C), 3.55 (2 H, t d, $^{3}J_{H-H}$ = 7 Hz, $^{4}J_{H-P}$ = 1 Hz, C**H**$_2$-Cl). ^{1}H{^{31}P}-NMR (300 MHz; $CDCl_3$): δ_H 1.2 (18 H, 6(C**H**$_3$)), 1.7 (2 H, m, C**H**$_2$-P), 2.0 (2 H, m, C-C**H**$_2$-C), 3.55 (2 H, t , $^{3}J_{H-H}$ = 7 Hz, C**H**$_2$-Cl). ^{13}C{H}-NMR (75.5 MHz; $CDCl_3$): δ_c 14.3 (d, $^{1}J_{C-P}$ = 30 Hz, P-**C**H$_2$), 26.7 (d, $^{2}J_{C-P}$ = 1 Hz, **C**H$_3$), 28.7 (d, $^{2}J_{C-P}$ = 1 Hz, C-**C**H$_2$-C), 31.2 (d, $^{1}J_{C-P}$ = 29 Hz, P-**C**(CH_3)$_3$), 36.0 (d, $^{3}J_{C-P}$ = 13.5 Hz, **C**H$_2$-Cl). ^{31}P{^{1}H}-NMR (121.5 MHz; $CDCl_3$): δ_P 44.8

(m). IR (cm^{-1}), KBr, 2900-3000, 2400, 2250, 1475, 1375. MS ES+: *m/z* 259.11 $([M+Na]^+$ (^{35}Cl) requires 259.15), 261.13 $([M+Na]^+$ (^{37}Cl) requires 261.15)

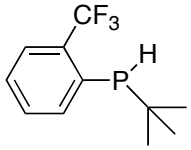
7.2.8. Di-*tert*-butyl(3-bromopropyl)phosphinoborane (2.9).



Di-*tert*-butylphosphinoborane (3.00 g, 18.75 mmol) was dissolved in THF (60 ml) and cooled to -78 °C with good stirring. *N*-butyllithium (7.6 cm^3, 19 mmol as a 2.5M solution in hexane) was added to this dropwise and then the solution was allowed to warm to room temperature for complete conversion to the anion. The solution was again cooled to -78°C and 1,3-dibromopropane (8ml, 78.4 mmol) was added rapidly, to avoid disubstitution. The temperature was maintained overnight until the dry ice was exhausted, at which point the solvent and excess 1,3-dibromopropane were removed under vacuum. The residue was partitioned between CH_2Cl_2/water and the organic phase washed twice with water before being dried over $MgSO_4$, filtered and the solvent removed under vacuum. Flash chromatography (10 % diethyl ether in hexane) yielded the product in the second fraction as a white crystalline solid (4.15 g, 14.6 mmol, 78 % yield). An analytical sample was prepared by recrystallisation from hexane at low temperature (-78 °C)

Anal. Calcd for $C_{11}H_{27}BBrP$: C, 47.01; H, 9.68 % found: C, 47.13; H, 9.83 %. ^{1}H-NMR (300 MHz; $CDCl_3$): δ_H 1.2 (18 H, d, $^3J_{H-P}$ = 12.5 Hz, 6(C**H**$_3$)), 1.55 (2 H, m, C**H**$_2$-P), 2.0 (2 H, m, C-C**H**$_2$-C), 3.3 (2 H, t d, $^3J_{H-H}$ = 7 Hz, $^4J_{H-P}$ = 1 Hz, C**H**$_2$-Br). ^{1}H{^{31}P}-NMR (300 MHz; $CDCl_3$): δ_H 1.2 (18 H, 6(C**H**$_3$)), 1.55 (2 H, m, C**H**$_2$-P), 2.0 (2 H, m, C-C**H**$_2$-C), 3.3 (2 H, t , $^3J_{H-H}$ = 7 Hz, C**H**$_2$-Br). ^{13}C{H}-NMR (75.5 MHz; $CDCl_3$): δ_c 17.0 (d, $^1J_{C-P}$ = 29.5 Hz, P-**C**H_2), 28.2 (d, $^2J_{C-P}$ = 1 Hz, **C**H_3), 28.7 (d, $^2J_{C-P}$ = 1 Hz, C-**C**H_2-C), 32.6 (d, $^1J_{C-P}$ = 27.1 Hz, P-**C**$(CH_3)_3$), 36.0 (d, $^3J_{C-P}$ = 14 Hz, Cl-**C**H_2). ^{31}P{^{1}H}-NMR (121.5 MHz; $CDCl_3$): δ_P 44.3 (m). IR (cm^{-1}), KBr, 2900-3000, 2400, 2250, 1475, 1375. MS ES+: *m/z* 303.21 $([M+Na]^+$ (^{71}Br) requires 303.10), 305.22 $([M+Na]^+$ (^{81}Br) requires 305.10).

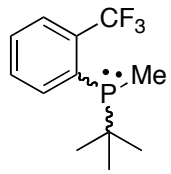
7.2.9. (*Ortho*-trifluoromethylphenyl)*tert*-butylphosphine (2.10).



(*Ortho*-trifluoromethylphenyl)(*tert*-butyl)phosphinoborane (248 mgs, 1 mmol) was dissolved in CH_2Cl_2 (10 ml) and cooled to -20 °C then $HBF_4.OMe_2$ (350 μl, 5 mmol), was added dropwise. Once addition was complete, the reaction was allowed to warm to room temperature and stirred overnight before being cooled to 0 °C and hydrolysis by the addition of a saturated degassed solution of $NaHCO_3$ (20 ml). After vigorous stirring of the biphasic mixture for 10 minutes the organic layer was removed and the aqueous layer extracted with CH_2Cl_2 (10 ml x 2) and the combined organic extracts dried over $MgSO_4$. This was then filtered off and the solvent removed under vacuum to yield the title compound as a clear oil (219 mgs, 0.94 mmol, 94%).

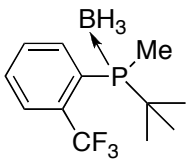
^{1}H-NMR (400 MHz; CD_2Cl_2): δ 7.62 (dm, 1 H $^3J_{H-H}$ = 7.0 Hz, Ar**H** o-CF_3), 7.56 (dd, 1 H, $^3J_{H-H}$ = 7.0 Hz, $^3J_{H-P}$ = 7.0 Hz, Ar**H** *o*-P), 7.40 (t, 1 H, $^3J_{H-H}$ = 7.0 Hz, Ar**H**), 7.50 (t, 1 H, $^3J_{H-H}$ = 7.0 Hz, Ar**H**), 4.08 (dm, 1 H, $^1J_{H-P}$ = 218 Hz, P-**H**), 1.04 (d, 9 H, J = 12.5 Hz, C(C**H$_3$**)). 1H{P}-NMR (400 MHz; CD_2Cl_2): δ 7.62 (dm, 1 H, $^3J_{H-H}$ = 7.0 Hz, Ar**H** o-CF_3), 7.56 (d, 1 H, $^3J_{H-H}$ = 7.0 Hz, Ar**H** *o*-P), 7.40 (t, 1 H, $^3J_{H-H}$ = 7.0 Hz, Ar**H**), 7.50 (t, 1 H, $^3J_{H-H}$ = 7.0 Hz, Ar**H**), 4.08 (m, 1 H, P-**H**), 1.04 (s, 9 H, C(C**H$_3$**)). ^{13}C{H}-NMR (100 MHz; CD_2Cl_2): δ_c 138.15 (d, $^2J_{C-P}$ = 11 Hz, Ar**C** *o*-P), 133.33 (dm, $^1J_{C-P}$ = 33 Hz, Ar**C**-P), 132.82(q, $^2J_{C-F}$ = 29.5 Hz, Ar**C**-CF_3), 129.95 (m, Ar**C**), 127.73 (m, Ar**C**), 125.6 (dq $^4J_{C-F}$ = 6 Hz, $^4J_{C-P}$ = 2 Hz, Ar**C** *o*-CF_3), 123.55(q, $^1J_{C-F}$ = 274 Hz, **C**F_3), 29.50 (d, $^2J_{C-X}$ = 13 Hz, C(**C**H_3)), 29.0 (M, $^1J_{C-P}$ = 13 Hz, P-**C**(CH_3)). ^{19}F NMR (376 MHz; CD_2Cl_2): δ -57.37 (dd, $^4J_{P-F}$ = 27 Hz, $^5J_{P-H}$ = 4.7 Hz). ^{19}F{H} NMR (376 MHz; CD_2Cl_2): δ -57.37 (d, $^4J_{F-P}$ = 27 Hz). ^{31}P NMR (162 MHz; CD_2Cl_2): δ -16.34 (q, $^4J_{P-F}$ = 27.3 Hz). Single Mass Analysis as oxide MS ES+: *m/z* 251.0811 ($[M + H]^+$ ($C_{11}H_{15}F_3P_1O$) requires 251.0813)

7.2.10. (*Ortho*-triflouromethylphenyl)(*tert*-butyl)methylphosphine (2.11).



(*Ortho*-trifluoromethyphenyl)*tert*-butylchlorophosphine (0.3184 g, 1.18 mmol) was dissolved in diethyl ether (10 ml) and cooled to -78˚C. MeLi (1.38 ml, 2.208 mmol, 1.6 equivalents as a 1.6 M solution in hexanes) was added slowly and the reaction allowed to warm to room temperature gradually over 3 hours. The solvent was then removed under vacuum to near dryness and degassed CH_2Cl_2 (15 ml) added. The reaction was then quenched with degassed water (2ml) which was then removed by syringe, and the remaining CH_2Cl_2 layer dried using Na_2SO_4 which was filtered off. The solvent was then removed to give the product as an air sensitive light brown oil (165 mg, 0.665 mmol) in 56 % yield.
^{1}H-NMR (300 MHz; C_6D_6): δ_H 0.76 (9 H, d, $^3J_{H-P}$ = 12 Hz, C(C**H**$_3$)$_3$, 0.91 (3 H, d, $^2J_{H-P}$ = 7 Hz, P-C**H**$_3$), 6.8 (1 H, t, $^3J_{H-H}$ = 8 Hz, Ar**H**), 6.9 (1 H, t, $^3J_{H-H}$ = 8 Hz, Ar**H**), 7.3 (1 H, d, $^3J_{H-H}$ = 8 Hz, Ar**H**), 7.4 (1 H, d, $^3J_{H-H}$ = 8 Hz, Ar**H**). ^{13}C{H}-NMR (75 MHz; C_6D_6): δ_c 27.7 (d, $^3J_{C-P}$ = 15 Hz, **C**H$_3$ *tert*-butyl), 29.6 (d, $^2J_{C-P}$ = 17 Hz, **C**H$_3$ methyl), 29.77 (d, $^1J_{C-P}$ = 15 Hz, **C**(CH$_3$)), 125.4 (q, $^1J_{C-F}$ = 278 Hz, **C**F$_3$), 126.7 (d q, $^3J_{C-F}$ = 6 Hz, $^3J_{C-P}$ = 6 Hz, Ar**C**H *o*-CF$_3$), 129.5 (s, Ar**C**H), 130.9 (s, Ar**C**H), 130.9 (s, Ar**C**H), 134.5 (d, $^2J_{C-P}$ = 4 Hz, Ar**C**H *o*-P), 136.6 (q d, $^2J_{C-F}$ = 31 Hz, $^2J_{C-P}$ = 2 Hz, Ar**C**-CF$_3$), 138.2 (d, $^1J_{C-P}$ = 39 Hz, Ar**C**-P). ^{19}F-NMR (282 MHz; C_6D_6): δ_F -54.9 (d, $^4J_{F-P}$ = 58 Hz), ^{31}P-NMR (121 MHz; C_6D_6): δ_P -20.0 (q, J_{P-F} = 58Hz). MS CI+: *m/z* 249.0 ([M + H]$^+$ requires 249.09)

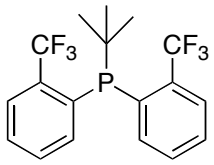
7.2.11. (*Ortho*-triflouromethylphenyl)(*t*-butyl)methylphosphineborane (2.12).



A THF (8 ml) solution of (*ortho*-triflouromethylphenyl)(*tert*-butyl)methylphosphine (0.332 g 1.34 mmol) was cooled to 0 °C whilst stirring. $BH_3.SMe_2$ (1.5 ml as a 1M solution in THF) was added and the reaction allowed to gradually warm to room temperature. After two hours

the reaction was complete and the solvent was removed. Flash chromatography (3 % diethyl ether in hexane) yielded the title compound in the second fraction (44 % yield).
^{1}H-NMR (300 MHz; C_6D_6): δ_H 0.6 (3H,m br, B**H**$_3$), 1.1 (9 H, d, $^{3}J_{H-P}$ = 14.3 Hz, 3(C**H**$_3$) *tert*-butyl), 1.7 (3 H, d m, $^{2}J_{H-P}$ = 10.1 Hz, P-C**H**$_3$), 7.54 (1 H, t, $^{3}J_{H-H}$ = 8.2 Hz, Ar**H**), 7.58 (1 H, t, $^{3}J_{H-X}$ = 7.6 Hz, Ar**H**), 7.77 (1 H,d m, $^{3}J_{H-H}$ = 7.2 Hz, Ar**H** *o*-CF_3), 8.25 (1 H, dd, $^{3}J_{H-P}$ = 13.9 Hz , $^{3}J_{H-H}$ = 7.1 Hz, Ar**H** *o*-P). ^{19}F-NMR (282 MHz; C_6D_6): δ_F -55.8 (s). ^{31}P{^{1}H}-NMR (121 MHz; C_6D_6): δ_P 36.7 (br m). MS CI+: *m/z* 261 ([M - H]$^+$ requires 261.1).

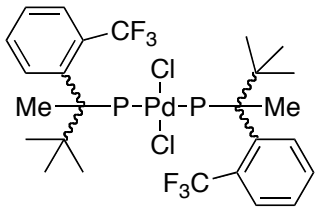
7.2.12. *Tert*-butylbis(*ortho*-(trifluoromethyl)phenyl)phosphine (2.13).



