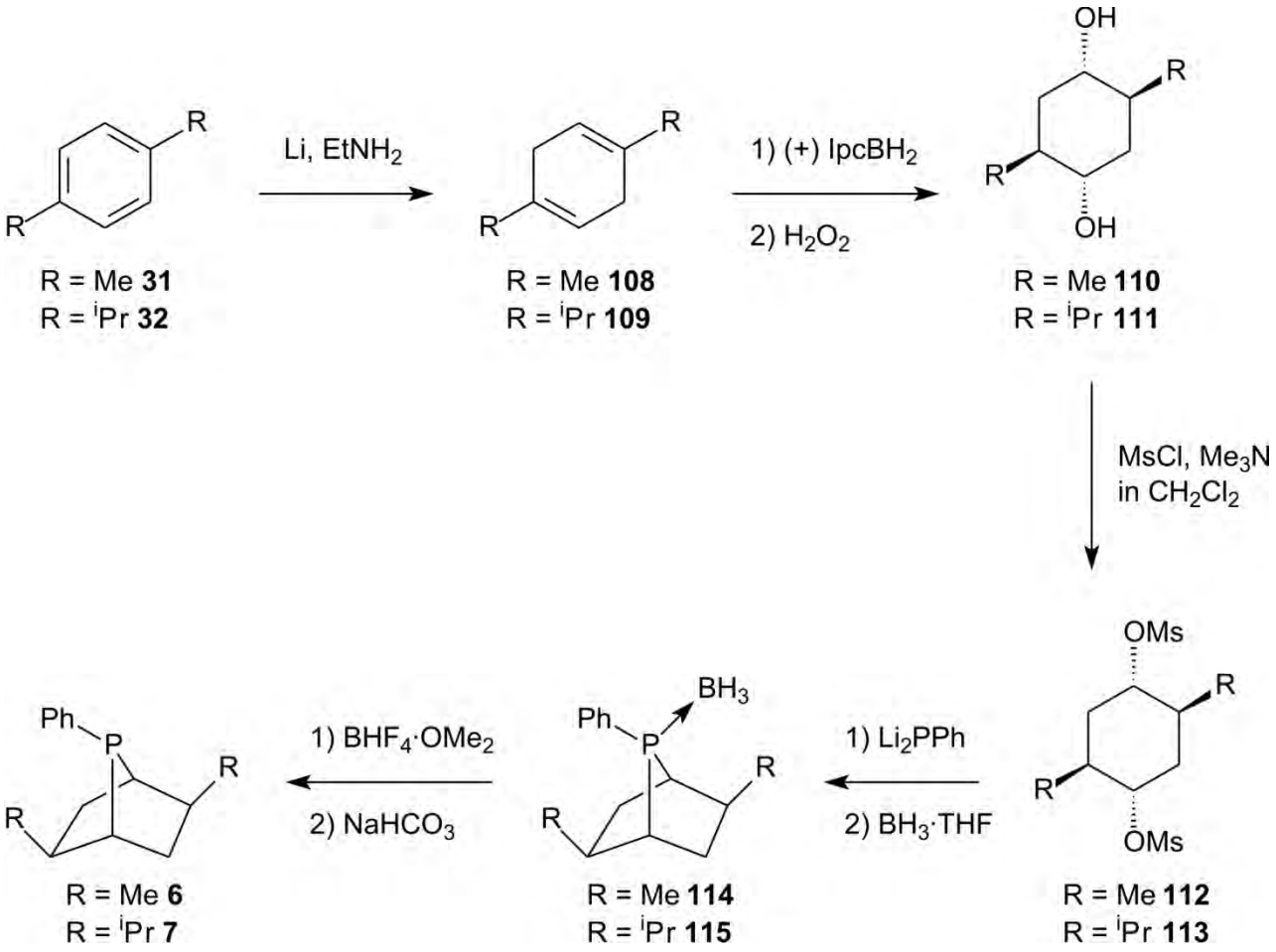
4. Preliminary Experimental Study

4.1 Introduction

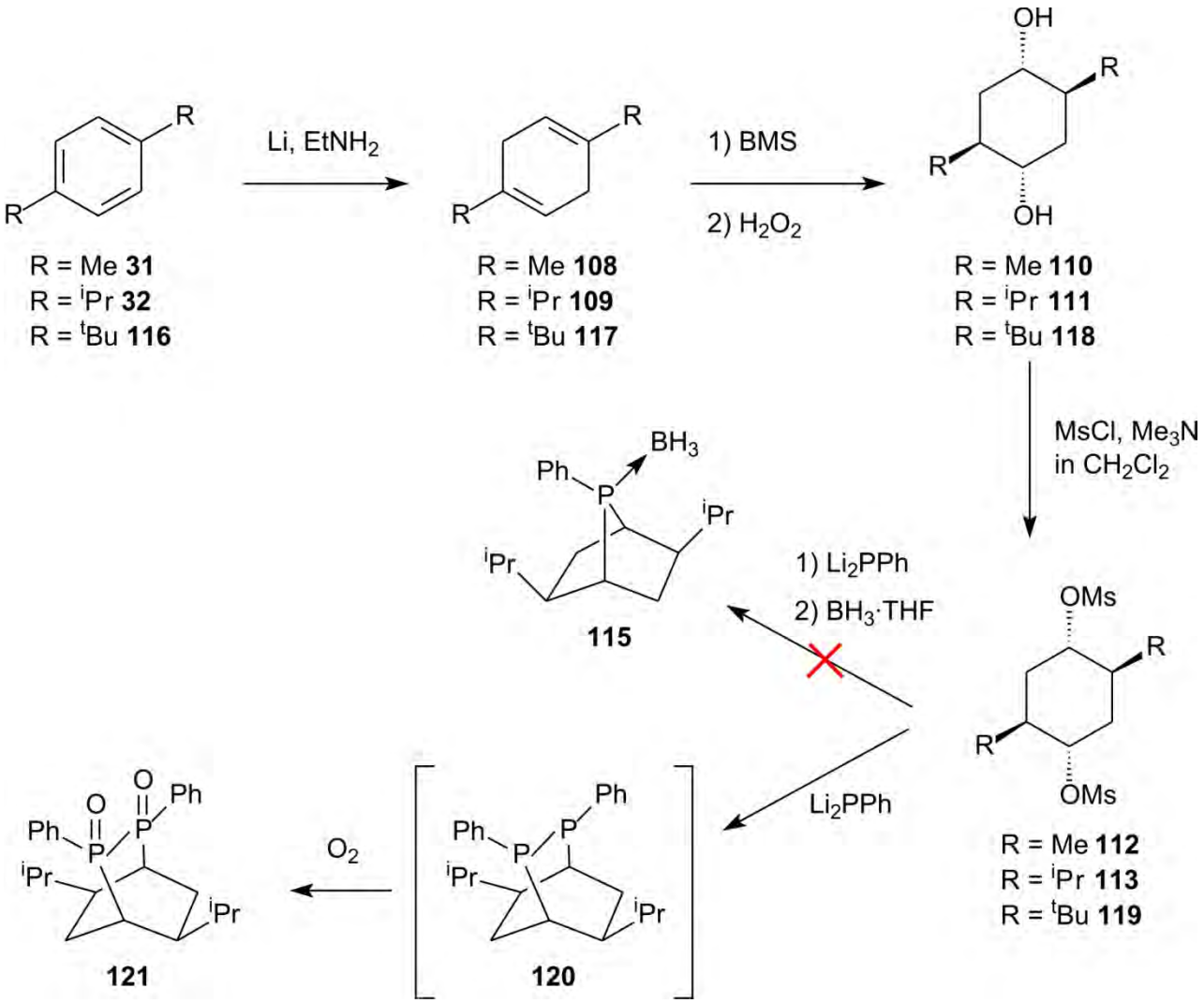
For a ligand to be useful in the synthesis of a new precatalyst, the following three criteria should be kept in mind: cost, ease of synthesis, and the environmental impact of the synthesis. The syntheses of **6** and **7** were first reported by Zhu *et al*.[1] in 1997 (**Scheme 4.1**). No evidence could be found in the literature that **6** or **7** have been used as ligands for metathesis catalysts. The compounds **6** and **7** offer a potential method to manipulate the steric bulk and electronic properties of the ligands. By manipulating the functional group R in the starting compound, ligands can be synthesised that can potentially be used to synthesise new Grubbs 1 type precatalysts. The aim of this preliminary experimental investigation was to study the synthetic feasibility of **6**, **7** and **8** according to the three criteria listed and not to synthesise new Grubbs precatalysts.