A stirred solution of *ortho*-bromobenzotrifluoride (8.491 g, 5.26 cm^3, 37.7 mmol) diethyl ether (40 ml) was cooled to -78 °C, and *n*-butyllithium (15 cm^3 as a 2.5M solution in hexanes, 37.7 mmol) added slowly, after which the reaction was allowed to warm to room temperature. The solution was then cooled to -78 °C and t-butyldichlorophosphine (2.00 g as a solution in 10 ml diethyl ether, 12.57 mmol) added slowly by dropping funnel. The solution was then allowed to warm slowly to room temperature. After 16 hours the dark green solution was washed with water. The diethyl ether layer retained and dried with $MgSO_4$, filtered and the solvent removed. Recrystalisation from methanol yielded the product as an air stable white crystals (3.880 g, 10.25 mmol) in 81.6 % yield.
Anal. Calcd for $C_{18}H_{17}F_6P$: C, 57.15; H, 4.53 % found: C, 56.66; H, 4.73 % ^{1}H-NMR (300 MHz; C_6D_6): δ_H 1.2 (9H, d, $^{3}J_{P-H}$ = 13.3, (C**H**$_3$)$_3$), 7.32 (2H, t d, $^{3}J_{H-H}$ = 7.5 Hz, Ar**H**), 7.4 (2H, t d, $^{3}J_{H-H}$ = 7.5 Hz, Ar**H**), 7.6 (2H, d d d, $^{3}J_{H-P}$ = 5.3 Hz, $^{3}J_{H-H}$ = 8 Hz, Ar**H** *o*-P), 7.75 (2 H, d m, $^{3}J_{H-H}$ = 7.5 Hz, Ar**H** *o*-CF_3). ^{1}H{^{31}P}-NMR (300 MHz; C_6D_6): δ_H 1.2 (9 H, s, (C**H**$_3$)$_3$), 7.32 (2H, t d, $^{3}J_{H-H}$ = 7.5 Hz, Ar**H**), 7.4 (2H, t d, $^{3}J_{H-H}$ = 7.5 Hz, Ar**H**), 7.6 (2H, d d, $^{3}J_{H-H}$ = 8 Hz, Ar**H** *o*-P), 7.75 (2 H, d m, $^{3}J_{H-H}$ = 7.5 Hz, Ar**H** *o*-CF_3). ^{13}C{H}-NMR (100 MHz; $CDCl_3$): δ_c 29.3 (d, $^{3}J_{C-P}$ = 16 Hz, **C**H$_3$), 31.7 (d, $^{1}J_{C-P}$ = 21 Hz, P-**C**(CH$_3$)$_3$), 124.15 (q, $^{1}J_{C-F}$ = 275 Hz, **C**F$_3$), 127.15 (m, Ar**C**H *o*-CF_3), 128.50 (s, Ar**C**H), 130.5 (s, Ar**C**H), 135.3 (m, Ar**C**-CF_3), 136.0 (s, Ar**C**H), 136.1 (d, $^{1}J_{C-P}$ = 40 Hz, Ar**C**H), ^{19}F-NMR: δ -55.8 (6F, d, $^{4}J_{F-P}$ = 51.1Hz),

$^{31}P\{H\}$ NMR δ: -2.6 (sep, $^{4}J_{P-F}$ = 51.2 Hz), IR (cm^{-1}), KBr, 3050, 2900-3000, 2200, 1300. MS ES+: *m/z* 401.02 ($[M + Na]^+$ requires 401.09)

7.2.13. Bis((*ortho*-trifluoromethylphenyl)*tert*-butylmethylphosphine)palladiumdichloride (2.16).



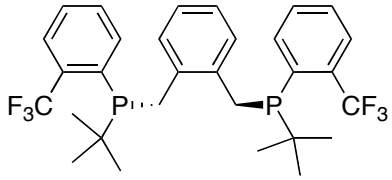
(*Ortho*-trifluoromethylphenyl)*tert*-butylmethylphosphine (55 mgs, 0.220 mmol) was dissolved in dry degassed CH_2Cl_2 (2 ml). $[Pd(PhCN)_2Cl_2]$ (42 mg, 0.110 mmol) was added and the mixture stirred at room temperature for 24 hours. The solvent was then reduced to near dryness and diethyl ether added resulting in a yellow precipitate, which was filtered off and washed with further diethyl ether to yield the title compound (45 mgs, 73 mmol, 67 % yield). The complex is present as a mixture of the *rac* and *meso* isomers leading to two sets of signals in the ratio 1:2.5 by ^{19}F NMR. Recrystallisation by slow diffusion of hexane into a CH_2Cl_2solution of the product yielded crystals suitable for X-ray crystallography.
^{1}H-NMR (400 MHz; CD_2Cl_2): δ 7.79 (2H, m, Ar**H**), 7.69 (2 H, m, Ar**H**), 7.49 (4H, m, Ar**H**), 1.86 (3H, t app, J_{P-H} = 7.4 Hz, P-C**H**$_3$ major isomer), 1.85 (3H, t app, J_{P-H} = 7.4 Hz, P-C**H**$_3$ minor isomer), 1.21 (9 H, t app, J_{P-H} = 7.4 Hz, C(C**H**$_3$)$_3$ minor isomer), 1.20 (9 H, t app, J_{P-H} = 7.4 Hz, C(C**H**$_3$)$_3$ major isomer). $^{1}H\{F\}$-NMR (400 MHz; CD_2Cl_2): δ 7.79 (1H, m, Ar**H**), 7.69 (1 H, m, Ar**H**), 7.49 (2H, m, Ar**H**), 1.86 (3H, t app, J_{P-H} = 7.4 Hz, P-C**H**$_3$ major isomer), 1.85 (3H, t app, J_{P-H} = 7.4 Hz, P-C**H**$_3$ minor isomer), 1.21 (t app, J_{P-H} = 7.4 Hz, C(C**H**$_3$)$_3$ minor isomer), 1.20 (t app, J_{P-H} = 7.4 Hz, C(C**H**$_3$)$_3$ major isomer). $^{1}H\{P\}$-NMR (400 MHz; CD_2Cl_2): δ 7.79 (1H, m, Ar**H**), 7.69 (1 H, m, Ar**H**), 7.49 (2H, m, Ar**H**), 1.86 (3H, s, P-C**H**$_3$ major isomer), 1.85 (3H, s, P-C**H**$_3$ minor isomer), 1.21 (s, C(C**H**$_3$)$_3$ minor isomer), 1.20 (s, C(C**H**$_3$)$_3$ major isomer).

$^{13}C\{H\}$-NMR (101 MHz; CD_2Cl_2): δ 134.65 (m, Ar**C**H), 132.01 (m, Ar**C**), 129.40 (m, Ar**C**H), 129.23 (s, Ar**C**H), 128.93 (m, Ar**C**), 127.46 (m, Ar**C**H), 123.46 (q, *J* = 275.5 Hz, **C**F$_3$), 34.57 (t app, J_{C-P} = 11.1 Hz, **C**(CH)$_3$ major isomer), 34.37 (t app, J_{C-P} = 11.1 Hz, **C**(CH)$_3$, minor isomer), 26.80 (m, C(**C**H)$_3$), 8.19 (m, P-**C**H$_3$). ^{19}F-NMR (376 MHz; CD_2Cl_2):

δ -52.95 (t, J_{F-P} = 6.9 Hz, major isomer), -53.09 (t, J_{F-P} = 6.9 Hz, minor isomer). ^{31}P-NMR (162 MHz; CD2Cl2): δ 27.37 (m). IR (cm^{-1}), KBr, 3200, 3500, 2900-3000, 2200, 1300. MS ES+ 697.02 (M+ Na).

7.3. Bisphosphine Compounds

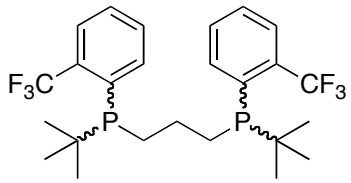
7.3.1. 1,2-Bis[(*ortho*-trifluoromethylphenyl)*tert*-butylmethylenephosphine]benzene (3.2) (*rac*).



(*Ortho*-trifluoromethylphenyl)*tert*-butylphosphineborane (0.595 g, 2.4 mmol) was dissolved in THF (15 cm^3) and was cooled to -78 ˚C. *N*-butyllithium (0.94 ml, 2.4 mmol as a 2.5 M solution in hexanes) was added slowly whilst stirring and the reaction allowed to gradually warm to room temperature. After 1 hour the solution was cooled to -78 ˚C, *ortho*-α,α-dichloroxylene (0.175 g, 1 mmol) was added and the reaction allowed to warm to room temperature. ^{31}P NMR showed a mixture of products which gradually converted to the product upon extended heating over 5 days. The solvent was then removed under vacuum and the residue redissolved in dichloromethane (20 cm^3) followed by workup with water (10 cm^3). The organic layer was retained and dried with $MgSO_4$, which was removed by filtration and washed with further dichloromethane yielding a light yellow solution. The solvent was then removed under vacuum yielding 0.659 g of the crude product. Recrystallisation from dichloromethane/ethanol (4 cm^3, 1/2) yielded the product (120 mgs, 0.21 mmol, 21% yield) as clear needles suitable for X-ray analysis which showed these to be the *rac* isomer.
Anal. Calc'd for $C_{30}H_{34}F_6P_2$: C, 63.16; H, 6.01% found: C, 63.97; H, 6.53%
^{1}H-NMR (300 MHz; C_6D_6): δ_H1.15 (18 H, d, $^3J_{H-P}$ = 15 Hz, 2(C(C**H**$_3$)$_3$), 3.4 (2 H, d, $^2J_{H-H}$ = 14 Hz, P-C**H**H), 3.85 (2 H, ddd, $^2J_{H-H}$ = 14 Hz, $^2J_{H-P}$ = 7.5 Hz, $^5J_{H-P}$ = 4 Hz, P-C**H**H), 6.7 (2 H, m, Ar**H** xylyl), 6.8 (2 H, m, Ar**H** xylyl), 6.9 (2 H, t, $^3J_{H-H}$ = 8 Hz, Ar**H**), 7.15 (2 H, t, $^3J_{H-H}$ = 8 Hz, Ar**H**), 7.45 (2 H, dd, $^3J_{H-H}$ = 8 Hz, $^3J_{H-P}$ = 3 Hz, Ar**H** *o*-P), 7.8 (2 H, dm, $^3J_{H-H}$ = 8 Hz, Ar**H** *o*-CF_3). ^{1}H{^{31}P}-NMR (300 MHz; C_6D_6): δ_H1.15 (18 H, 2(C(C**H**$_3$)$_3$), 3.4 (2 H, d, $^2J_{H-H}$ = 14 Hz, P-C**H**H), 3.85 (2 H, d, $^2J_{H-H}$ = 14 Hz), 6.7 (2 H, m, Ar**H** xylyl), 6.8 (2 H, m, Ar**H** xylyl),

6.9 (2 H, t, $^{3}J_{H-H}$ = 8 Hz, Ar**H**), 7.15 (2 H, t, $^{3}J_{H-H}$ = 8 Hz, Ar**H**), 7.45 (2 H, d, $^{3}J_{H-H}$ = 8 Hz, Ar**H** *o*-P), 7.8 (2 H, dm, $^{3}J_{H-H}$ = 8 Hz, Ar**H** *o*-CF_3). $^{13}C\{H\}$-NMR (75 MHz; C_6D_6): δ_c 28.5 (d, $^{2}J_{C-P}$ = 15 Hz, C(**C**H_3)$_3$), 29.4 (dd, $^{1}J_{C-P}$ = 24 Hz, $^{4}J_{C-P}$ = 12 Hz, P-**C**H_2), 31.0 (d, $^{1}J_{C-P}$ = 18.5 Hz, **C**$(CH_3)_3$), 125.2 (q, $^{1}J_{C-F}$= 275 Hz, **C**F_3), 126.6 (s, Ar**C**),126.7 (dq, $^{3}J_{C-F}$ = 6 Hz, $^{3}J_{C-P}$ = 6 Hz, Ar**C** *o*-CF_3), 130.1 (s, Ar**C**), 130.5 (s, Ar**C**), 131.2 (d, $^{2}J_{C-P}$ = 6 Hz, Ar**C** *o*-P), 135.4 (d, $^{3}J_{C-P}$ = 3 Hz, Ar**C** *m*-P), 136.25 (d, $^{1}J_{C-P}$ = 40.5 Hz, Ar**C**-P), 136.8 (dd, $^{2}J_{C-P}$ = 6 Hz, $^{3}J_{C-P}$ = 3 Hz, Ar**C**-CH_2). 137.5 (m, Ar**C**-CF_3). ^{19}F-NMR (282 MHz; C_6D_6): δ_F -54.95 (d, $^{4}J_{F-P}$ = 58 Hz). $^{31}P\{^{1}H\}$-NMR (121.5 MHz; C_6D_6): δ_P -7.6 (q, $^{4}J_{P-F}$ = 58 Hz). MS ES+: *m/z* 593.13 ($[M+ Na]^+$ requires 593.19), 571.15 ($[M+ H]^+$ requires 571.21).

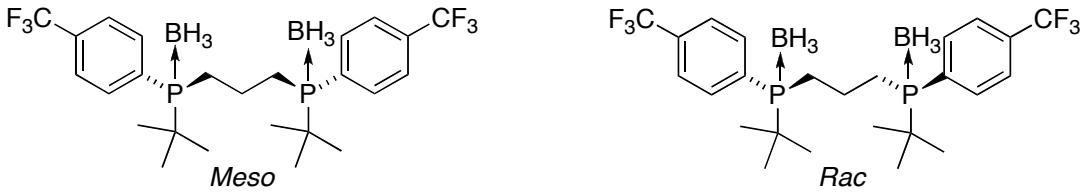
7.3.2. 1,3-bis(*tert*-butyl(*ortho*-(trifluoromethyl)phenyl)phosphino)propane (3.3).



(*Ortho*-trifluoromethylphenyl)*tert*-butylphosphineborane (0.542 g, 2.2 mmol) was dissolved in THF (15 cm^3) and was cooled to -78 ˚C. *N*-butyllithium (0.88 ml, 2.2 mmol as a 2.5 M solution in hexanes) was diluted in diethyl ether (10 cm^3) and added drop-wise over an hour and the reaction allowed to gradually warm to room temperature. Then the solution was again cooled to -78 ˚C and 1,3-diidopropane (0.296 g, 1 mmol) was added and the reaction allowed to warm to room temperature. After 24 hours $^{31}P\{H\}$NMR showed that the reaction of the anion was complete. Addition of 2 ml pyrolidine led to complete decomplexation of boranes after 24 hours at room temperature, yielding deprotected products. The solvent was then reduced under vacuum and the residue extracted with hexane, filtered and the solvent removed. Flash chromatography (gradient elution from 0.5-10 % diethyl ether/hexane) of this mixture was performed using degassed solvents under nitrogen pressure and fractions were collected in round bottomed flasks under a stream of argon and the solvent quickly removed by rotary evacuation and the resulting oil stored under argon. Fractions containing the product were identified by $^{31}P\{H\}$NMR and combined and a further short column (20 % diethyl ether/hexane) was performed to remove any oxide formed during fraction collection, and the solvent removed under vacuum to give the title compound as a mixture of *rac* and *meso isomers* (0.460 g, 90 % yield).