Scheme 4.1 The literature synthesis of the phosphine ligands **6** and **7**.

4.2 Discussion

In this study, the depicted syntheses in **Scheme 4.2** were done. Minor adjustments were made where the cost of the reagents required a different approach to that of **Scheme 4.1**.



Scheme 4.2 The preliminary experimental study of phosphine ligand synthesis.

The Birch reduction of **31**, **32** and **116** to **108**, **109** and **117**, as described by Kwart *et al*.,[2] requires the use of anhydrous ethylamine. A 70% amine in water solution was distilled. Synthesis with the amine distillate gave identical yields to that reported by Kwart *et al*.[2] for all the Birch reductions. The mixtures were used as is in the next reactions, since Kwart *et al*.[2] showed that a slightly purer product could only be obtained with significant loss of product.

The synthesis of the diols **110**, **111** and **118** with monoisopinocamphenylborane ($IpcBH_2$), **122** (**Figure 4.1**), according to the method of Lane *et al.,*[3] again proved to be a very expensive route to follow. Fortunately, Sun *et al.*[4] reported that the same reaction could be done with the less expensive borane dimethyl sulphide complex (BMS). The yields of 39% for **110** and 43% for **111**

are slightly lower than those obtained by using $IpcBH_2$,[3] but from a cost point of view this is acceptable. No evidence could be found in literature that the diol **118** has been synthesised before. From an environmental point of view, large quantities of chemicals are used to synthesise several unusable by-products. The racemic mixture of the diols also proved to be troublesome to separate from each other to obtain the desired stereoisomer. The ^{t}Bu-diol could in one instance be obtained in the pure form by recrystallisation from ethyl acetate, but in all instances time-consuming column separation was still necessary to obtain a pure product. Due to the low solubility of the diols in the eluent, it was necessary to dry-load the compounds onto silica gel. The method is described in **§ 4.3.3** below. For all the compounds, a pure compound was only obtained with this method if a recrystallisation was performed beforehand to separate out most of the undesired stereoisomer of the diol. The large quantities of the diols needed required that several columns had to be run for every batch of diol synthesised. From an environmental and cost point of view, it is not ideal that a large quantity of non-reusable solvent had to be used every time.

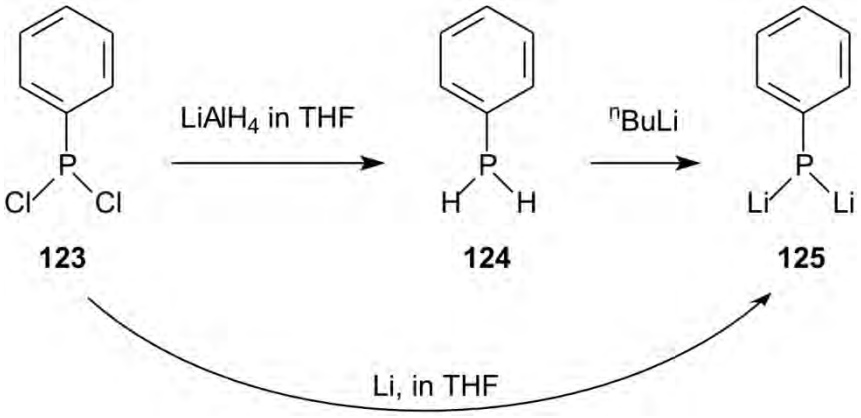
122

Figure 4.1 The monoisopinocamphenylborane ($IpcBH_2$) **122**.

The synthesis of the bis(methanesulphonate) esters **112**, **113** and **119** proceeded as described by Chen *et al*.[5] without any problems. High yields of greater than 99% could be obtained every time. XRD data were obtained for **113** and **119** (**Figures 4.6** and **4.7**). The data show sterically crowded compounds. The steric bulk of the isopropyl and tertiary butyl groups can potentially hinder the attack of the phosphine in the next step of the reaction.

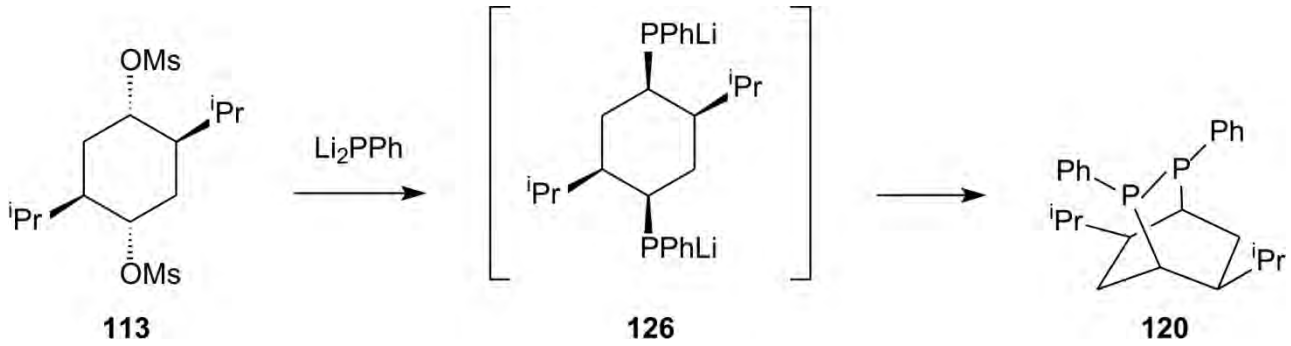
The synthesis of the phosphine ligand proved to be very problematic. Phenylphosphine, **124** (**Scheme 4.3**), is very flammable and highly poisonous. Shipping costs made the commercial anhydrous reagent expensive and it was decided to synthesise the reagent on site. A synthesis method in a tetraglyme solution was reported by Bourumeau *et al.*[6] It was pointed out by Otto[7] that the same result could be achieved in THF, which is more convenient since the phosphine ligand synthesis has to be done in THF. The synthesis of **124** was performed successfully with very little impurities present in the product according to GC-MS analysis. The next step was to synthesise the dilithium phenylphosphine **125**. There are two possible methods available: the direct synthesis method of Riermeier *et al.*[8] from **123** with lithium metal and the synthesis method of Zhu *et al*.[1] with ^{n}BuLi from **124**. Riermeier *et al.*[8] refluxed **123** with lithium metal, which led to several unwanted by-products forming according to the GC-MS analyses. The longer the mixture was refluxed, the more

impurities formed. It was much easier to synthesise **125** according to the method of Zhu *et al*.[1] from ^{n}BuLi and **124** without the formation of the same impurities.



Scheme 4.3 The synthesis of dilithium phenylphosphine **125**.

Once **125** was synthesised, the attempted synthesis of compound **115** was done. This compound is the main focus of the rest of the discussion since the available literature indicated that it should provide the highest yield.[1] Only the synthesis of **115** was attempted for the purposes of this feasibility study. The desired product could not be isolated. The formation of the diphosphine **120** was observed instead. The reason for this is still not clear at this point in time. Due to the reported[1] inversion of symmetry when starting with **113** to form the phosphine, a normal S_N2 type reaction was expected. The XRD analysis of **113** (**Figure 4.6**) shows a distorted chair conformation, while the dioxide **121** shows a boat conformation according to XRD analysis (**Figure 4.9**). Why the phosphine reacts with itself before completing the bridging reaction could not be explained, since this diphosphine compound has not been reported in literature. The initial thought was that due to a solution of **113** being added to a solution of **125**, the higher concentration of the phosphine might lead to it reacting at both ends of the substrate to form **126** and only thereafter bridging takes place (**Scheme 4.4**).



Scheme 4.4 A possible method of diphosphine formation.

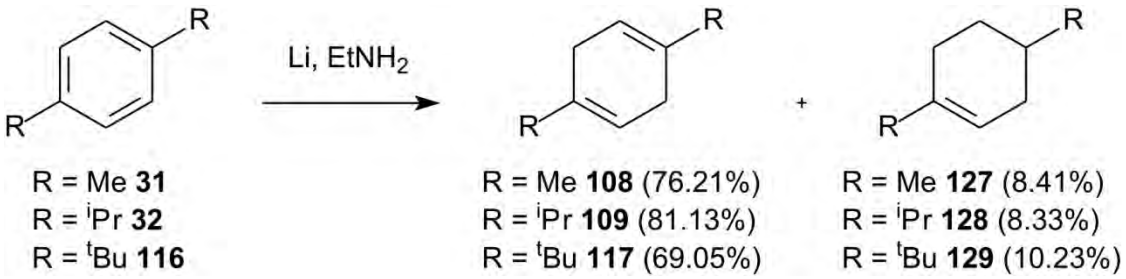
To investigate this, the order of addition was changed so that the phosphine was always the limiting reagent. This did not affect the formation of the diphosphine at all. Next, it was thought that a change in temperature might affect the products formed since up to this point all the reactions were done at room temperature. The thought was that one of the products might be the kinetic product and one the thermodynamic product so a change in temperature should provide an indication of this. The phosphine synthesis reaction with **113** was repeated at -78 °C and by refluxing it at 70 °C without having an influence on the products formed.

4.3 Experimental procedures

4.3.1 Reagents and general procedures

All reactions of the phosphorous compounds with the organolithium reagents were done under an argon atmosphere in oven-dried flasks. All other air-sensitive reactions were done under either a nitrogen or argon atmosphere. Dry diethyl ether and THF were prepared by refluxing the solvents over Na/benzophenone, and distilling an aliquot as required. Dry dichloromethane was prepared by refluxing the solvent over $CaCl_2$, and distilling an aliquot as required. All reagents were received from Sigma-Aldrich unless stated otherwise. All reagents were used without further purification unless stated otherwise. Afrox supplied all the gases used during this study. When transferring one solution from one flask to another, under inert conditions, cannula needles were used. The needle was flushed with a stream of argon before transferring liquids.

4.3.2 Birch reduction of 1,4-disubstituted-benzenes



Scheme 4.5 Birch reduction of **31**, **32** and **116** to **108**, **109** and **117**.

General procedures for all Birch reductions

A three-necked, oven-dried, 500-ml round-bottom flask equipped with thermometer, magnetic stirrer, and a nitrogen inlet and outlet was used for all reductions. The flask was cooled in an ice bath and kept at 0 °C for the duration of the reaction. The aromatic substrate, 125 mL ethylamine (distilled from a 70% solution in water, boiling point (bp) of the fraction collected: 30 °C), and the first portion of alcohol were added. The alcohol and lithium were usually added in three portions.

The alcohol was always added before the lithium and was always in slight excess. The lithium was cut into small pieces and washed with petroleum ether (bp 40-60 °C). The lithium was added when the flask cooled to 0 °C. After two hours, the second portion of alcohol and lithium was added and after four hours the third and last portion of alcohol and lithium was added. The total reaction time after the first lithium addition was six hours. The reaction was quenched by adding 200 mL of ice water followed by 300 mL diethyl ether. In some cases, a white cake forms upon the addition of water, but this breaks up when the diethyl ether is added. The aqueous layer was extracted with two 150 mL portions of diethyl ether. The combined diethyl ether layers were washed with 3 x 50 mL of a 10% HCl solution to remove the remaining ethylamine, thereafter the reaction mixture was washed with two 100 mL portions of water and dried over magnesium sulphate. The diethyl ether solution was then rotary evaporated or fractional distillation was performed to isolate the crude product.

Birch reduction of ρ-xylene (**31**) to 1,4-dimethyl-1,4-cyclohexadiene (**108**):

A solution of 15.5 mL of p-xylene (**31**) in ethylamine was reduced with three 7.2 mL portions of ethanol and three portions of lithium (first portion 0.7171 g, second portion 0.7134 g, third portion 0.7176 g). GC-MS analysis after fractional distillation showed that the product distribution was as follows: 76.21% diolefin (**108**), 8,41% monoolefin (**127**) and 15.38% unreacted (**31**). In the subsequent reaction, the product mixture was used as is.

Mass spectrum: (GC-MS-EI): (**31**) *m/z* 106 ([M^+]); (**108**) *m/z* 108 ([M^+]); (**127**) *m/z* 110 ([M^+]).

Birch reduction of ρ-diisopropyl-benzene (**32**) to 1,4-diisopropyl-1,4-cyclohexadiene (**109**):

A solution of 12.75 mL of p-diisopropyl-benzene (**32**) in ethylamine was reduced with three 7.2 mL portions of ethanol and three portions of lithium (first portion 0.7058 g, second portion 0.7081 g, third portion 0.7098 g). GC-MS analysis after fractional distillation showed that the product distribution was as follows: 81.13% diolefin (**109**), 8.33% monoolefin (**128**) and 10.54% unreacted (**32**). In the subsequent reaction, the product mixture was used as is.

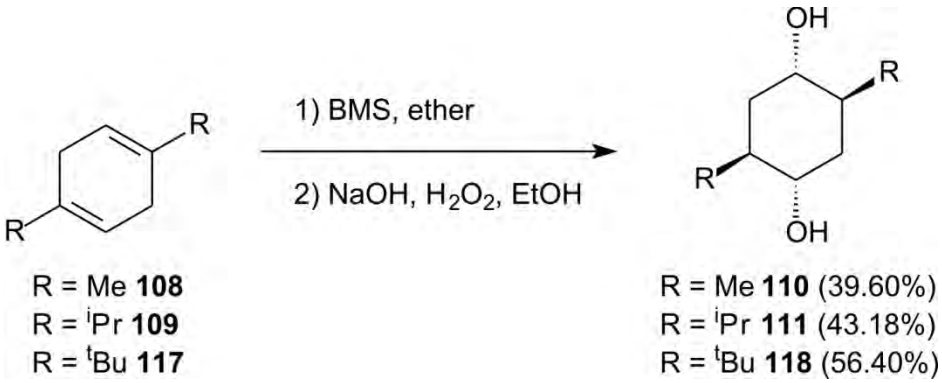
Mass spectrum: (GC-MS-EI): (**32**) *m/z* 162 ([M^+]); (**109**) *m/z* 164 ([M^+]); (**128**) *m/z* 166 ([M^+]).