^{1}H-NMR (300 MHz; C_6D_6): δ_H 0.98 (18 H of one diastereomer, d, $J_{H\text{-}p}$ = 12.1 Hz, C(C**H$_3$**)$_3$, 1.03 (18 H of one diastereomer, d, $J_{H\text{-}p}$ = 12.1 Hz, C(C**H$_3$**)$_3$), 1.40 (2 H, m, C**H$_2$**), 1.70 (2 H, m, C**H$_2$**) 1.90 (1H, m, CH**H**), 2.08 (1 H, m, CH**H**). ^{1}H{^{31}P}-NMR (300 MHz; C_6D_6): δ_H 0.98 (18 H of one diastereomer, s, C(C**H$_3$**)$_3$, 1.03 (18 H of one diastereomer, s, C(C**H$_3$**)$_3$, 1.40 (2 H, m, C**H$_2$**), 1.70 (2H, m, C**H$_2$**) 1.90 (1 H, m, CH**H**), 2.08 (1 H, m, CH**H**) 7.0 (3 H, m, Ar**H**), 7.15 (1H, t, Ar**H**) 7.38 (1H, m, Ar**H**) 7.60 (3H, m, Ar**H**). ^{13}C{H}-NMR (75 MHz; C_6D_6): δ_c 23.2 (t, $^{2}J_{C\text{-}P}$ = 15.7 Hz, C-**C**H$_2$C), 23.9 (dd, $^{1}J_{C\text{-}P}$ = 18.3 Hz, $^{3}J_{C\text{-}P}$ = 11.6 Hz,P-**C**H$_2$), 24.6 (m, **C**H$_2$), 28.3 (d, $^{2}J_{C\text{-}P}$ = 14.7 Hz, **C**H$_3$), 30.1 (d, $^{1}J_{C\text{-}P}$ = 16.2 Hz, **C**(CH)$_3$), 125.4 (q, $J_{C\text{-}F}$ = 275.3 Hz, $^{3}J_{C\text{-}P}$ = 1.5 Hz, **C**F$_3$), 126.7 (dq, $^{3}J_{C\text{-}F}$ = 5.8 Hz, $J_{C\text{-}P}$ = 9.4 Hz, Ar**C** *o*-P), 129.5 (d, $J_{C\text{-}P}$= 14.9 Hz, Ar**C**), 130.8 (d, $J_{C\text{-}P}$= 12.1 Hz, Ar**C**), 134.6 (dm, $J_{C\text{-}P}$ = 26.9 Hz, Ar**C**), 134.9 (d, $J_{C\text{-}P}$= 43.1 Hz, Ar**C**) 137.5 (m, Ar**C**-CF$_3$). ^{19}F{^{1}H}-NMR (282 MHz; C_6D_6): δ_F -54.8 (d, $^{4}J_{F\text{-}P}$ = 57.1 Hz), -54.7 (d, $^{4}J_{F\text{-}P}$ = 56.9 Hz); δ_P(121 MHz; C_6D_6) -10.2 (q, $^{4}J_{P\text{-}F}$ = 57.0 Hz), -8.6 (q, $^{4}J_{P\text{-}F}$ = 57.3 Hz). Single Mass Analysis MS ES+: *m/z* 509.1953 ($[M + H]^+$ ($C_{25}H_{33}F_6P_2$) requires 509.1962).

7.3.3. 1,3-bis(*tert*-butyl(*para*-(trifluoromethyl)phenyl)phosphino)propanediborane *(rac/meso)* (3.4).



(*para*-trifluoromethylphenyl)*tert*-butylphosphineborane (1.05 g, 4.2 mmol) was dissolved in THF (20 ml) and was cooled to -100 ˚C. *N*-butyllithium (1.8 cm^3, 4.5 mmol as a 2.5 M solution in hexanes) was diluted in THF (10 ml) and added drop-wise over two hours and the reaction vessel transferred to a cold bath cooled to -40 °C and the temperature maintained for 30 minutes. Then the solution was again cooled to -78 ˚C and 1,3-diidopropane (0.230 cm^3, 2.0 mmol) was added and the reaction allowed to gradually warm to room temperature. After 16 hours ^{31}P{H}NMR showed that the reaction was complete. The solvent was then reduced under vacuum and the residue extracted with dichloromethane, filtered and the solvent removed. Flash chromatography (1-5 % diethyl ether in hexane) allowed partial separation of the *rac* and *meso* diastereomers, which were further purified by recrystallisation from hexane.

Samples suitable for X-ray crystallography were prepared by diffusion of hexane into saturated dichloromethane solutions of the products. The yields were as follows; *rac* 355 mgs, *meso* 145 mgs, mixed *rac*/*meso* 275 mgs, (total, 775 mgs, 1.44 mmol, 72% yield).

Meso.

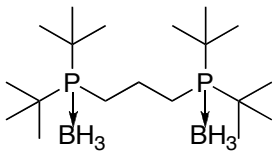
^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.66 (dd, 4 H, $^{3}J_{H-H}$ = 8.5 Hz, $^{3}J_{H-P}$ = 8.5 Hz, Ar**H** *o*-P), 7.52 (dq, 4 H, $^{3}J_{H-P}$ = 7.6 Hz, $^{3}J_{H-P}$ = 1.2 Hz, Ar**H** *o*-CF_3), 1.94 (m, 2 H, 2CH**H**), 1.78 (m, 1 H, CH**H**), 1.64 (m, 2 H, 2CH**H**), 1.47 (m, 1 H, CH**H**), 0.77 (d, 18 H, $^{3}J_{H-P}$ = 14.0 Hz, C**H**$_3$), -0.1 – 0.8 (m br, 6H, B**H**$_3$). ^{1}H{P}-NMR (300 MHz, $CDCl_3$): δ 7.66 (d, 4 H, $^{3}J_{H-H}$ = 8.5 Hz, Ar**H** *o*-P), 7.52 (d, 4 H, $^{3}J_{H-H}$ = 7.6 Hz, Ar**H** *o*-CF_3), 1.94 (m, 2 H, 2CH**H**), 1.78 (m, 1 H, CH**H**), 1.64 (m, 2 H, 2CH**H**), 1.47 (m, 1 H, CH**H**), 0.77 (s, 18 H, C**H**$_3$), -0.1 – 0.8 (m br, 6H, B**H**$_3$). ^{13}C{H}-NMR (75 MHz; $CDCl_3$): δ 134.07 (d, $^{2}J_{C-P}$ = 8.1 Hz, Ar**C** *o*-P), 133.32 (dq, $^{2}J_{C-F}$ = 33.1 Hz, $^{4}J_{C-P}$ = 2.5 Hz, Ar**C**-CF_3), 130.72 (d, $^{1}J_{C-P}$ = 44.8 Hz, Ar**C**-P), 125.15 (dq, $^{2}J_{C-P}$ = 12.9 Hz, $^{4}J_{C-F}$ = 3.6 Hz, Ar**C** *o*-P), 123.63 (qd, $^{1}J_{C-F}$ = 273.3 Hz, $^{5}J_{C-P}$ = 0.8 Hz, **C**F_3), 29.28 (d, $^{1}J_{C-P}$ = 32.2 Hz, P-**C**$(CH_3)_3$), 25.22 (d, $^{2}J_{C-P}$ = 2.2 Hz, **C**H_3), 20.24 (dd, $^{1}J_{C-P}$ = 36.8 Hz, $^{3}J_{C-P}$ = 9.5 Hz P-**C**H_2), 17.73 (s, C-**C**H_2-C).

Rac.

Anal. Calcd for $C_{24}H_{32}B_2F_{10}P_2$: C, 56.01; H, 7.14 % found: C, 55.85; H, 5. 7.13 %.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.66 (dd, 4 H, $^{3}J_{H-H}$ = 8.5 Hz, $^{3}J_{H-P}$ = 8.5 Hz, Ar**H** *o*-P), 7.52 (dd, 4 H, $^{3}J_{H-P}$ = 7.6 Hz, $^{3}J_{H-P}$ = 1.2 Hz, Ar**H** *o*-CF_3), 2.50 (m, 2 H, CH**H**), 1.83 (m, 2 H, CH**H**), 1.59 (m, 2 H, CH**H**), 1.01 (d, 18 H, $^{3}J_{H-P}$ = 14.0 Hz, C**H**$_3$), -0.1 – 0.8 (m br, 6H, B**H**$_3$). ^{1}H{P}-NMR (300 MHz, $CDCl_3$): δ 7.66 (d, 4 H, $^{3}J_{H-H}$ = 8.5 Hz, Ar**H** *o*-P), 7.52 (d, 4 H, $^{3}J_{H-P}$ = 7.6 Hz, Ar**H** *o*-CF_3), 2.50 (m, 2 H, CH**H**), 1.83 (m, 2 H, CH**H**), 1.59 (m, 2 H, CH**H**), 1.01 (s, 18 H, C**H**$_3$), -0.1 – 0.8 (m br, 6H, B**H**$_3$). ^{13}C{H}-NMR (75 MHz; $CDCl_3$): δ 134.35 (d, $^{2}J_{C-P}$ = 8.1 Hz, Ar**C** *o*-P), 133.32 (dq, $^{2}J_{C-F}$ = 33.1 Hz, $^{4}J_{C-P}$ = 2.5 Hz, Ar**C**-CF_3), 130.72 (d, $^{1}J_{C-P}$ = 44.8 Hz, Ar**C**-P), 125.38 (m, Ar**C** *o*-P), 123.86 (qd, $^{1}J_{C-F}$ = 273.3 Hz, $^{5}J_{C-P}$ = 0.8 Hz, **C**F_3), 29.72 (d, $^{1}J_{C-P}$ = 32.3 Hz, P-**C**$(CH_3)_3$), 25.64 (d, $^{2}J_{C-P}$ = 2.2 Hz, **C**H_3), 20.24 (dd, $^{1}J_{C-P}$ = 33.8 Hz, $^{3}J_{C-P}$ = 9.9 Hz P-**C**H_2), 17.69 (s, C-**C**H_2-C). ^{19}F-NMR (376 MHz; $CDCl_3$): δ -63.25 (s, *meso*) -63.79 (s, *rac*). ^{31}P-NMR (162 MHz; $CDCl_3$): δ 33.40 (m br, *meso/rac*). IR (cm^{-1}), KBr, 3050, 2900-3000, 2300, 1400. MS ES+: *m/z* 559.30 ($[M + Na]^+$ requires 559.24).

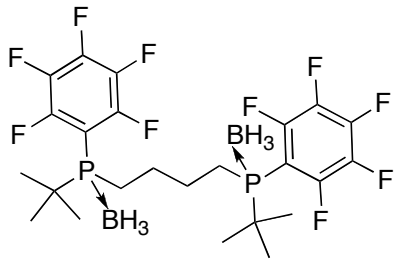
7.3.4. 1,3-Bis(di-*tert*-butylphosphino)propanediborane (3.5).



A solution of di-*tert*-butylphosphinoborane (1.00 g, 6.25 mmol) in THF was cooled to -78 °C and *n*-butyllithium (2.75 cm^3, 6.87 mmol as a 2.5 M solution in hexanes) was added drop-wise. When addition was complete, the mixture was allowed to warm to room temperature and then cooled to -78 °C again before addition of 1,3-dibromopropane (300 μL, 2.95 mmol). The reaction was again allowed to warm to room temperature and stirred overnight. The solvent was then removed under vacuum before workup using CH_2Cl_2/water. After drying with magnesium sulphate the solvent was reduced under vacuum and flash chromatography (10 % diethyl ether in hexane) performed to yield the title compound (0.803 g, 2.42 mmol. 82 % yield) as a clear oil that crystallised on standing. Further purification was possible by recrystallisation from hexane at low temperature (-78 °C).

^{1}H-NMR (400 MHz; $CDCl_3$): δ_H 0.43 (6 H, b m, 2B**H**$_3$), 1.28 (36 H, d, $^3J_{H-P}$ = 12.5 Hz, 12(C**H**$_3$), 1.75 (4 H, m, 2(P-C**H**$_2$)), 2.07 (2 H, m, C-C**H**$_2$-C). ^{1}H{^{31}P}-NMR (400 MHz; $CDCl_3$): δ_H 0.43 (6 H, b m, 2B**H**$_3$), 1.28 (36 H, s, 12(C**H**$_3$),1.75 (4 H, m, 2(P-C**H**$_2$)), 2.07 (2 H, m, C-C**H**$_2$-C). ^{13}C{H}-NMR (100 MHz; $CDCl_3$): δ_c 20.8 (d d, $^1J_{C-P}$ = 21 Hz, $^3J_{C-P}$ = 11 Hz, P-**C**H_2), 20.9 (s, C-**C**H_2-C), 28.0 (d, $^2J_{C-P}$ = 1 Hz, **C**H_3), 32.1 (d, $^1J_{C-P}$ = 27 Hz, P-**C**$(CH_3)_3$). ^{31}P{^{1}H}-NMR (162 MHz; $CDCl_3$): δ_P 43.8 (b m). MS: *m/z* 383.3 (100 %, [M] + Na^+ requires 383.3)

7.3.5. 1,4-bis[(Pentafluorophenyl)(*t*-butyl)phosphino]butanediborane (3.7).

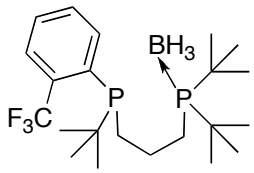


Mg cuttings (0.060 g, 2.48 mmol) were activated by stirring dry for 1 hour in the presence of a catalytic amount of I_2. THF (10 ml) was added and the suspension cooled to 0 °C prior to the addition of 1,4dibromobutane (0.261 g, 1.24 mmol). The reaction was allowed to continue until the magnesium was consumed. The diGrignard was then transferred to a dropping funnel and added dropwise to a stirred solution of (pentafluorophenyl)(*tert*-butyl)phosphinochloride (0.723 g, 2.48 mmol) in THF which was stirred at -78 °C. When the diGrignard addition was completed, the reaction was allowed to warm gradually to room temperature. After 16 hours, the reaction was reduced to near dryness and redissolved in CH_2Cl_2 which was washed with a saturated solution of NH_4Cl. The organic layer was retained and dried over $MgSO_4$ then at this stage $^{31}P\{H\}$ NMR of the solution showed two triplets in the spectrum indicating a mixture of *rac* and *meso* isomers (**3.6**) δ: -0.1 (t, J_{P-F} = 38.6 Hz) 0.3 (t, J_{P-F} = 38.6 Hz). This compound was more fully characterised as it's diborane derivative. The solution of 1,4-bis[(Pentafluorophenyl)(*t*-butyl)phosphino]butane was cooled to -20 °C and BH_3.THF (2.5 ml as a 1M solution in THF) was added. The reaction was allowed to gradually warm to room temperature prior to the solvent being removed. Column chromatography (1-10 % diethyl ether in hexane) under atmospheric conditions yielded the product in the second fraction as a mixture of diastereomers (206 mg, 0.34 mmol, 28 %.yield).