Birch reduction of ρ-di-tert-butyl-benzene (**116**) to 1,4-di-tert-buthyl-1,4-cyclohexadiene (1**17**):

A solution of 12.4062 g of p-di-tert-butylbenzene (**116**) in ethylamine was reduced with three 7.2 mL portions of ethanol and three portions of lithium (first portion 0.7094 g, second portion 0.7092 g, third portion 0.7085 g). GC-MS analysis after concentration showed that the product distribution was as follows: 69.05% diolefin (**117**), 10.23% monoolefin (**129**) and 20.72% unreacted (**116**). In the subsequent reaction, the product mixture was used as is. mp 55-60 °C, Lit. 53-56 °C.

Mass spectrum: (GC-MS-EI): (**116**) *m/z* 190 ([M^+]); (**117**) *m/z* 192 ([M^+]); (**129**) *m/z* 194 ([M^+]).

4.3.3 Hydroboration of olefins with borane dimethyl sulphide (BMS)



Scheme 4.6 Hydroboration of **108**, **109** and **117** to **110**, **111** and **118**.

General procedures for all hydroboration reactions with BMS

All starting materials, including the borane dimethyl sulphide complex (BMS), were used directly as obtained from the Aldrich Chemical Co. Since BMS is decomposed by atmospheric moisture, all manipulations of liquid BMS and the hydroboration reactions were carried out in dry glassware under a nitrogen atmosphere. The method described below is based on the method of Lane *et al*.[3] with BMS being used instead of (+)-IpcBH$_2$, since Sun *et al*.[4] found that hydroboration of these diolefins can be successfully achieved using this less expensive borane.

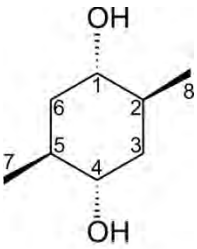
Hydroboration of the 1,4-di-methyl-alkene mixture (**31**, **108** and **127**) to **110**:

A dry 500 mL flask equipped with a mechanical stirrer, pressure-equalising dropping funnel, and reflux condenser was flushed with dry nitrogen and maintained under a positive nitrogen pressure. In the flask was placed 13.5232 g of the 1,4-dimethyl alkene mixture (**31** (39.96%), **108** (53.07%) and **127** (7.03%)), obtained as described above, dissolved in 200 mL dry diethyl ether and cooled to 0-5 °C with an ice water bath. Hydroboration was achieved by the dropwise addition of 12.65 mL BMS over 30 minutes. Following the addition of the borane, the cooling bath was removed and the solution was stirred for 3 hr at 20-25 °C. Then 150 mL ethanol was added dropwise, otherwise a vigorous effervescence takes place. Directly after 50 mL 3 *N* aqueous sodium hydroxide was added; again, caution should be taken since the first drops cause a vigorous effervescence. After cooling to 0-5 °C in an ice water bath, 56 mL hydrogen peroxide (30% solution) was added dropwise at such a rate that the reaction mixture never warmed to more than 35 °C. Immediately following the addition of the peroxide (1 hour), the cooling bath was removed and the reaction mixture was heated at reflux for one hour. The reaction mixture was then poured into 600 mL of ice water. After adding 300 mL of diethyl ether and mixing thoroughly, the layers were separated. The lower aqueous layer was extracted with 2 x 150 mL diethyl ether. The combined organic layers were washed twice with water (2 x 100 mL), washed with saturated aqueous sodium chloride (100 mL), dried over anhydrous potassium carbonate, filtered, and

concentrated on a rotary evaporator. The product, **110**, is highly soluble in the water fraction. To increase the yield, the water fraction was removed on a rotary evaporator. The residue obtained was twice dissolved in 200 mL ethyl acetate. The mixture was filtered to remove the inorganic salt. The solvent was removed and the residue obtained was combined with that obtained from the initial extraction. The reaction mixture was purified by recrystallisation from benzene. The mother liquor contained the desired stereoisomer plus a small fraction of the undesired isomer, while almost pure crystals of the undesired product were obtained. The recrystallisation was repeated until all the desired isomer was removed from the crystals. After concentration, the residue obtained from the mother liquor was dissolved in ethyl acetate, 26 g silica gel was added and the solvent was removed. The silica gel mixture was applied to a wet column and separated with a 1:1 diethyl ether:dichloromethane eluent. The column was washed out with a 1:2 mixture of methanol:ethyl acetate to yield 3.8097 g (39.60%) of the desired product, **110**, as a white powder. mp. 92-94 °C, Lit. 95-97 °C.

IR spectrum (**110**): 3295 (OH), 2961 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 2925 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 2890 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 2867 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 1451, 1421, 1375, 1329, 1086, 732 cm^{-1}.

Mass spectrum: (GC-MS-EI): (**110**) *m/z* 144 ([M^+]).



110

Figure 4.2 The 1,4-methyldiol (**110**).

A ^1H and ^{13}C NMR investigation in $CDCl_3$ was done and supports the assigned structure of **110**. The ^1H and ^{13}C NMR data are summarised in **Table 4.1**. Assignment of the resonant signals to specific nuclei was done by comparison with the data of Chen *et al*.[5] The NMR spectra were identical to those reported in literature.

Table 4.1 ^{1}H-NMR-[a] and ^{13}C-NMR-data[a] of (**110**)

Proton/Carbon	δ_H[b] (ppm)	J_H (Hz)	δ_C[b] (ppm)
1, 4	3.49, 3.50 dt[c]	13.26 (6.60)	71.41 D[d]
2, 5	1.81-2.16 m[c]		35.24 D[d]
3, 6	1.63-1.81 m[c] & 1.33-1.53 m[c]		35.48 T[d]
7, 8	0.96 d[c]	6.96	17.88 Q[d]
-OH	1.55 s[c]		

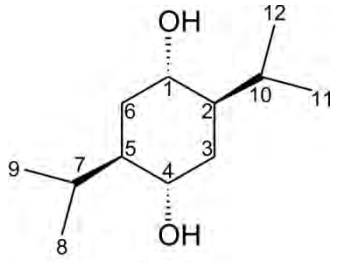
[a] ^{1}H-Spectrum: 600 MHz, ^{13}C-Spectrum: 150 MHz.
[b] Solvent $CDCl_3$. Capital letters refer to splitting patterns resulting from directly bonded protons and small case letters indicates couplings over more than one bond. S/s = Singlet, D/d = Doublet, T/t = Triplet, Q = Quartet, m = Multiplet .
[c] Protons could not be differentiated.
[d] Two equivalent carbons that cannot be differentiated.

Hydroboration of the 1,4-di-isopropyl alkene mixture (**32**, **109** and **128**) to **111**:

A dry 500 mL flask equipped with a mechanical stirrer, pressure-equalising dropping funnel, and reflux condenser was flushed with dry nitrogen and maintained under a positive nitrogen pressure. In the flask was placed 10.397 g of the 1,4-di-isopropyl alkene mixture (**32** (26.49%), **109** (56.75%) and **128** (13.95%)) obtained as described above, dissolved in 100 mL dry diethyl ether and cooled to 0-5 °C with an ice water bath. Hydroboration was achieved by the dropwise addition of 7.30 mL BMS over 30 minutes. Following the addition of the borane, the cooling bath was removed and the solution was stirred for 3 hr at 20-25 °C. Then 90 mL ethanol was added, followed by 28 mL 3 *N* aqueous sodium hydroxide. After cooling to 0-5 °C in an ice water bath, 32 mL hydrogen peroxide was added dropwise at such a rate that the reaction mixture never warmed to more than 35 °C. Immediately following the addition of the peroxide (1 hour), the cooling bath was removed and the reaction mixture was heated at reflux for one hour. The reaction mixture was then poured into 600 mL of ice water. After adding 200 mL of diethyl ether and mixing thoroughly, the layers were separated. The lower aqueous layer was extracted with 2 x 100 mL diethyl ether, and thereafter it was discarded. The combined organic layers were washed twice with water (2 x 100 mL), washed with saturated aqueous sodium chloride (100 mL), dried over anhydrous potassium carbonate, filtered, and concentrated on a rotary evaporator. The reaction mixture was purified by recrystallisation from ethyl acetate. The mother liquor contained the desired stereoisomer plus a small fraction of the undesired isomer, while almost pure crystals of the undesired product were obtained. After concentration, the residue obtained from the mother liquor was dissolved in ethyl acetate, 20 g silica gel was added and the solvent was removed. The silica gel mixture was applied to a wet column and separated with a 30% ethyl acetate:petroleum ether eluent. The column was washed out with pure ethyl acetate to yield 3.20 g (43.18%) of the desired product, **111**, as a white powder. mp. 139-140 °C, Lit. 139-140 °C.

IR spectrum (**111**): 3306 (OH), 2953 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 2917 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 2869 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 1468, 1384, 1365, 1179, 1162, 1054, 1019, 999, 981 cm^{-1}.

Mass spectrum: (GC-MS-EI): (**111**) *m/z* 200 ($[M^+]$).



111

Figure 4.3 The 1,4-di-isopropyldiol **111**.

A ^1H and ^{13}C NMR investigation in $CDCl_3$ was done and supports the assigned structures of **111**. The ^1H and ^{13}C NMR data are summarised in **Table 4.2**. Assignment of the resonant signals to specific nuclei was done by comparison with the data of Chen *et al*.[5] The NMR spectra were identical to those reported in literature.

Table 4.2 ^1H-NMR-[a] and ^{13}C-NMR-data[a] of (**111**)

Proton/Carbon	δ_H[b] (ppm)	J_H (Hz)	δ_C[b] (ppm)
1, 4	3.54-4.25 m[c]		67.61 D[d]
2, 5	1.45-1.55 m[c]		46.16 D[d]
3, 6	1.55-1.75 m[c]		29.20 T[d]
7, 10	1.75-1.95 m[c]		26.75 D[d]
8, 9, 11, 12	0.83, 0.91 dd[c]	11.94 (6.78)	18.83 & 21.08 Q[d]
-OH	1.43 s[c]		

[a] ^1H-Spectrum: 600 MHz, ^{13}C-Spectrum: 150 MHz.
[b] Solvent $CDCl_3$. Capital letters refer to splitting patterns resulting from directly bonded protons and small case letters indicates couplings over more than one bond. S/s = Singlet, D/d = Doublet, T/t = Triplet, Q = Quartet, m = Multiplet.
[c] Protons could not be differentiated.
[d] Equivalent carbons that cannot be differentiated.

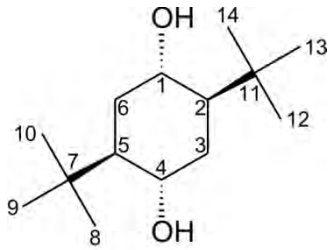
Hydroboration of the 1,4-di-tert-buthyl alkene mixture (**116**, **117** and **129**) to **118**:

A dry 500 mL flask equipped with a mechanical stirrer, pressure-equalising dropping funnel, and reflux condenser was flushed with dry nitrogen and maintained under a positive nitrogen pressure. In the flask was placed 1.9233 g of the 1,4-di-tert-buthyl alkene mixture (**116** (20.72%), **117** (69.05%) and **129** (10.23%)) obtained as described above, dissolved in 30 mL of dry diethyl ether and cooled to 0-5 °C with an ice water bath. Hydroboration was achieved by the dropwise addition of 2.6 mL BMS over 20 minutes. Following the addition of the borane, the cooling bath was

removed and the solution was stirred for 3 hr at 20-25 °C. Then, 25 mL ethanol was added, followed by 8.25 mL 3 *N* aqueous sodium hydroxide. After cooling to 0-5 °C in an ice water bath, 9.25 mL hydrogen peroxide was added dropwise at such a rate that the reaction mixture never warmed to more than 35 °C. Immediately following the addition of the peroxide (30 minutes), the cooling bath was removed and the reaction mixture was heated at reflux for one hour. The reaction mixture was then poured into 300 mL of ice water. After adding 100 mL of diethyl ether and mixing thoroughly, the lower aqueous layer was removed and discarded. The upper organic layer was washed twice with water (2 x 50 mL), washed with saturated aqueous sodium chloride (50 mL), dried over anhydrous potassium carbonate, filtered, and concentrated on a rotary evaporator. The product mixture was further purified by using the method similar to that described by Chen *et al*.[5] A quarter portion of the product mixture was dissolved in ethyl acetate, applied to a silica gel column and separated with a 30% ethyl acetate:petroleum ether eluent. Only the last fraction contained the desired stereoisomer. This was repeated until the entire product mixture was separated. The yield of the combined fractions of **118** was 0.8942 g (55.40%) of a white powder. mp. 191-192 °C.

IR spectrum (**118**): 3353 (OH), 2949 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 2912 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 2869 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 1451, 1393, 1356, 1291, 1258, 1242, 1022, 1004, 977, 944, 888 cm^{-1}.

Mass spectrum: (GC-MS-EI): (**118**) *m/z* 228 ([M^+]).



118

Figure 4.4 The 1,4-di-tert-buthyldiol (**118**).

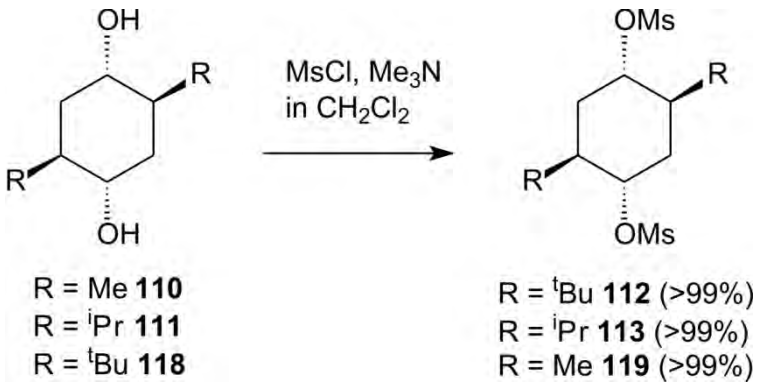
A ^1H and ^{13}C NMR investigation in $CDCl_3$ was done and supports the assigned structure of **118**. The ^1H and ^{13}C NMR data are summarised in **Table 4.3**.