Anal. Calcd for $C_{24}H_{32}B_2F_{10}P_2$: C, 48.52; H, 5.43 % found: C, 48.67; H, 5.43 %. ^{1}H-NMR (300 MHz, $CDCl_3$): δ_H 0.6 (3 H, br,m,w, B**H**$_3$), 1.15 (18 H, d, $^3J_{H-P}$ = 15 Hz, 2x (C(C**H**$_3$)$_3$)), 1.3 (2 H, m, C**H**$_2$), 1.65 (2 H, m, C**H**$_2$), 1.85 (2 H, m, C**H**$_2$), 2.4 (2 H, m, C**H**$_2$). $^1H\{^{31}P\}$-NMR (300 MHz; $CDCl_3$): δ_H 0.6 (3 H, br,m,w, B**H**$_3$), 1.15 (18 H, s, 2x (C(C**H**$_3$)$_3$)), 1.3 (2 H, m, C**H**$_2$), 1.65 (2 H, m, C**H**$_2$), 1.85 (2 H, m, C**H**$_2$). 2.4 (2 H, m, C**H**$_2$). $^{13}C\{H\}$-NMR (100 MHz; $CDCl_3$): δ_c 20.5 (d t, $^1J_{C-P}$ = 33 Hz, $^4J_{C-F}$ = 5 Hz, P-**C**H$_2$), 24.2 (d d, $^2J_{C-P}$ = 15 Hz, $^3J_{C-P}$ = 2 Hz, C-**C**H$_2$-C), 24.4 (d, $^2J_{C-P}$ = 2.3 Hz, (C(**C**H$_3$)$_3$)), 30.5 (d, $^1J_{C-P}$= 29.7 Hz, (**C**(CH$_3$)$_3$)), 100.5 (m, **C**-P), 136.8 (d m, $^1J_{C-F}$ = 255 Hz, Ar**C** *m*-P), 142.5 (d m, $^1J_{C-F}$ = 260 Hz, Ar**C** *p*-P), 147.7

(d m, $^{1}J_{C\text{-}F}$ = 254 Hz, Ar**C** *o*-P).^{19}F-NMR (282 MHz; $CDCl_3$): δ_F -125.75 (4 F ,br m, *o*-**F**), -146.1 (2 F, t t d, $^{3}J_{F\text{-}F}$ = 23 Hz, $^{4}J_{F\text{-}F}$ = 6 Hz, $^{5}J_{F\text{-}P}$ = 2 Hz, *p*-**F**), -159.3 (4 F, t d, $^{3}J_{F\text{-}F}$ = 20 Hz, $^{4}J_{F\text{-}P}$ = 9 Hz, *m*-F). $^{31}P\{^{1}H\}$-NMR (121.5 MHz; $CDCl_3$): δ_P 43.6 (br m). IR (cm^{-1}), KBr, 2900-3000, 2500, 2350, 1500, 1350, 1300. MS ES+: *m/z* 617.15 ($[M + Na]^+$ requires 617.19).

7.3.6.1. Di-*tert*-butyl(3-(*tert*-butyl(*ortho*-(trifluoromethyl)phenyl)phosphino)propyl)phosphineborane (3.8), using 1,3-bromo,chloro-propane.



(*Ortho*-trifluoromethylphenyl)*tert*-butylphosphineborane (0.496 g, 2.0 mmol) was dissolved in THF (15 ml) and was cooled to -78 ˚C. *N*-butyllithium (0.84 ml, 2.1 mmol as a 2.5 M solution in hexanes) was diluted in 10 ml THF and added drop-wise over an hour and the reaction allowed to gradually warm to room temperature. The solution was then cooled to -78 °C and 1-bromo,3-chloropropane (200 ul, 2.0 mmol) was added and the After 24 hours $^{31}P\{H\}$NMR showed that the reaction of the anion was complete giving a mixture of borane protected and unprotected 3-chloropropyl phosphine products. In a separate vessel di-*tert*-butylphosphinoborane (320 mgs, 2 mmol) was dissolved in THF and cooled to -78 °C before the addition of *n*-butyllithium (0.84 ml, 2.1 mmol). The solution was then allowed to return to room temperature and the resulting di-*tert*-butylphosphine anion solution was then added dropwise over 20 minutes to the solution containing the 3-chloropropyl phosphine products, which had been cooled to -78 °C. the reaction was left to stir for 24 hours. At each of the following stages ^{31}P-NMR monitoring showed a degree of conversion to the desired product. The solution was again cooled to -78 °C and the addition of a further of the di-*tert*butylphosphine anion (1 mmol). This was followed by the three additions of (0.4 ml, 1mmol) at 24 hr intervals which regenerated the di-*tert*butylphosphine anion and thus allowed further conversion. When acceptable conversion to the desired product was observed the solvent was then reduced under vacuum and the residue extracted with hexane, filtered and the solvent removed. Flash chromatography (gradient elution from 0.5-3 % diethyl ether in hexane) of this mixture was performed using degassed solvents under nitrogen pressure and

fractions were collected in round bottomed flasks under a stream of argon and the solvent quickly removed by rotary evacuation and the resulting oil stored under argon. Fractions containing the product were identified by $^{31}P\{H\}$NMR and combined and a further short column (20 % diethyl ether in hexane) was performed to remove any oxide formed during fraction collection, and the solvent removed under vacuum to give the title compound (0.460 g, 90 % yield).

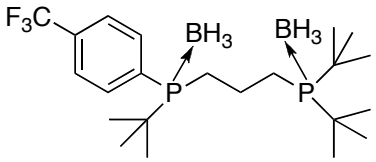
^{1}H-NMR (400 MHz, C_6D_6) δ 7.66 (dm, 2 H, $^{3}J_{H-H}$ = 7.6 Hz Ar**H**), 7.55 (d, 1 H, $^{3}J_{H-H}$ = 7.4 Hz, Ar**H**), 7.18 (t, 1 H, $^{3}J_{H-H}$ = 7.6, Ar**H**), 7.05 (dm, 1 H, $^{3}J_{H-H}$ = 7.2 Hz, Ar**H**), 2.06 (m, 1 H, CH**H**), 1.74 (m, 1 H, CH**H**), 1.51 (m, 1 H, CH**H**), 1.30 (m, 3 H, CH**H**), 0.99 (s, C(C**H**$_3$)), 0.97 (s, C(C**H**$_3$))), 0.94 (s, C(C**H**$_3$))). $^{13}C\{H\}$-NMR (75 MHz, C_6D_6): δ 137.29 (dq, $^{2}J_{C-F}$ = 28.5 Hz, $^{2}J_{C-P}$ = 1 Hz, Ar**C**-CF$_3$), 136.42 (d, $^{1}J_{C-P}$ = 40 Hz, Ar**C**-P), 135.19 (d, $^{2}J_{C-P}$ = 3.5 Hz, Ar**C** *o*-P), 131.08 (s, Ar**C**), 129.76 (s, Ar**C**), 126.88 (dq, $^{2}J_{C-F}$ = 6 Hz, $^{2}J_{C-P}$ = 6 Hz, Ar**C** *o*-CF$_3$), 125.42 (q, $^{1}J_{C-F}$ = 275.5 Hz, **C**F$_3$), 32.31 (d, $^{1}J_{C-P}$ = 26.5 Hz, P(**C**(CH$_3$)$_3$)(C(CH$_3$)$_3$)), 32.29 (d, $^{1}J_{C-P}$ = 26.5 Hz, P(C(CH$_3$)$_3$)(**C**(CH$_3$)$_3$)), 30.14 (d, $^{1}J_{C-P}$ = 15.5 Hz, P(**C**(CH$_3$)$_3$)Ar), 28.34 (d, $^{2}J_{C-P}$ = 14.5 Hz, P(C(**C**H$_3$)$_3$)Ar), 28.07 (d, $^{2}J_{C-P}$ = 7.5Hz, P(C(**C**H$_3$)$_3$)(C(CH$_3$)$_3$)), 28.05 (d, $^{2}J_{C-P}$ = 7.5 Hz, P(C(CH$_3$)$_3$)(C(**C**H$_3$)$_3$)), 25.18 (ddq,$^{1}J_{C-P}$ = 20 Hz, $^{3}J_{C-P}$ = 11 Hz, $^{5}J_{C-F}$ = 2 Hz, **C**H$_2$-P(C(CH$_3$)$_3$)Ar), 22.84 (d, $^{2}J_{C-P}$ = 15 Hz, CH$_2$-**C**H$_2$-CH$_2$), 19.47 (dd, $^{1}J_{C-P}$ = 28 Hz, $^{3}J_{C-P}$ = 12 Hz, **C**H$_2$-P(C(CH$_3$)$_3$)$_2$).^{19}F-NMR (282 MHz, C_6D_6): δ -54.74 (d, $^{4}J_{P-F}$ = 56.7 Hz). $^{31}P\{H\}$-NMR (121 MHz, C_6D_6): δ 46.2 (m, $^{1}J_{P-B}$ = 50 Hz, **P**(C(CH$_3$)$_3$)$_2$) **P**(C(CH$_3$)$_3$)Ar) -11.6 (q, $^{4}J_{P-F}$ = 57 Hz, P(C(CH$_3$)$_3$)Ar). Single Mass Analysis MS ES+: *m/z* 421.2388 ([M + H]$^{+}$ ($C_{22}H_{38}F_3P_2$) requires 421.2401).

7.3.6.2. 1-(Di-*tert*-butylphosphino)-3-(*tert*-butyl(*ortho*-(trifluoromethyl)phenyl)phosphino)propaneborane (3.8) from di-*tert*-butyl(3-bromopropyl)phosphinoborane (2.9).

Tert-butyl(*ortho*-(trifluoromethyl)phenyl)phosphinoborane (1.100 g 4.43 mmol) was dissolved in THF (40 ml) and cooled to -100 °C with good stirring. *N*-butyllithium was added to diluted with THF (10 ml) and added dropwise over 1 hour to the cooled phosphine borane solution. When the addition was complete the solution was allowed to warm to -40 °C for 20 minutes then cooled again to -78 °C prior to the addition of di-*tert*-butyl(3-bromopropyl)phosphinoborane (1.24 g, 4.43 mmol). The solution was allowed to stir for 1 hour at -78 °C before being allowed to warm to room temperature and stirred for 16 hours, the solvent was then reduced under vacuum and the residue extracted with hexane, filtered and

the solvent removed. Flash chromatography (gradient elution from 0.5-3 % diethyl ether in hexane) of this mixture was performed using degassed solvents under nitrogen pressure and fractions were collected in round bottomed flasks under a stream of argon and the solvent quickly removed by rotary evacuation and the resulting oil stored under argon. Fractions containing the product were identified by $^{31}P\{H\}$NMR and combined and a further short column (20 % diethyl ether in hexane) was performed to remove any oxide formed during fraction collection, and the solvent removed under vacuum to give the title compound (0.460 g, 90 % yield). Data identical to previous method.

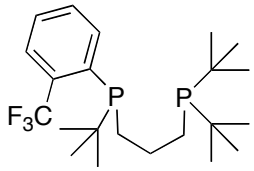
7.3.7. 1-(Di-*tert*-butylphosphino)-3-(*tert*-butyl(*para*-(trifluoromethyl)phenyl)phosphino)propanediborane (3.9).



Tert-butyl(*para*-(trifluoromethyl)phenyl)phosphinoborane (1.100 g 4.43 mmol) was dissolved in THF (40 ml) and cooled to -100 °C with good stirring. *N*-butyllithium was added to diluted with THF (10 ml) and added dropwise over 1 hour to the cooled phosphine borane solution. When the addition was complete the solution was allowed to warm to -40 °C for 20 minutes then cooled again to -78 °C prior to the addition of di-*tert*-butyl(3-bromopropyl)phosphinoborane (1.24 g, 4.43 mmol). The solution was allowed to stir for 1 hour at -78 °C before being allowed to warm to room temperature and stirred for 16 hours. The solvent was then removed under vacuum and (under atmospheric conditions) diethyl ether (50 ml) was added followed by water (20 ml), the mixture was stirred, and the resulting phases separated, the organic layer retained and dried over $MgSO_4$, filtered and the solvent removed under vacuum. Recrystallisation from hexane at -40 °C gave the product at fine white needles (1.45 g, 3.23 mmol, 73 % yield). A sample suitable for X-ray analysis was obtained by slow diffusion of hexane into a CH_2Cl solution of the product.
Anal. Calcd for: C, 58.96; H,9.67 % found: C,59.37; H,10.04 %. ^{1}H-NMR (300 MHz C_6D_6): δ 7.68 (2 H, m, Ar**H** *o*-P), 7.48 (2 H, m, Ar**H** *o*-CF_3), 2.22 (1 H,m, C**H**H), 1.73 (2 H, m, C**H**H), 1.55 (2 H, m, C**H**H), 1.32 (1 H, m, C**H**H), 0.97 (9 H, d, $^3J_{H-P}$ = 12.5 Hz, P(C(C**H**$_3$)$_3$)(C(CH$_3$)$_3$)), 0.90 (9 H, d, $^3J_{H-P}$ = 12.5 Hz, P(C(CH$_3$)$_3$)(C(C**H**$_3$)$_3$)), 0.87 (9 H, d, $^3J_{H-}$

$_P$ = 13.8 Hz, P(C(C**H**$_3$)$_3$)Ar), 0.62 (1 H, m, C**H**H), 0.33 (6 H, m, br, 2B**H**$_3$). ^{1}H{P}-NMR (300 MHz, C_6D_6): δ 7.68 (2 H, m, Ar**H** *o*-P), 7.48 (2 H, m, Ar**H** *o*-CF_3), 2.22 (1 H,m, C**H**H), 1.73 (2 H, m, C**H**H), 1.55 (2 H, m, C**H**H), 1.32 (1 H, m, C**H**H), 0.97 (9 H, s, P(C(C**H**$_3$)$_3$)(C(CH$_3$)$_3$)), 0.90 (9 H, s, P(C(CH$_3$)$_3$)(C(C**H**$_3$)$_3$)), 0.87 (9 H, s, P(C(C**H**$_3$)$_3$)Ar), 0.62 (1 H, m, C**H**H), 0.33 (6 H, m, br, 2B**H**$_3$). ^{13}C{H}-NMR (75 MHz, C_6D_6): δ 134.51 (d, $^2J_{C-P}$ = = 8.0 Hz, Ar**C** *o*-P), 133.45 (qd, $^2J_{C-F}$ = 35.2 Hz, $^3J_{C-P}$ = 2.5 Hz, Ar**C**-CF_3), 131.53 (d, $^1J_{C-P}$ = 45.1 Hz, Ar**C**-P), 125.32 (d q, $^3J_{C-P}$ = 9.2 Hz, $^3J_{C-F}$ = 3.7 Hz, Ar**C** *o*-CF_3), 124.01 (q, $^1J_{C-F}$ = 273.3 Hz, **C**F$_3$), 32.51 (d, $^1J_{C-P}$ = 26.8 Hz, P(**C**(CH$_3$)$_3$)(C(CH$_3$)$_3$)), 32.37 (d, $^1J_{C-P}$ = 27.2 Hz, P(C(CH$_3$)$_3$)(**C**(CH$_3$)$_3$)), 29.68 (d, $^1J_{C-P}$ = 32.2 Hz, P(**C**(CH$_3$)$_3$)Ar), 28.11 (m, P(C(**C**H$_3$)$_3$)(C(CH$_3$)$_3$)), 25.77 (d, $^2J_{C-P}$ = 2.2 Hz, P(C(**C**H$_3$)$_3$)Ar), 21.22 (dd, $^1J_{C-P}$ = 32.3 Hz, $^3J_{C-P}$ = 9.5 Hz, **C**H$_2$-P(C(CH$_3$)$_3$)Ar), 20.07 (dd, $^1J_{C-P}$ = 35.6 Hz, $^3J_{C-P}$ = 10.8 Hz , **C**H$_2$-P(C(CH$_3$)$_3$)(C(CH$_3$)$_3$)), 19.58 (s, CH$_2$-**C**H$_2$-CH$_2$).^{19}F-NMR (282 MHz, C_6D_6): δ -63.59 (s). ^{31}P-NMR (121 MHz, C_6D_6): δ 45.15 (m, **P**(C(CH$_3$)$_3$)$_2$), 34.00 (**P**(C(CH$_3$)$_3$)Ar). IR (cm^{-1}), KBr, 3100, 2900-3000, 2400, 2200, 1300. MS ES-: *m/z* 447.18 ([M – H]$^-$ requires 447.30).

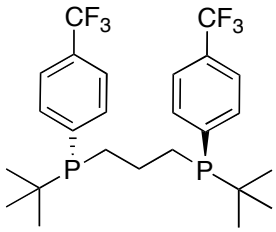
7.3.8. Di-*tert*-butyl(3-(*tert*-butyl(*ortho*-(trifluoromethyl)phenyl)phosphino)propyl)phosphine (3.10).



Di-*tert*-butyl(3-(*tert*-butyl(*ortho*-(trifluoromethyl)phenyl)phosphino)propyl)phosphineborane (150 mgs, 0.33 mmol) was dissolved in CH_2Cl_2 (10 ml) and cooled to -20 °C then $HBF_4.OMe_2$ (175 µl, 2.26 mmol), was added dropwise. Once addition was complete the reaction was allowed to warm to room temperature and stirred overnight before being cooled to 0 °C and hydrolysis by the addition of a saturated degassed solution of $NaHCO_3$ (10 ml). After vigorous stirring of the biphasic mixture for 10 minutes the organic layer was removed and the aqueous layer extracted with CH_2Cl_2 (5 ml x 2) and the combined organic extracts dried over $MgSO_4$. This was then filtered off and the solvent removed under vacuum to yield the title compound as a clear oil (130 mgs, 0.31 mmol 94 % yield).
^{1}H-NMR (400 MHz, C_6D_6) δ 7.66 (m, 2 H, Ar**H**), 7.45 (d, 1 H, $^3J_{H-H}$ = 7.5 Hz, Ar**H**), 7.37 (t, 1 H, $^3J_{H-H}$ = 7.5 Hz, Ar**H**), 2.06 (m, 1 H, CH**H**), 1.74 (m, 1 H, CH**H**), 1.51 (m, 1 H, CH**H**), 1.30

(m, 3 H, CH**H**), 0.99 (d, 9 H, $^{2}J_{P\text{-}H}$ = 11 Hz, C(C**H**$_3$)), 0.96 (d, 9 H, $^{2}J_{P\text{-}H}$ = 11 Hz, C(C**H**$_3$))), 0.94 (d, 9 H, $^{2}J_{P\text{-}H}$ = 11 Hz, C(C**H**$_3$)). ^{1}H{P}-NMR (400 MHz, C_6D_6) δ 7.66 (m, 2 H, Ar**H**), 7.45 (d, 1 H, $^{3}J_{H\text{-}H}$ = 7.5 Hz, Ar**H**), 7.37 (t, 1 H, $^{3}J_{H\text{-}H}$ = 7.5 Hz, Ar**H**), 2.06 (m, 1 H, CH**H**), 1.74 (m, 1 H, CH**H**), 1.51 (m, 1 H, CH**H**), 1.30 (m, 3 H, CH**H**), 0.99 (s, 9 H, C(C**H**$_3$)), 0.96 (s, 9 H, C(C**H**$_3$)), 0.94 (s, 9 H, C(C**H**$_3$))).^{13}C{H}-NMR (75 MHz, C_6D_6): δ 134.18 (s, Ar**C**), 130.37 (s, Ar**C**) 129.04 (s, Ar**C**) 126.31 (m, Ar**C** *o*-CF_3) 124.68 (q, $^{1}J_{C\text{-}F}$ = 275 Hz, CF_3) 29.59 (m, P(**C**(CH$_3$)$_3$)$_2$), 27.95 (d, $^{2}J_{C\text{-}P}$ = 14 Hz, P(**C**(CH$_3$)$_3$)Ar)), 27.00 (m, **C**H$_2$) 24.29 (m, **C**H$_2$), 22.72 (m, **C**H$_2$). ^{19}F-NMR (376 MHz, C_6D_6) δ -54.75 (d, $^{4}J_{P\text{-}F}$ = 55.8 Hz). ^{31}P NMR (162 MHz, C_6D_6) δ_P 27.39 (m, **P**(C(CH$_3$)$_2$), -10.04 (q, $J_{P\text{-}F}$ = 55.8 Hz, **P**(C(CH$_3$)$_3$)Ar). Single Mass Analysis MS ES+: *m/z* 421.2388 ([M + H]$^+$ ($C_{22}H_{38}F_3P_2$) requires 421.2401).

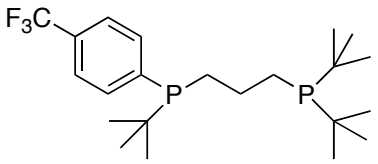
7.3.9. 1,3-Bis(*tert*-butyl(*para*-(trifluoromethyl)phenyl)phosphino)propane (*rac*) (3.11).



1,3-Bis(*tert*-butyl(*para*-(trifluoromethyl)phenyl)phosphino)propanediborane (*rac*) (400 mgs, 0.74 mmol) was dissolved in dichloromethane (10 ml) and cooled to -20 °C before $HBF_4.OMe_2$ (0.9 ml, 7.4 mmol) was added dropwise. Once addition was complete, the reaction was allowed to warm to room temperature and stirred overnight before being cooled to 0 °C. Hydrolysis was then achieved by the addition of a saturated solution of $NaHCO_3$ (10 ml). After vigorous stirring of the biphasic mixture for 10 minutes the organic layer was removed, the aqueous layer extracted with dichloromethane two further times and the combined extracts dried over $MgSO_4$. The solution was then filtered off and the solvent removed under vacuum to yield the title compound as a clear oil (358 mgs, 95.2 % yield). ^{1}H-NMR (300 MHz; C_6D_6): δ_H 0.88 (18 H, d, $^{3}J_{H\text{-}P}$ = 12 Hz, 6(C**H**$_3$)), 1.43 (2 H, m, 2C**H**H), 1.65 (2 H, m, 2C**H**H), 2.15 (2 H, m, 2C**H**H), 7.4 (8 H, m, 8 Ar**H**). ^{1}H{^{31}P}-NMR (300 MHz; $CDCl_3$): δ_H 0.88 (18 H, s, 6(C**H**$_3$)), 1.43 (2 H, m, 2C**H**H), 1.65 (2 H, m, 2C**H**H), 2.15 (2 H, m, 2C**H**H), 7.4 (8 H, m, 8 Ar**H**). ^{13}C{H}-NMR (100 MHz; $CDCl_3$): δ_c 21.7 (dd, $^{1}J_{C\text{-}P}$ = 16 Hz,

$^{3}J_{C\text{-}P}$ = 12 Hz, P-**C**H_2), 22.8 (t, $^{2}J_{C\text{-}P}$ = 16 Hz, **C**H_2 centre), 27.3 (d, $^{2}J_{C\text{-}P}$ = 13 Hz, **C**H_3), 29.1 (d, $^{1}J_{C\text{-}P}$ = 11.5 Hz, **C**(CH_3)), 124.0 (q, $^{1}J_{C\text{-}F}$ = 272 Hz, **C**F_3), 124.4 (m, Ar**C** *o*-CF_3), 130.9 (q, $^{2}J_{C\text{-}F}$ = 32.5 Hz, Ar**C**-CF_3), 134.3 (d, $^{2}J_{C\text{-}P}$ = 19 Hz, Ar**C** *o*-P), 139.9 (d, $^{1}J_{C\text{-}P}$ = 23 Hz, Ar**C**-P). ^{19}F-NMR (376 MHz; $CDCl_3$): δ_F -62.9 (s). ^{31}P{H}-NMR (162 MHz; $CDCl_3$): δ_P 2.03 (s). Single Mass Analysis MS ES+ 509.1962 ($[M + H]^+ C_{25}H_{33}F_6P_2$ requires 509.1962).

7.3.10. 1-(Di-*tert*-butylphosphino)-3-(*tert*-butyl(*para*-(trifluoromethyl)phenyl)phosphino)propane (3.12).

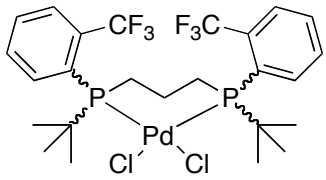


1-(Di-*tert*-butylphosphino)-3-(*tert*-butyl(*para*-(trifluoromethyl)phenyl)phosphino)propanediborane (250 mg, 0.56 mmol) was dissolved in CH_2Cl_2 (10 ml) and cooled to -20 °C then $HBF_4.OMe_2$ (0.57 ml, 5.6 mmol) was added dropwise. Once addition was complete, the reaction was allowed to warm to room temperature and stirred overnight before being cooled to 0 °C for and the addition of a saturated solution of $NaHCO_3$ (10 ml). After vigorous stirring of the resulting biphasic mixture for 10 minutes the organic layer was removed and the aqueous layer extracted with CH_2Cl_2 (10 ml x 2). The combined organic extracts were dried over $MgSO_4$. This was then filtered off and the solvent was then removed under vacuum to yield the title compound as a clear oil (214 mgs, 0.51 mmol, 92 % yield).

^{1}H-NMR (400 MHz): δ 8.29 (2 H, m, Ar**H** *o*-P), 7.64 (2 H, m, Ar**H** *o*-CF_3), 2.20 (2 H, m C**H**H) 1.98 (1 H, m, C**H**H) 1.64 (1 H, m, C**H**H), 1.52 (1 H, m, C**H**H), 1.47 (9 H, d, $^{3}J_{H\text{-}P}$ = 14.7 Hz, P(C(C**H**$_3$)$_3$)(C$(CH_3)_3$)), 1.42 (9 H, d, $^{3}J_{H\text{-}P}$ = 16.2 Hz, P-(C(C**H**$_3$)$_3$)Ar) 1.34 (9 H, d, $^{3}J_{H\text{-}P}$ = 14.5 Hz, P(C$(CH_3)_3$)(C(C**H**$_3$)$_3$)), 1.29 (1 H, m, C**H**H). ^{1}H{P}-NMR (400 MHz): δ 8.29 (2 H, m, Ar**H** *o*-P), 7.64 (2 H, m, Ar**H** *o*-CF_3), 2.20 (2 H, m C**H**H) 1.98 (1 H, m, C**H**H) 1.64 (1 H, m, C**H**H), 1.52 (1 H, m, C**H**H), 1.47 (9 H, s, P(C(C**H**$_3$)$_3$)(C$(CH_3)_3$)), 1.42 (9 H, s, P-(C(C**H**$_3$)$_3$)Ar), 1.34 (9 H, s, P(C$(CH_3)_3$)(C(C**H**$_3$)$_3$)), 1.29 (1 H, m, C**H**H).^{13}C{H}-NMR (101 MHz): δ 141.27 (d, $^{1}J_{C\text{-}P}$ = 26.0 Hz, Ar**C**-P), 134.73 (d, $^{3}J_{C\text{-}P}$ = 19.7 Hz, Ar**C** *o*-P), 130.69 (q, $^{2}J_{C\text{-}F}$ = 32.1 Hz, Ar**C**-CF_3), 124.76 (q, $^{1}J_{C\text{-}F}$ = 272.0 Hz, **C**F_3), 124.42 (dq, $^{3}J_{C\text{-}P}$ = 6.7, $^{3}J_{C\text{-}F}$ = 3.7 Hz, Ar**C** *o*-CF_3), 31.08 (d, $^{1}J_{C\text{-}P}$ = 22.5 Hz, P(**C**$(CH_3)_3$)(C$(CH_3)_3$)), 31.01 (d, $^{1}J_{C\text{-}P}$ = 21.9

Hz, P(**C**$(CH_3)_3$)($C(CH_3)_3$)), 29.53 (d, $^2J_{C\text{-}P}$ = 13.8 Hz, P(C(**C**$H_3)_3$)($C(CH_3)_3$)), 29.50 (d, $^2J_{C\text{-}P}$ = 13.8 Hz, P($C(CH_3)_3$)(C(**C**$H_3)_3$)), 28.84 (d, $^1J_{C\text{-}P}$ = 13.2 Hz, P(**C**$(CH_3)_3$)Ar), 27.33 (d, $^1J_{C\text{-}P}$ = 13.4 Hz, P (C(**C**$H_3)_3$)Ar), 26.86 (dd, $^2J_{C\text{-}P}$ = 26.5, $^2J_{C\text{-}P}$ = 17.5 Hz, CH_2-**C**H_2-CH_2), 22.93 (dd $^1J_{C\text{-}P}$ = 28.6, $^3J_{C\text{-}P}$ = 12.4 Hz, **C**H_2- P($C(CH_3)_3$Ar), 21.83 (dd, $^1J_{C\text{-}P}$ = 21.8 Hz, $^3J_{C\text{-}P}$ 13.2 Hz, **C**H_2- P($C(CH_3)_3)_2$).^{19}F-NMR (376 MHz): δ -63.45 (s).^{31}P{H}-NMR (162 MHz): δ 40.87 (s, **P**$(C(CH_3)_3)_2$), 29.98 (s, **P**($C(CH_3)_3$Ar)). Single Mass Analysis MS ES+: *m/z* 421.2401 ([M + H]$^+$ ($C_{22}H_{38}F_3P_2$) requires 421.2401).

7.3.11.1. [(1,3-Bis(*tert*-butyl(*ortho*-(trifluoromethyl)phenyl)phosphino)propane)palladium]dichloride (*rac*) (3.14).



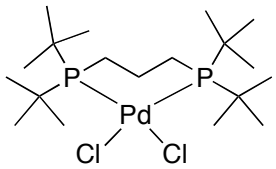
1,3-Bis(*tert*-butyl(*ortho*-(trifluoromethyl)phenyl)phosphino)propane (220 mg, 0.433 mmol) was dissolved in dichloromethane (10 ml), stirred at room temperature and [palladium(benzonitrile)$_2$dichloride] (166 mg, 0.433 mmol) was added before the reaction allowed to stir overnight. The reaction was reduced to near dryness by removal of solvent under vacuum, (under atmospheric conditions) hexane was then slowly added to form a precipitate which was isolated by filtration and washed with further hexane. The precipitate was then redissolved and precipitated several times to yield the product as a orange powder (70 mgs 0.102 mmol, 23.5 % yield). A sample suitable for X-ray analysis was prepared by slow diffusion of hexane into a dichloromethane solution of the product. This showed the product to be present as the *rac* isomer.