Table 4.3 ^{1}H-NMR-[a] and ^{13}C-NMR-data[a] of (**118**)

Proton/Carbon	δ_H[b] (ppm)	J_H (Hz)	δ_C[b] (ppm)
1, 4	3.96 s[c]		68.10 D[d]
2, 5	1.53, 1.65 dd[c]	12.57 (5.43)	46.89 D[d]
3, 6	1.15, 1.55 dt[c] & 1.74, 1.77 dt[c]	14.49 13.98 (4.53, 4.53)	29.42 T[d]
7, 11	-		32.33 S[d]
8, 9, 10, 12, 13, 14	0.88 s[c]		27.24 Q[d]
-OH	2.45 s[c]		

[a] ^{1}H-Spectrum: 600 MHz, ^{13}C-Spectrum: 150 MHz.
[b] Solvent $CDCl_3$. Capital letters refer to splitting patterns resulting from directly bonded protons and small case letters indicates couplings over more than one bond. S/s = Singlet, D/d = Doublet, T/t = Triplet, Q = Quartet.
[c] Protons could not be differentiated.
[d] Equivalent carbons that cannot be differentiated.

4.3.4 Synthesis of bis(methanesulphonate) esters



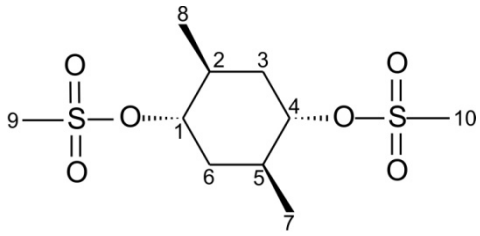
Scheme 4.7 Synthesis of bis(methanesulphonate) esters **112**, **113** and **119**.

Synthesis of bis(methanesulphonate) ester (**112**):

A dry 100 mL flask equipped with a mechanical stirrer, pressure-equalising dropping funnel, and reflux condenser was flushed with dry nitrogen and maintained under a positive nitrogen pressure. A stirred solution of the diol **110** *(*0.5433 g) and dry trimethylamine (1 mL) in CH_2Cl_2 (40 mL) was prepared at 0 °C; to this, methanesulphonyl chloride (0.6 mL) in CH_2Cl_2 (10 mL) was added dropwise over 10 min. The mixture was stirred at 0 °C for 30 min and then at room temperature for another 30 min and was quenched with saturated NH_4Cl solution in ice water (50 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phase was dried over anhydrous Na_2SO_4, and the solvent was removed by rotary evaporation to give **112** as a light off-white solid (1.24 g, >99%): mp. 93-97 °C, lit 68-77 °C.

IR spectrum (**112**): 3027, 2963 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 2945 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 1463, 1332, 1164, 898 cm^{-1}.

Mass spectrum: (GC-MS-EI): (**112**) *m/z* 108 ($[M^+]$ = 300 - $(SO_3CH_4)_2$).



112

Figure 4.5 Bis(methanesulphonate) ester (**112**).

A ^{1}H and ^{13}C NMR investigation in $CDCl_3$ was done and supports the assigned structure of **112**. The ^{1}H and ^{13}C NMR data are summarised in **Table 4.4**. Assignment of the resonant signals to specific nuclei was done by comparison with the data of Chen *et al*.[5] The NMR spectra were identical to those reported in literature.

Table 4.4 ^{1}H-NMR-[a] and ^{13}C-NMR-data[a] of (**112**)

Proton/Carbon	δ_H[b] (ppm)	J_H (Hz)	δ_C[b] (ppm)
1, 4	4.53, 4.54 dt[c]	7.02 (3.48)	81.42 D[d]
2, 5	2.12-2.35 m[c]		33.12 D[d]
3, 6	1.77, 1.78, 1.79, 1.80 qd[c] & 2.02, 2.04, 2.05, 2.06 qd[c]	14.09 (7.57, 3.49) 13.98 (7.56, 4.80)	33.36 T[d]
7, 8	1.04 d[c]	7.02	17.35 Q[d]
9, 10	3.00 s[c]		38.73 Q[d]

[a] ^{1}H-Spectrum: 600 MHz, ^{13}C-Spectrum: 150 MHz.
[b] Solvent $CDCl_3$. Capital letters refer to splitting patterns resulting from directly bonded protons and small case letters indicates couplings over more than one bond. S/s = Singlet, D/d = Doublet, T/t = Triplet, Q = Quartet, m = Multiplet.
[c] Protons could not be differentiated.
[d] Two equivalent carbons that cannot be differentiated.

Synthesis of bis(methanesulphonate) ester (**113**):

A dry 500 mL flask equipped with a mechanical stirrer, pressure-equalising dropping funnel, and reflux condenser was flushed with dry nitrogen and maintained under a positive nitrogen pressure. A stirred solution of the diol **111** *(*5.5051 g) and dry trimethylamine (10 mL) in CH_2Cl_2 (200 mL) was prepared at 0 °C; to this, methanesulphonyl chloride (4.60 mL) in CH_2Cl_2 (10 mL) was added dropwise over 10 min. The mixture was stirred at 0 °C for 30 min and then at room temperature for another 30 min and was quenched with saturated NH_4Cl solution in ice water (100 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic phase was dried over anhydrous Na_2SO_4, and the solvent was removed by rotary evaporation to give **113** as a light off-white solid (11.00 g, >99%): mp. 120-124 °C, lit 128-129 °C.

IR spectrum (**113**): 3025, 2962 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 2939 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 2880 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 1460, 1343, 1314, 1167, 895 cm^{-1}.

Mass spectrum: (GC-MS-EI): (**113**) *m/z* 164 ([M^+] = 356 - $(SO_3CH_4)_2$).

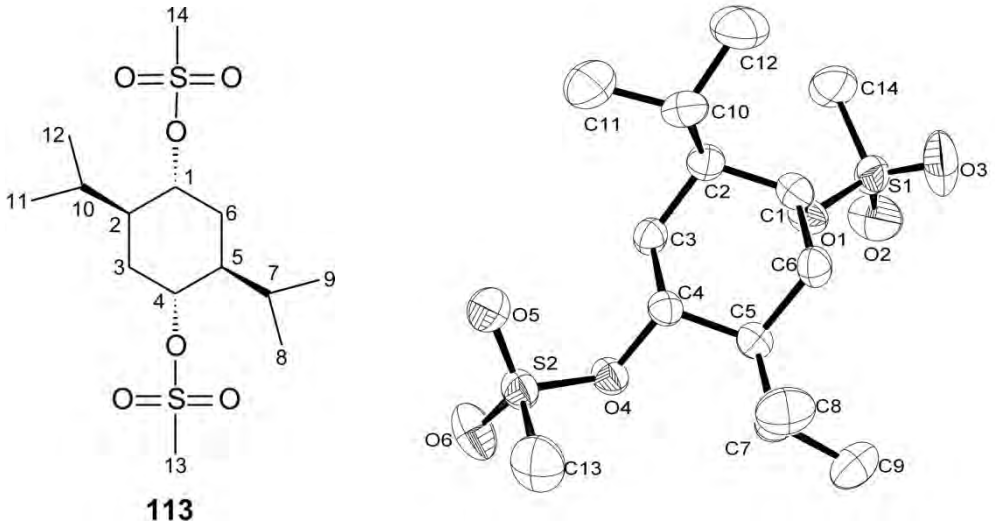


Figure 4.6 Bis(methanesulphonate) ester **113** (XRD hydrogen atoms are omitted for clarity).