Anal. Calcd for $C_{25}H_{32}Cl_2F_6P_2Pd$: C, 43.78; H, 4.70 % found: C, 43.86; H, 4.42 %. ^{1}H-NMR (300 MHz; $CDCl_3$): δ_H 1.4 (18 H, d, $^3J_{H\text{-}P}$ = 16 Hz, 6(CH_3)), 1.95, 2.15, 2.4 (6 H, m, 6C**H**H), 7.55 (4 H, m, 4Ar**H**), 7.8 (2 H, m, 2Ar**H** *o*-CF_3), 9.05 (2 H, m br, 2Ar**H** *o*-P). ^{1}H{^{31}P}-NMR (300 MHz; $CDCl_3$): δ_H 1.4 (18 H, s, 6(CH_3)), 1.95, 2.15, 2.4 (6 H, m, 6C**H**H), 7.55 (4 H, m, 4Ar**H**), 7.8 (2 H, m, 2Ar**H** *o*-CF_3), 9.05 (2 H, m br, 2Ar**H** *o*-P). ^{19}F-NMR (282 MHz; $CDCl_3$): δ_F -53.2 (s). ^{31}P{^{1}H}-NMR (121 MHz; CD_2Cl_2): δ_P(121 MHz; $CDCl_3$): δ_P 33.7 (s). IR (cm^{-1}), KBr, 2900-3000, 2200, 1300. MS ES+: *m/z* 651.08 (100 %), ([M – Cl]$^+$ requires 651.06).

7.3.11.2. [(1,3-bis(*tert*-butyl(*ortho*-(trifluoromethyl)phenyl)phosphino)propane)palladium]dichloride (3.14) via $Pd_2(dba)_3$

$Pd_2(dba)_3$ (50 mgs, 0.055 mmol), was added to a stirred solution of 1,3-bis(*tert*-butyl(*ortho*-(trifluoromethyl)phenyl)phosphino)propane (57 mgs, 0.11 mmols) in THF (10 ml). After 1hour, the dark orange solution was filtered and the solvent removed under vacuum yielding orange oil. This was dissolved in diethyl ether and HCl (0.6 cm^3, 1.2 mmol as 2M solution in diethyl ether) was added to form the product as a yellow precipitate. The product was purified under atmospheric conditions by filtration to isolate the precipitate followed by re-dissolving in 5 cm^3 dichloromethane and precipitation by the slow addition of hexane (42 mgs, 0.61 mmol, 55 % yield). Further recrystallisation allowed the isolation of the *rac* isomer. Data identical to previous preparation.

7.3.12. 1,3-bis(di-*tert*-butylphosphino)propane palladium dichloride (3.15).

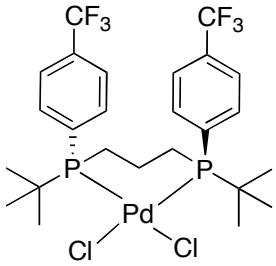


$Pd_2(dba)_3$ (260 mgs 0.28 mmol), was added to a stirred solution of 1,3-bis(di-*tert*-butylphosphino)propane (190 mgs, 0.57 mmols) in THF (10 ml). After 1 hour, the dark orange solution was filtered and the solvent removed under vacuum yielding orange oil. This was dissolved in ether and HCL (0.6 ml, 1.2 mmol as 2M solution in diethyl ether) was added to form the product as a yellow precipitate. The product was purified under atmospheric conditions by filtration to isolate the precipitate followed by redissolving in 5ml CH_2Cl_2 and precipitation by the slow addition of hexane (171 mgs, 0.33 mmol 59 % yield). Crystals suitable X-ray crystallography were obtained by slow diffusion of hexane into a CH_2Cl_2 solution of the product.

Anal. Calcd for $C_{19}H_{42}Cl_2P_2Pd$: C, 44.76; H, 8.30 % found: C, 45.40; H, 8.57 %. ^{1}H-NMR (400 MHz; CD_2Cl_2) δ_H 1.45 (36 H, d, $^2J_{H-P}$ = 14.2 Hz, 2(C**H$_3$**)$_3$, 1.7 (4 H, m, 2(P-C**H$_2$**), 1.95 (2 H, m, C-C**H$_2$**-C). ^{1}H{^{31}P}-NMR (400 MHz; CD_2Cl_2) δ_H 1.45 (36 H, s, 2(C**H$_3$**)$_3$, 1.7 (4 H, m, 2(P-C**H$_2$**), 1.95 (2 H, m, C-C**H$_2$**-C). ^{13}C{H}-NMR (100 MHz; CD_2Cl_2) δ_c 20.2 (m, **C**H_2-P), 22.0 (t, $^2J_{C-P}$ = 2 Hz, C-**C**H_2-C), 31.3 (m, (**C**H_3)), 39.3 (d d, $^1J_{C-P}$ = 21.2 Hz, $^3J_{C-P}$ = 1.6 Hz

P-**C**(CH_3)), $^{31}P\{^1H\}$-NMR (162 MHz; CD_2Cl_2): δ: 40.9(s). IR (cm^{-1}), KBr, 2900-3000, 2200.MS ES^+: *m/z* 475.1 $[M - Cl]^+$.

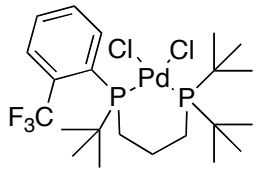
7.3.13. [1,3-bis(*tert*-butyl(*para*-(trifluoromethyl)phenyl)phosphino)propanepalladium]dichloride-(*rac)* (3.16).



1,3-Bis(*tert*-butyl(*para*-(trifluoromethyl)phenyl)phosphino)propane-(*rac*) (248 mg, 0.49 mmol) was dissolved in CH_2Cl_2 (10 ml) and [palladium(benzonitrile)$_2$dichloride] (188 mgs, 0.49 mmol) added. There followed an almost instant colour change from deep red to yellow. Hexane was added and a precipitate formed which was filtered, washed with further hexane and dried under vacuum to yield the title compound as bright yellow crystalline powder (325 mgs, 0.475 mmol 97 % yield).

Anal. Calcd for $C_{25}H_{32}Cl_2F_6P_2Pd$: C, 43.78; H, 4.70 % found: C, 43.82; H, 4.45 %. ^{1}H-NMR (400 MHz; CD_2Cl_2): δ_H 1.28(18 H, d, $^3J_{H-P}$ = 18 Hz, 6(C**H**$_3$)), 1.85 (4 H, 4 m, C**H**H), 2.05 (2 H, 2 m, C**H**H), 7.71 (4 H, d, $^3J_{H-H}$ = 8 Hz, Ar**H** *o*-CF_3), 8.22 (4 H, dd, $^3J_{H-H}$ = 8 Hz, $^3J_{H-P}$ = 9 Hz, Ar**H** *o*-P). $^1H\{^{31}P\}$-NMR (400 MHz; CD_2Cl_2): δ_H 1.28 (18 H, s, 6(C**H**$_3$)), 1.85 (4 H, 4 m, C**H**H), 2.05 (2 H, 2 m, C**H**H), 7.70 (4 H, d, $^3J_{H-H}$ = 8 Hz, Ar**H** *o*-CF_3), 8.21 (4 H, d, $^3J_{H-H}$ = 8 Hz, Ar**H** *o*-P). $^{13}C\{H\}$-NMR (100 MHz; CD_2Cl_2): δ_c 19.15 (s, CH_2-**C**H_2-CH_2), 20.32 (m, P-**C**H_2), 29.5 (m, **C**H_3), 37.30 (d d, $^1J_{C-P}$ = 32 Hz, $^3J_{C-P}$ = 3 Hz, **C**$(CH_3)_3$), 124.20 (q, $^1J_{C-F}$ = 275 Hz, **C**F_3), 125.60 (d q, $^2J_{C-P}$ = 10 Hz, $^4J_{C-F}$ = 4 Hz, Ar**C** *o*-P), 133.45 (q, $^2J_{C-F}$ = 33 Hz, Ar**C**-CF_3), 134.40 (d, $^1J_{C-P}$ = 43 Hz, Ar**C**-P), 135.42 (d q, $^3J_{C-P}$ = 5 Hz, $^3J_{C-F}$ = 4 Hz Ar**C** *o*-CF_3). ^{19}F-NMR (376 MHz; CD_2Cl_2): δ_F 63.18 (s), $^{31}P\{H\}$-NMR (161 MHz; CD_2Cl_2): δ_P 28.10 (s). IR (cm^{-1}), KBr, 2900-3000, 2250, 1350. MS ES+: *m/z* 649.15 ($[M - Cl]^+$ requires 649.06).

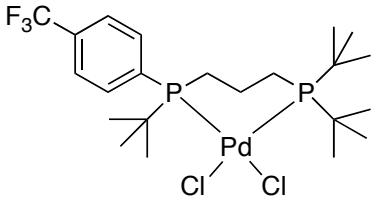
7.3.14. Di-*tert*-butyl(3-(*tert*-butyl(*ortho*-(trifluoromethyl)phenyl)phosphino)propyl)phosphine palladium dichloride (3.17).



$Pd_2(dba)_3$ (210 mgs, 0.23 mmol) was added to a stirred solution of di-*tert*-butyl(3-(*tert*-butyl(*ortho*-(trifluoromethyl)phenyl)phosphino)propyl)phosphine (196 mgs, 0.46 mmol) in THF (10 ml). After 1hour the dark orange solution was filtered and the solvent removed under vacum yielding an orange oil. This was redissolved in diethyl ether and 2.5 eq of HCL in diethyl ether was added slowly to form the product as a yellow precipitate. After filtration the product was redisolved in CH_2Cl_2 and precipitated by the addition of hexane (49 mgs, 0.08 mmol, 18 % yield) . Crystals suitable X-ray crystallography were obtained by slow diffusion of hexane into a CH_2Cl_2 solution of the product.

Anal. Calcd for $C_{22}H_{37}Cl_2F_3P_2Pd$: C, 44.20; H, 6.24 % found: C, 44.45; H, 6.47 %. ^{1}H-NMR (400 MHz; CD_2Cl_2): δ_H 1.1 (9 H, d, $^3J_{H-P}$ = 14 Hz, (C**H**$_3$)$_3$), 1.35 (9 H, d, $^3J_{H-P}$ = 16 Hz, (C**H**$_3$)$_3$), 1.48 (1 H, m, C**H**H) 1.5 (9 H, d, $^3J_{H-P}$ = 15 Hz, (C**H**$_3$)$_3$), 1.85 (1 H, m, C**H**H), 2.15 (1 H, m, C**H**H), 2.2 (1 H, m, C**H**H), 2.3 (1 H, m, C**H**H), 2.75 (1 H, m, C**H**H), 7.55 (1 H, t, $^3J_{H-H}$ = 8 Hz, ArC**H**), 7.65 (1 H, t, $^3J_{H-H}$ = 8 Hz, ArC**H**), 7.75 (1 H, d d, $^3J_{H-H}$ = 10 Hz, $^4J_{H-P}$ = 3 Hz, Ar**C** *o*-CF_3), 9.30 (1 H, d d, $^3J_{H-P}$ = 16 Hz, $^3J_{H-H}$ = 8.5 Hz, Ar**H** *o*-P). ^{1}H{^{31}P}-NMR (400 MHz; CD_2Cl_2): δ_H 1.1 (9 H, s, (C**H**$_3$)$_3$), 1.35 (9 H, s, (C**H**$_3$)$_3$), 1.48 (1 H, m, C**H**H) 1.5 (9 H, s, (C**H**$_3$)$_3$), 1.85 (1 H, m, C**H**H), 2.15 (1 H, m, C**H**H), 2.2 (1 H, m, C**H**H), 2.3 (1 H, m, C**H**H), 2.75 (1 H, m, C**H**H), 7.55 (1 H, t, $^3J_{H-H}$ = 8 Hz, Ar**H**), 7.65 (1 H, t, $^3J_{H-H}$ = 8 Hz, Ar**H**), 7.75 (1 H, d, $^3J_{H-H}$ = 10 Hz, Ar**H** *o*-CF_3), 9.30 (1 H, d, $^3J_{H-H}$ = 8.5 Hz, Ar**H** *o*-P). ^{13}C{H}-NMR (75 MHz; CD_2Cl_2): δ_c 144.39 (d, $^2J_{C-P}$ = 22 Hz, Ar**C** *o*-P), 133.69 (s, Ar**C**) 133.34 (d, $^3J_{C-P}$ = 13 Hz, Ar**C** *p*-CF_3),128.46 (m, Ar**C** *o*-CF_3), 39.05 (d, $^2J_{P-C}$ = 24 Hz, **C**(CH_3)), 38.90 (d, $^2J_{P-C}$ = 21.5 Hz, **C**(CH_3)), 38.78 (d, $^2J_{P-C}$ = 19 Hz, **C**(CH_3)), 31.32(s, C(**C**H$_3$)) 29.89 (s, C(**C**H$_3$)), 31.32 (s, C(**C**H$_3$)) 18.62 (m, **C**H$_2$-P), 18.45 (s, CH$_2$-**C**H$_2$-CH$_2$) 16.11 (dd, $^1J_{C-P}$ = 21 Hz, $^3J_{C-P}$ = 18 Hz). ^{19}F-NMR (376 MHz; CD_2Cl_2): δ_F 55.01 (s). ^{31}P-NMR (162 MHz, CD_2Cl_2): δ 43.84 (s, **P**((C(CH_3)$_3$)$_2$), 33.54 (s, **P(**C(CH_3)$_3$)Ar). IR (cm^{-1}), KBr, 2900-3000, 2325, 1300. MS ES+ *m/z* 560.15 ([M - Cl]$^+$ requires 560.11).

7.3.15.1. [1-(Di-*tert*-butylphosphino)-3-(*tert*-butyl(*para*-(trifluoromethyl)phenyl)phosphino)propane palladiumdichloride] (3.18).



Via [palladium(benzonitrile)$_2$dichloride]

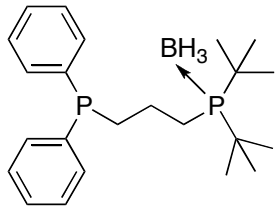
1-(Di-*tert*-butylphosphino)-3-(*tert*-butyl(*para*-(trifluoromethyl)phenyl)phosphino)propane (63 mg, 0.15 mmol) was dissolved in CH_2Cl_2 (5 cm^3) and [palladium(benzonitrile)$_2$dichloride] (57 mgs, 0.49 mmol) was added. The solvent was reduced under vacuum and hexane was added slowly to form a precipitate which was filtered off then redissolved in the minimum amount of CH_2Cl_2 and again precipitated, washed with further hexane and dried under vacuum to yield the title compound as an orange powder (47 mgs, 0.078 mmol 52 % yield). A sample suitable for X-ray analysis was prepared by slow diffusion of hexane into a CH_2Cl_2 solution of the product.