A ^1H and ^{13}C NMR investigation in $CDCl_3$ was done and supports the assigned structures of **113**. The ^1H and ^{13}C NMR data are summarised in **Table 4.5**. Assignment of the resonant signals to specific nuclei was done by comparison with the data of Chen *et al*.[5] The NMR spectra were identical to those reported in literature. XRD analysis confirmed the structure where MS analysis failed to provide the molecular mass ([M^+]).

Table 4.5 ^1H-NMR-[a] and ^{13}C-NMR-data[a] of (**113**)

Proton/Carbon	δ_H[b] (ppm)	J_H (Hz)	δ_C[b] (ppm)
1, 4	4.80-4.81 dt[c]	3.36, 3.12, 3.36	78.53 D[d]
2, 5	1.79-1.86 m[c]		43.99 D[d]
3, 6	1.86-2.13 m[c]		27.37 T[d]
7, 10	1.71-1.79 m[c]		26.39 D[d]
8, 9, 11, 12	0.92, 0.93 dd[c]	6.03	18.30 & 20.68 Q[d]
13, 14	3.00 s[c]		38.93 Q[d]

[a] ^1H-Spectrum: 600 MHz, ^{13}C-Spectrum: 150 MHz.
[b] Solvent $CDCl_3$. Capital letters refer to splitting patterns resulting from directly bonded protons and small case letters indicates couplings over more than one bond. S/s = Singlet, D/d = Doublet, T/t = Triplet, Q = Quartet, m = Multiplet.
[c] Protons could not be differentiated.
[d] Equivalent carbons that cannot be differentiated.

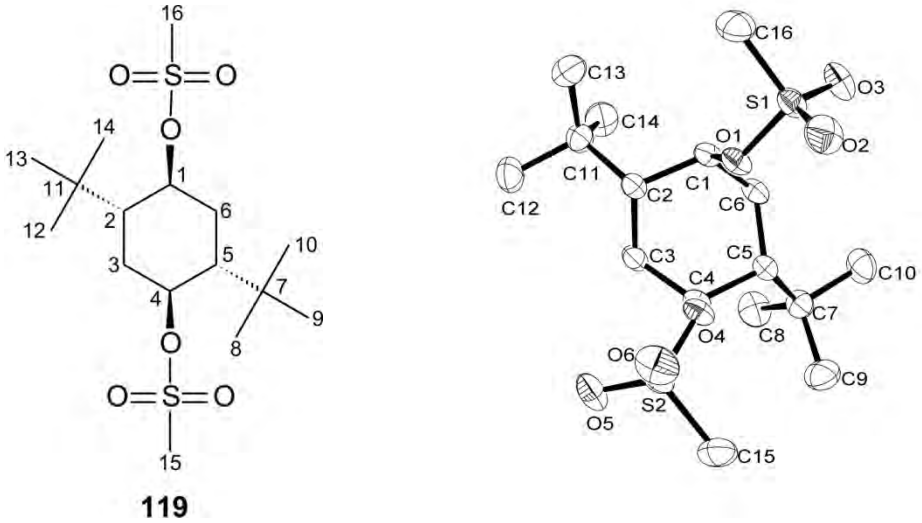
Synthesis of bis(methanesulphonate) ester (**119**):

A dry 100 mL flask equipped with a mechanical stirrer, pressure-equalising dropping funnel, and reflux condenser was flushed with dry nitrogen and maintained under a positive nitrogen pressure. A stirred solution of the diol **118** *(*0.6568 g) and dry trimethylamine (1.5 mL) in CH_2Cl_2 (50 mL) was prepared at 0 °C; to this, methanesulphonyl chloride (0.5 mL) in CH_2Cl_2 (5 mL) was added

dropwise over 10 min. The mixture was stirred at 0 °C for 30 min and then at room temperature for another 30 min and was quenched with saturated NH_4Cl solution in ice water (50 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phase was dried over anhydrous Na_2SO_4, and the solvent was removed by rotary evaporation to give **119** as a light yellow solid (1.41 g, >99%): mp. 97-101 °C.

IR spectrum (**119**): 3018, 2971 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 2947 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 2920 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 2874 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 1478, 1336, 1325, 1242, 1170, 897 cm^{-1}.

Mass spectrum: (GC-MS-EI): (**119**) *m/z* 192 ($[M^+]$ = 384 – $(SO_3CH_4)_2$).



119

Figure 4.7 Bis(methanesulphonate) ester (**119**) (XRD hydrogen atoms are omitted for clarity).

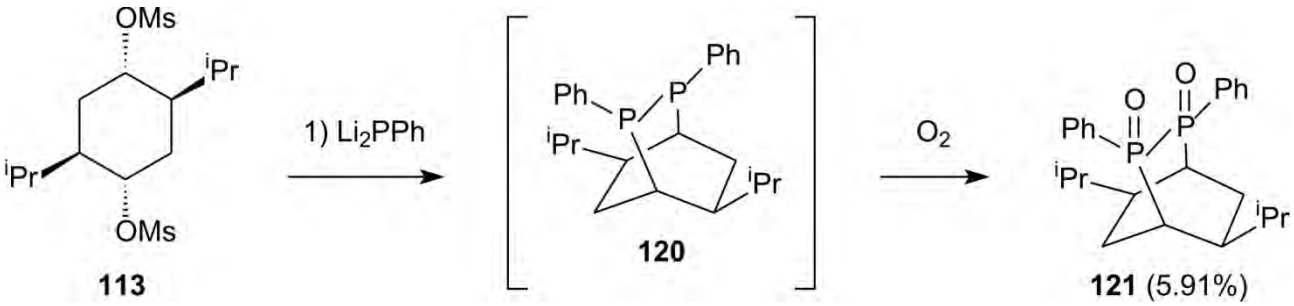
A ^1H and ^{13}C NMR investigation in $CDCl_3$ was done and supports the assigned structure of **119**. The ^1H and ^{13}C NMR data are summarised in **Table 4.6**. XRD analysis confirmed the structure where MS analysis failed to provide the molecular mass ($[M^+]$).

Table 4.6 ^{1}H-NMR-[a] and ^{13}C-NMR-data[a] of (**119**)

Proton/Carbon	δ_H[b] (ppm)	J_H (Hz)	δ_C[b] (ppm)
1, 4	4.85-5.25 m[c]		80.05 D[d]
2, 5	1.75, 1.77 dt[c]	13.62 (4.20, 4.23)	43.12 D[d]
3, 6	1.24, 1.25 dt[c] & 2.18, 2.20 dt[c]	16.05 15.30 (2.88, 2.85)	28.46 T[d]
7, 11	-		32.41 S[d]
8, 9, 10, 12, 13, 14	0.92 s[c]		27.18 Q[d] & 27.23 Q[d]
15, 16	3.00 s[c]		39.80 Q[d]

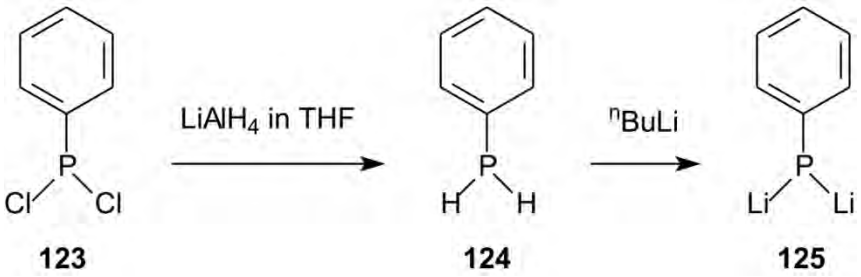
[a] ^{1}H-Spectrum: 600 MHz, ^{13}C-Spectrum: 150 MHz.
[b] Solvent $CDCl_3$. Capital letters refer to splitting patterns resulting from directly bonded protons and small case letters indicates couplings over more than one bond. S/s = Singlet, D/d = Doublet, T/t = Triplet, Q = Quartet.
[c] Protons could not be differentiated.
[d] Equivalent carbons that cannot be differentiated.