Anal. Calcd for $C_{22}H_{37}Cl_2F_3P_2Pd$: C, 44.20; H, 6.24 % found: C, 44.76; H, 6.38 %. ^{1}H-NMR (400 MHz; CD_3CN): δ 8.35 (m, 2 H, Ar**H** *o*-P), 7.71 (m, 2 H, Ar**H** *o*-CF_3), 2.25 (m, 1H, C**H**H), 2.02 (m, 1H, C**H**H), 1.78 (m, 1H, C**H**H), 1.60 (m, 1H, C**H**H), 1.46 (d, 9 H, $^3J_{H\text{-}P}$ = 14.7 Hz, P(C(C**H**$_3$)$_3$)(C(CH$_3$)$_3$)), 1.40 (d, 9 H, $^3J_{H\text{-}P}$ = 16.5 Hz, P(C(C**H**$_3$)$_3$)Ar), 1.32 (m, 9 H, $^3J_{H\text{-}P}$ = 14.3 Hz, P(C(CH$_3$)$_3$)(C(C**H**$_3$)$_3$)), 1.20 (m, 1H, C**H**H). ^{1}H{^{31}P}-NMR (400 MHz; CD_3CN): δ 8.38-8.33 (m, 2 H, Ar**H** *o*-P), 7.73-7.70 (m, 2 H, Ar**H** *o*-CF_3), 2.25 (m, 1H, C**H**H), 2.02 (m, 1H, C**H**H), 1.78 (m, 1H, C**H**H), 1.60 (m, 1H, C**H**H), 1.46 (s, 9 H, P(C(C**H**$_3$)$_3$)(C(CH$_3$)$_3$)), 1.40 (s, 9 H, P(C(C**H**$_3$)$_3$)Ar), 1.32 (s, 9 H, P(C(CH$_3$)$_3$)(C(C**H**$_3$)$_3$)), 1.20 (m, 1H, C**H**H). ^{13}C{H}-NMR (101 MHz, CD_3CN): δ 136.00 (d, $^2J_{C\text{-}P}$ = 10.2 Hz, Ar**C** *o*-P), 124.81 (dq, $^3J_{C\text{-}P}$ = 10.2 Hz, $^3J_{C\text{-}F}$ = 3.7 Hz, Ar**C** *o*-CF_3), 30.60 (d, $^2J_{C\text{-}P}$ = 2.9 Hz, P(C(**C**H$_3$)$_3$)Ar), 29.85 (d, $^2J_{C\text{-}P}$ = 2.9 Hz, P(C(**C**H$_3$)$_3$)(C(CH$_3$)$_3$)), 29.49 (d, $^2J_{C\text{-}P}$ = 3.4 Hz, P(C(CH$_3$)$_3$)(C(**C**H$_3$)$_3$)), 22.12 (dd, $^1J_{C\text{-}P}$ = 24.9; $^3J_{C\text{-}P}$ = 6.7 Hz, P-**C**H$_2$), 19.81 (s, CH$_2$-**C**H$_2$CH$_2$), 19.27 (dd, $^3J_{C\text{-}P}$ = 21.8, $^1J_{C\text{-}P}$ = 7.1 Hz, P-**C**H$_2$). ^{19}F-NMR (376 MHz, CD_3CN): δ -63.64 (s). ^{31}P{H}-NMR (162 MHz, CD_3CN): δ 41.42 (s), 31.21 (s). IR (cm^{-1}), KBr, 3050, 2900-3000, 2325, 1300. MS ES+: *m/z* 561.14 ([M - Cl]$^+$ requires 561.10).

7.3.15.2. Via $Pd_2(dba)_3$

$Pd_2(dba)_3$ (104 mgs, 0.11 mmol) was added to a stirred solution of di-*tert*-butyl(3-(*tert*-butyl(*para*-(trifluoromethyl)phenyl)phosphino)propyl)phosphine (96 mgs, 0.22 mmol) in THF (10 ml). After 1hour the dark orange solution was filtered and the solvent removed under vacuum yielding an orange oil. This was redissolved in diethyl ether and 2.5 eq of HCL in diethyl ether was added slowly to form the product as a yellow precipitate. After filtration the product was redisolved in CH_2Cl_2 and precipitated by the addition of hexane (49 mgs, 38 % yield) . Crystals suitable X-ray crystallography were obtained by slow diffusion of hexane into a CH_2Cl_2 solution of the product.

7.3.16. Di-*tert*-butyl(3-(diphenylphosphino)propyl)phosphineborane.



Di-*tert*-butyl(3-bromopropyl)phosphinoborane (70 mg, 0.25 mmol) was dissolved in THF (5 ml) and cooled to -78 °C. Potassium diphenylphosphide (0.275 mmol, 0.55 ml as a 0.5 M solution in THF) was added to this well stirred solution dropwise and the solution allowed to warm to room temperature gradually. At this stage ^{31}P-NMR indicated that the phosphide had been consumed and the solvent was reduced to about 1ml under vacuum, water was added followed by CH_2Cl_2. The organic layer was retained and washed two further times with water, dried over $MgSO_4$ and filtered before the solvent was removed under vacuum to yield a clear oil. Flash chromatography (gradient elution from 5-10 % diethyl ether in hexane) of this mixture was performed using degassed solvents under nitrogen pressure and fractions were collected in round bottomed flasks under a stream of argon and the solvent quickly removed by rotary evacuation and the resulting oil stored under argon. Fractions containing the product were identified by ^{31}P{H}NMR and combined and a further short column (20 % diethyl ether/hexane) was performed to remove any oxide formed during fraction collection, and the solvent removed under vacuum to give the title compound.

^{1}H-NMR (300 MHz; C_6D_6): δ_H 0.4 (3 H, m, B**H**$_3$), 1.1 (18 H, d, $^3J_{H-P}$ = 13 Hz, 6(CH_3)), 1.65 (2 H, m, C**H$_2$**), 1.75 (2 H, m, C**H$_2$**), 2.1 (2 H, t, $^3J_{H-H}$ = 7 Hz, $(Ph)_2$P-C**H$_2$**), 7.2 – 7.4 (10 H, m, 10Ar**H**). ^{1}H{^{31}P}-NMR (300 MHz; C_6D_6): δ_H 0.4 (3 H, m, B**H**$_3$), 1.1 (18 H, s, 6(CH_3)), 1.65 (2 H, m, C**H$_2$**), 1.75 (2 H, m, C**H$_2$**), 2.1 (2 H, t, $^3J_{H-H}$ = 7 Hz, $(Ph)_2$P-C**H$_2$**), 7.2 – 7.4 (10 H, m, 10Ar**H**). ^{13}C{H}-NMR (75.5 MHz; $CDCl_3$): δ_c 18.4 (d d, $^1J_{C-P}$ = 29 Hz, $^3J_{C-P}$ = 13 Hz, **C**H_2-P(C(CH_3)$_3$)$_2$.BH_3), 20.7 (d, $^2J_{C-P}$ = 17 Hz, **C**H_2 centre), 26.7 (d, $^2J_{C-P}$ = 1 Hz, **C**H_3). 29.5 (d d, $^1J_{C-P}$ = 12 Hz, $^3J_{C-P}$ = 12 Hz, **C**H_2-P$(Ph)_2$), 31.0 (d, $^1J_{C-P}$ = 27 Hz, **C**(CH_3)$_3$). ^{31}P{^{1}H}-NMR (121.5 MHz; $CDCl_3$): δ_P 45.5 (br m, **P**(C(CH_3)$_3$)$_2$.BH_3), 17.2 (s, **P**$(Ph)_2$). MS ES+: *m/z* 409.11 ($[M + Na]^+$ requires 409.24).

7.4. Catalytic Experiments.

7.4.1. Typical Hydroxycarbonylation Procedure.

Lithium chloride (8.4 mgs, 0.20 mmol), *para*-toluenesulphonic acid (34.4 mgs, 0.20 mmol), [Pd1,3-bis[(*ortho*-trifluoromethylphenyl)t-butylphosphine]propane]Cl_2 (6.8 mgs, 0.01 mmol) and 1,3-bis[(*ortho*-trifluoromethylphenyl)t-butylphosphine]propane (15 mgs, 0.03 mmol) were weighed into a Biotage 0.5-2 ml microwave vial, along with a stirring bar which was sealed with a crimp cap and put under an inert atmosphere. Styrene (114 µl, 1 mmol), water (45 µl, 2.5 mmol) and degassed butan-2-one (1.5 ml) were added before the cap was pierced with a capillary tube. The reaction tube was then placed in an autoclave which was purged with CO three times then pressurized to 50 bar then placed in a heating jacket and heated to 110 °C. After 16 hours the autoclave was cooled to room temperature and the pressure released slowly. The solvent was then removed from the reaction mixture and the residue dissolved in toluene and filtered to remove precipitate. The filtrate was then extracted with 3x saturated $NaHCO_3$ and the combined extracts acidified with conc. HCl until it remained decidedly acidic by litmus paper. This was then extracted using 3x dichloromethane and the combined extracts dried over $MgSO_4$, filtered and the solvent removed to give the viscous product, a mixture of 2-phenylpropanoic and 3-phenylpropanoic acids.
2-Phenylpropionic acid H^1 NMR δ: 1.45 (3H, d, C**H**$_3$), 3.7 (1H, q, C**H**), 7.2 (5H, m, Ar**H**).
3-Phenylpropanoic acid H^1 NMR δ: 2.6 (2H, t, CO-C**H**$_2$), 2.9 (2H, t, Ar-C**H**$_2$) 7.2 (5H, m, Ar**H**).

7.4.2.1. 2,2-difluoro-1,3-diphenylpropane-1,3-diol (catalytic reduction by H_2/[RuBINAP])

a) Catalyst preparation (from [Ru2(C6H6)$_2$Cl$_2$])

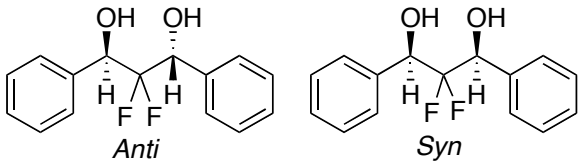
To a dried microwave tube was added benzeneruthenium chloride dimer (8.3 mg, 0.017 mmol) and S-BINAP (20.7 mg, 0.033 mmol) and the air displaced with argon. Dry THF (3ml) was added and the mixture heated in a microwave at 120 °C for 10 minutes. The solvent was removed under vacuum to give the catalyst as a dark red oil.

b) Reduction by H_2/[RuBINAP] catalyst

2,2-Difluoro-1,3-diphenylpropane-1,3-dione (0.866 g, 3.33 mmol) was dissolved in dry THF (20 ml) and the catalyst (1 mol% relative to the diketone) from the previous reaction added as a solution in THF (5ml). This mixture was then transferred to an autoclave which was quickly sealed before being purged and then pressurised with hydrogen (50 Bar) and heated to 60°C. After stirring overnight the solution was reduced to dryness under vacuum and the residue recrystallised from hot CH_2Cl_2 yielding the product as the *anti* isomer in fine white crystals (0.675 g, 2.55 mmol 77 % yield).

Anal. Calcd for $C_{15}H_{14}F_2O_2$: C, 68.17; H, 5.34 % found: C, 68.52; H, 5.12 %.
^{1}H-NMR (300 MHz; $CDCl_3$): *anti* δ_H 3.1 (2 H, br s, O-**H**), 5.0 (2 H, t, $^3J_{H-F}$ = 11 Hz, 2C**H**OH), 7.35 (10 H, m, 10 Ar-**H**). *syn* 2.6 (2 H, br s, O-**H**), 4.90 (2 H, d d, $^3J_{H-F}$ = 9 Hz, $^3J_{H-F}$ = 15 Hz, 2C**H**OH), 7.35 (10 H, m, 10 Ar-**H**). ^{1}H{^{19}F}-NMR (300 MHz; $CDCl_3$): *anti* δ_H 3.0 (2 H, br s, O-**H**), 5.0 (2 H, s, 2C**H**OH), 7.35 (10 H, m, 10 Ar-**H**).
^{13}C{H}-NMR (75 MHz; $CDCl_3$): *anti* δ_c 70.44 (t, $^2J_{C-F}$ = 28 Hz, **C**HOH), 121.5 (t, $^1J_{C-F}$ = 250.5 Hz; **C**F$_2$), 128.6, 128.1, 128.0 (Ar**C**H), 138.8 (Ar**C**). ^{19}F-NMR (282 MHz; $CDCl_3$): *anti* δ_F 119.2 (2 F, t, $^3J_{F-H}$ = 11 Hz). ^{19}F{^{1}H}-NMR (282 MHz; $CDCl_3$): *anti* δ_F 119.2 (s). MS ES-: *m/z* 263.04 ([M-H]$^-$ requires 263.09), MS ES+: *m/z* 287.04 ([M+Na]$^+$ requires 287.09)

7.4.2.2. 2,2-difluoro-1,3-diphenylpropane-1,3-diol (5.2) (reduction by $NaBH_4$).



2,2-Difluoro-1,3-diphenylpropane-1,3-dione (150 mg, 0.57 mmol) was dissolved in 10 ml dry THF and cooled to 0 °C prior to the addition of $NaBH_4$ (65 mg, 1.73 mmol). After 24 hours, the solvent was removed under vacuum and the residue was partitioned between CH_2Cl_2 and a saturated NH_4Cl solution and the organic layer washed two further times with water before it was dried ($MgSO_4$) and the solvent removed to yield the crude product as a brown oil (*anti:syn* 1:1.1). Recrystallisation from CH_2Cl_2 yielded the product as a white solid. ^{1}H-NMR showed some diastereo-enrichment on crystallisation (*anti:syn* 1:1.3). Only proton NMR is reported for the *syn* isomer.

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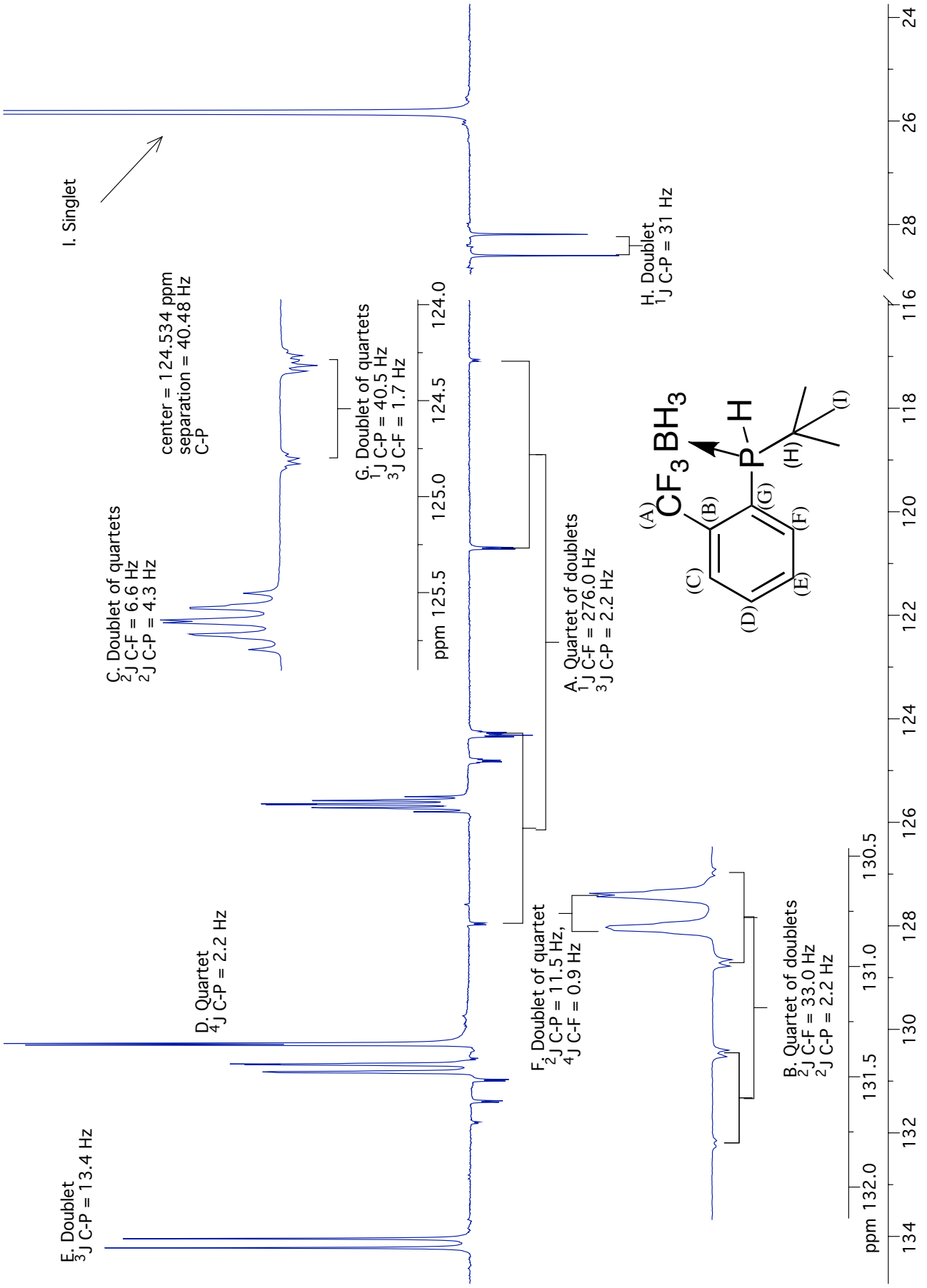
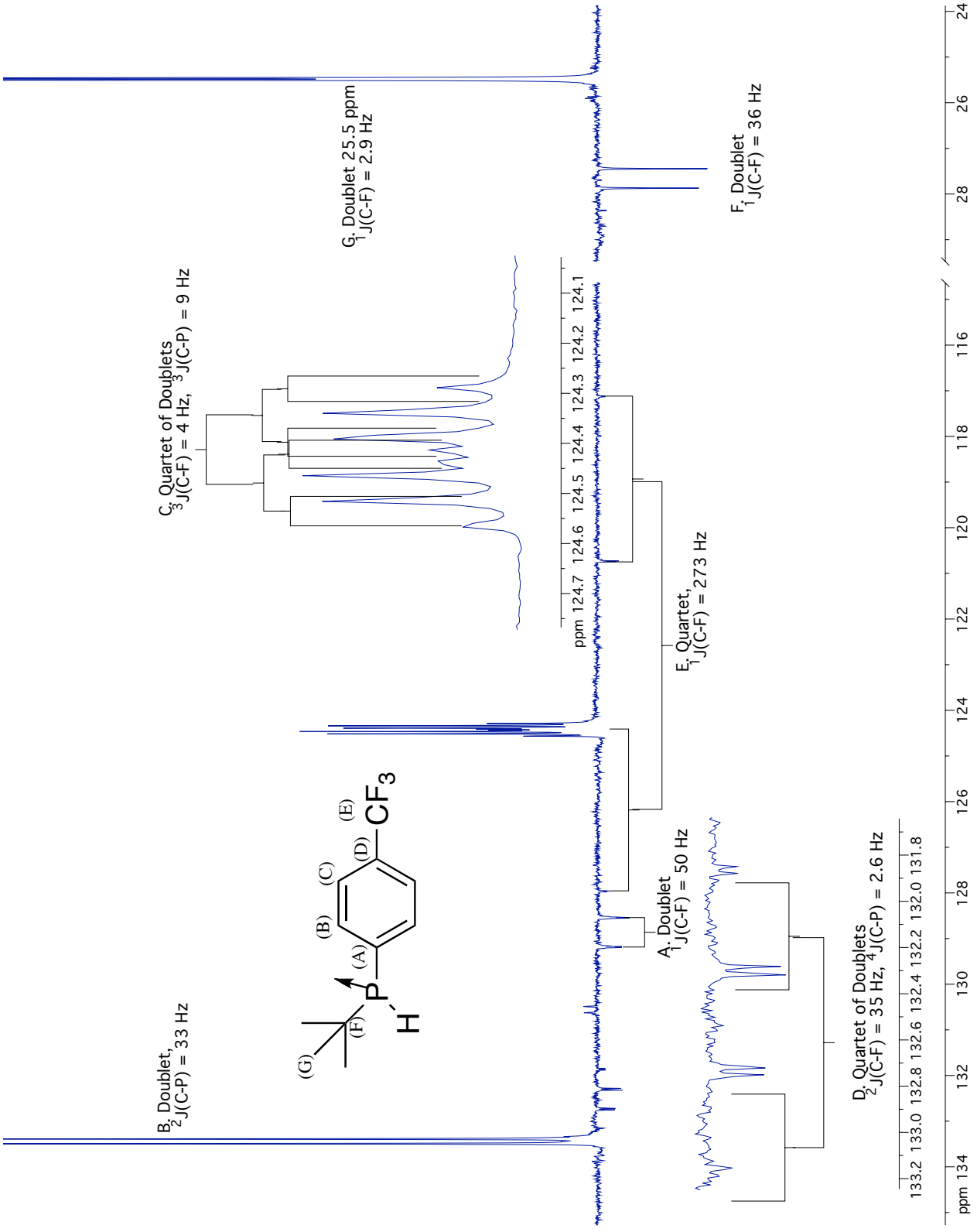
$^{13}C\{H\}$ NMR Spectrum of 2.4



$^{13}C\{H\}$ NMR Spectrum of 2.5



Appendix ii

Experiment No	Substrate	time (hours)	Pd complex	Amount Pd complex (mol%)	Added ligand (mol%)	Temp. (°C)	Pressure (Bar)	B/L Ratio	Selectivity	Yield
281005	styrene	2	3.14-rac	0.50	0.00	115	80	7.1	87.6%	52%
050406 A	styrene	16	3.14-rac	0.50	0.00	120	50	20.9	95.4%	51%
050406 B	styrene	16	Pd(DPPP)Cl2	0.50	0.00	120	50	3.8	79.0%	2%
020506 A	styrene	2	Pd(DTBPX)Cl2	2.00	0.00	130	50	10.6	91.3%	72%
020506 B	styrene	2	3.14-rac	2.00	0.00	130	50	9.6	90.6%	40%
020506 C	styrene	2	Pd(DPPP)Cl2	2.00	0.00	130	50	4.8	82.7%	2%
020506 D	styrene	2	Pd.DBA	2.00	6.00 (**3.3**)	130	50	8.0	88.8%	95%
40506	styrene	2	Pd.DBA	0.50	1.5 (**3.3**)	130	50	10.2	91.1%	52%
160506 A	**Methoxyvinylnapthalene**	**2**	**3.14-rac**	**0.50**	**0.00**	**110**	**50**	**46.0**	**97.9%**	**10%**
160506 B	**Fluorostyrene**	**2**	**3.14-rac**	**0.50**	**0.00**	**110**	**50**	**7.0**	**87.5%**	**23%**
160506 C	Styrene	2	3.14-rac	0.50	0.00	110	50	38.1	97.4%	26%
160506 D	styrene	2	3.14-rac	0.50	1.5 (**3.3**)	110	50	17.5	94.6%	46%
170506 A	**Methoxyvinylnapthalene**	**2**	**2.16**	**1.00**	**0.00**	**120**	**50**	**54.1**	**98.2%**	**60%**
170506 B	**Fluorostyrene**	**2**	**2.16**	**1.00**	**0.00**	**120**	**50**	**119.0**	**99.2%**	**38%**
180506 A	styrene	2	2.16	1.00	0.00	120	50	111.1	99.1%	82%
180506 B	**Methoxystyrene**	**2**	**2.16**	**1.00**	**0.00**	**120**	**50**	**45.2**	**97.8%**	**35%**
180506 C	styrene	2	2.16	1.00	0.00	120	50	89.9	98.9%	88%
180506 D	**Methoxystyrene**	**2**	**2.16**	**1.00**	**0.00**	**120**	**50**	**53.6**	**98.2%**	**41%**
060606 A	styrene	2	Pd.DBA	0.25	0.50 (**3.3**)	110	50	26.1	96.3%	13%
060606 B	styrene	2	Pd.DBA	0.25	1.00 (**3.3**)	110	50	18.7	94.9%	23%
060606 C	styrene	2	Pd.DBA	0.50	1.00 (**3.3**)	110	50	23.9	96.0%	31%
060606 D	styrene	2	Pd.DBA	0.50	2.00 (**3.3**)	110	50	17.0	94.5%	44%
080606 A	styrene	16	Pd.DBA	0.50	1.00 (**3.3**)	110	50	7.0	87.4%	63%
080606 B	styrene	16	Pd.DBA	0.50	1.50 (**3.3**)	110	50	11.7	92.1%	63%
080606 C	styrene	16	Pd.DBA	0.50	2.00 (**3.3**)	110	50	12.8	92.8%	60%
40706	styrene	16	Pd.DBA	0.50	1.50 (**3.3**)	130	50	15.7	94.0%	41%
280606 A	styrene	16	Pd.DBA	1.00	1.00 (**3.3**)	110	50	25.2	96.2%	39%
280606 B	styrene	16	Pd.DBA	1.00	4.00 (**3.3**)	110	50	10.9	91.6%	64%
280606 C	styrene	16	Pd.DBA	2.00	4.00 (**3.3**)	110	50	5.8	85.3%	76%
020706 A	styrene	16	Pd.DBA	1.00	3.00 (**3.3**)	120	50	13.2	93.0%	65%

Experiment No	Substrate	time (hours)	Pd complex	Amount Pd complex (mol%)	Added ligand (mol%)	Temp. (°C)	Pressure (Bar)	B/L Ratio	Selectivity	Yield
020706 B	styrene	16	Pd.DBA	0.50	1.50 (**3.3**)	120	50	14.1	93.4%	43%
020706 C	styrene	16	3.14-rac	1.00	0.00	120	50	13.2	93.0%	36%
020706 D	styrene	16	3.14-rac	1.00	3.00 (**3.3**)	120	50	11.3	91.9%	86%
070706 A	styrene	16	3.14-rac	1.00	3.00 (**3.3**)	120	50	13.4	93.0%	73%
070706 B	**Fluorostyrene**	**16**	**3.14-rac**	**1.00**	**3.00 (3.3)**	**120**	**50 Bar**	**9.4**	**90.4%**	**76%**
070706 C	**Methoxystyrene**	**16**	**3.14-rac**	**1.00**	**3.00 (3.3)**	**120**	**50 Bar**	**14.8**	**93.7%**	**50%**
070706 D	**Methoxyvinylnapthalene**	**16**	**3.14-rac**	**1.00**	**3.00 (3.3)**	**120**	**50 Bar**	**9.6**	**90.6%**	**41%**
300307 A	styrene	16	3.16-rac	1.00	0.00	120	50	24.9	96.1%	82%
300307 B	styrene	16	3.16-rac	1.00	3.00 (**3.11-rac**)	120	50	1.1	52.4%	1%
070407 A	styrene	16	3.16-rac	1.00	3.00 (**3.11-rac**)	120	50	1.0	49.8%	1%
070407 B	styrene	16	3.16-rac	0.50	0.00	120	50	29.0	96.7%	47%
070407 C	styrene	16	3.16-rac	0.25	0.00	120	50	0.6	37.4%	13%
070407 D	styrene	16	Pd(DPPP)Cl2	5.00	0.00	120	50	75.3	98.7%	52%
010507 A	styrene	16	PdDiPPF)Cl2	1.00	0.00	120	50	58.0	98.3%	45%
010507 B	styrene	16	3.15	1.00	0.00	120	50	15.2	93.8%	20%
010507 C	styrene	16	3.17	1.00	0.00	120	50	27.1	96.4%	83%
010507 D	styrene	16	3.18	1.00	0.00	120	50	52.3	98.1%	71%
070507 A	styrene	2	3.16-rac	2.00	0.00	130	50	14.7	93.6%	82%
070507 B	styrene	2	3.17	2.00	0.00	130	50	9.4	90.4%	48%
070507 C	styrene	2	3.18	2.00	0.00	130	50	23.2	95.9%	42%
070507 D	styrene	2	3.15	2.00	0.00	130	50	3.0	74.8%	18%
080507 A	styrene	16	3.16-rac	1.00	0.00	130	50	21.9	95.6%	83%
080507 A	styrene	16	3.15	1.00	0.00	130	50	4.1	80.3%	46%
080507 A	styrene	16	3.17	1.00	0.00	130	50	11.9	92.2%	65%
010707 A	styrene	16	3.14-rac	1.00	0.00	120	30	30.8	96.9%	72%
010707 B	styrene	16	3.16-rac	1.00	0.00	120	30	43.0	97.7%	81%
010707 C	styrene	16	3.17	1.00	0.00	120	30	25.5	96.2%	87%
010707 D	styrene	16	3.18	1.00	0.00	120	30	75.5	98.7%	84%
020707 A	styrene	16	3.14-rac	1.00	0.00	120	10	8.3	89.3%	12%
020707 B	styrene	16	3.16-rac	1.00	0.00	120	10	3.7	78.6%	21%

Experiment No	Substrate	time (hours)	Pd complex	Amount Pd complex (mol%)	Added ligand (mol%)	Temp. (°C)	Pressure (Bar)	B/L Ratio	Selectivity	Yield
020707 C	styrene	16	3.17	1.00	0.00	120	10	1.5	59.7%	7%
020707 D	styrene	16	3.18	1.00	0.00	120	10	4.8	82.6%	15%
030707 A	styrene	16	3.17	1.00	3.00 (**3.10**)	120	50	9.3	90.3%	62%
030707 B	styrene	16	3.18	1.00	3.00 (**3.12**)	120	50	0.2	18.3%	44%
030707 C	styrene	16	3.17	0.50	0.00	120	50	25.8	96.3%	64%
030707 D	styrene	16	3.18	0.50	0.00	120	50	35.4	97.3%	23%
040707 A	styrene	16	3.14-rac	1.00	0.00	100	50	56.3	98.3%	82%
040707 B	styrene	16	3.16-rac	1.00	0.00	100	50	66.7	98.5%	83%
040707 C	styrene	16	3.17	1.00	0.00	100	50	13.3	93.0%	71%
040707 D	styrene	16	3.18	1.00	0.00	100	50	23.0	95.8%	42%
no LiCl	styrene	16	3.16-rac	1.00	0.00	100	50	0.2	15.4%	52%
no TsOH	styrene	16	3.16-rac	1.00	0.00	100	50	0.4	28.6%	18%
NaBF4 LiCl	styrene	16	3.16-rac	1.00	0.00	100	50	0.7	40.0%	12%
NaI TsOH	styrene	16	3.16-rac	1.00	0.00	100	50			0%
HCL/LiCl	styrene	16	3.16-rac	1.00	0.00	100	50	21.7	95.6%	59.0
HCl	styrene	16	3.16-rac	1.00	0.00	100	50	37.0	97.4%	73.0

Enantio- and Diastereoselective Hydrogenation of a Fluorinated Diketone

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Palladium complexes of new bulky fluorinated diphosphines give particularly active and regioselective catalysts for hydroxycarbonylation of styrene†

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