4.3.5 Synthesis of the oxidised diphosphine 121



Scheme 4.8 Synthesis of the oxidised diphosphine **121**.

Synthesis of the dilithium phosphine salt (**125**):



Scheme 4.9 The synthesis of dilithium phenylphosphine **125**.

Phenylphosphine (**124**) was prepared by slow addition of 1.24 ml of dichlorophenylphosphine (**123**) to lithium aluminium hydride (0.4260 g) dissolved in 20 mL of THF at -20 °C in a Schlenk tube. The orange reaction mixture was then stirred for 1 h at room temperature. The solution was then transferred via a cannula needle to a short column and filtered through celite under an argon atmosphere into a 100 mL three-necked-flask under an argon atmosphere (**Figure 4.8**). The

$LiAlH_4$ residues were washed with a further 47 mL of THF and filtered as described above. The solution of **124** was used without more analysis than GC-MS. Immediately after filtration, the column was removed and replaced with a septum. The solution was cooled to -78 °C and 7.31 mL of a 2.5 M solution of ^{n}BuLi in hexanes was added dropwise at such a rate that the temperature never rose above -70 °C. Immediately after the addition, the cooling bath was removed and the solution was stirred for 1 h at room temperature. The orange solution of the dilithium salt, **125**, was then ready for further reactions.

Mass spectrum: (GC-MS-EI): (**123**) *m/z* 178 ([M^+]).

Mass spectrum: (GC-MS-EI): (**124**) *m/z* 110 ([M^+]).

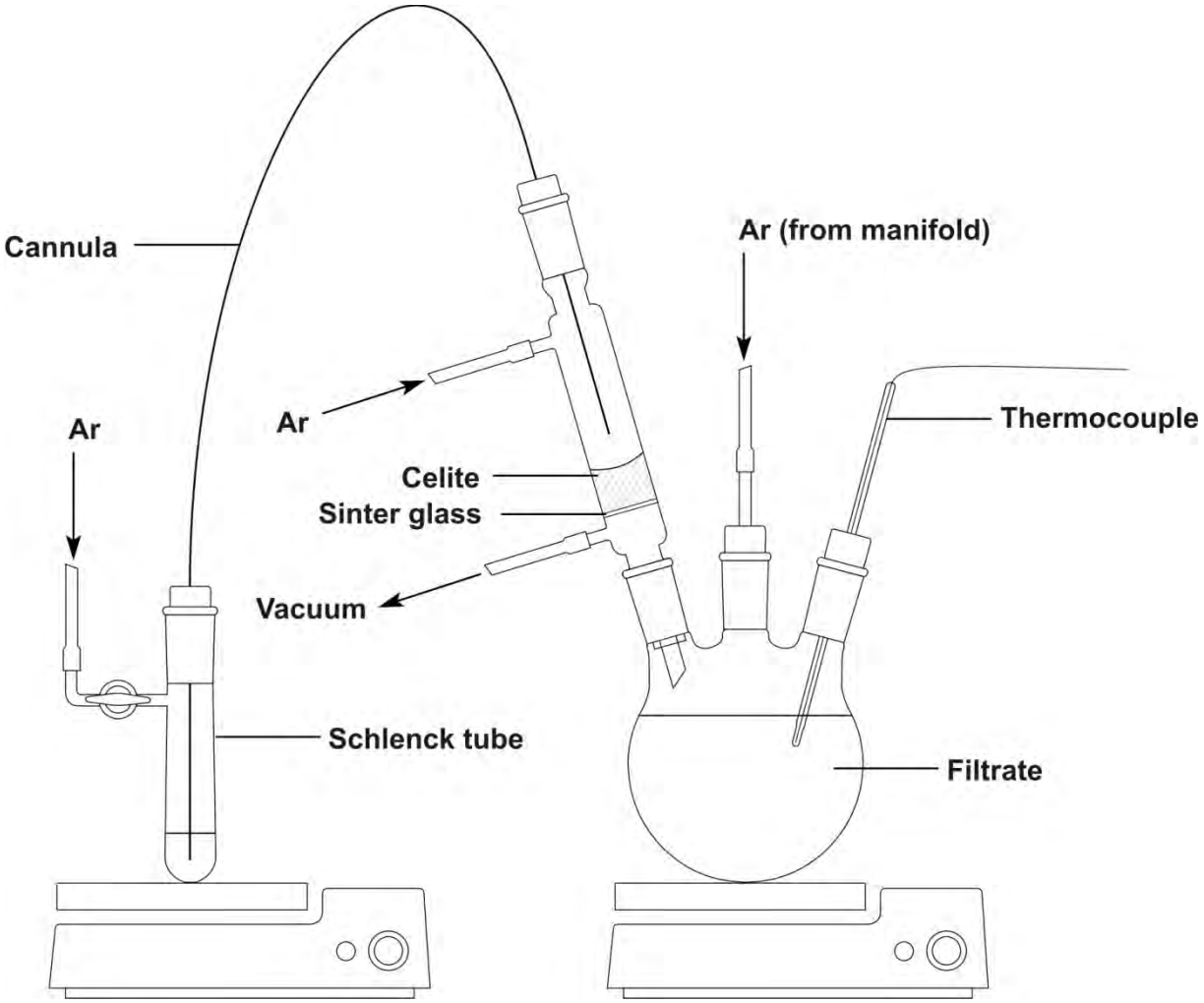


Figure 4.8 Setup for filtration of $LiAlH_4$ solution of the phosphine.

Synthesis of the oxidised diphosphine (**121**):

To phenylphosphine (1.0 ml) in THF (67 mL) was added n-BuLi (7.31 mL of a 2.5 M solution in hexane) via syringe at -78 °C over 20 min. Then the orange solution was warmed to room temperature and stirred for 1 h at room temperature. The resulting orange-yellow suspension was added to a solution of **113** (3.2650 g) in THF (33 mL) over 30 min. After the mixture was stirred

overnight at room temperature, the pale-yellow suspension was hydrolysed with a saturated NH_4Cl solution. The mixture was extracted with ether (2 x 50 mL), and the combined organic solution was dried over anhydrous sodium sulphate and filtered. The solvents were removed under reduced pressure. The residue was allowed to oxidise in the atmosphere. After complete oxidation, the residue was dissolved in chloroform, 20 g silica gel was added and the solvent was removed. The silica gel mixture was applied to a wet column (diethyl ether) and separated by washing with a diethyl ether eluent. The column was washed out with methanol to yield a pure white powder of **121**. Yield: 0.2243 g (5.91%). mp. 358-363 °C.

IR spectrum (**121**): 3056 (unsaturated aromatic hydrocarbons, CH), 2958 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 2868 (saturated aliphatic hydrocarbons, CH_3, CH_2 and CH), 1591, 1467, 1436, 1386, 1366, 1161, 1138, 1052, 991, 745, 693 cm^{-1}.

Mass spectrum: (GC-MS-EI): (**121**) *m/z* 414 ($[M^+]$).

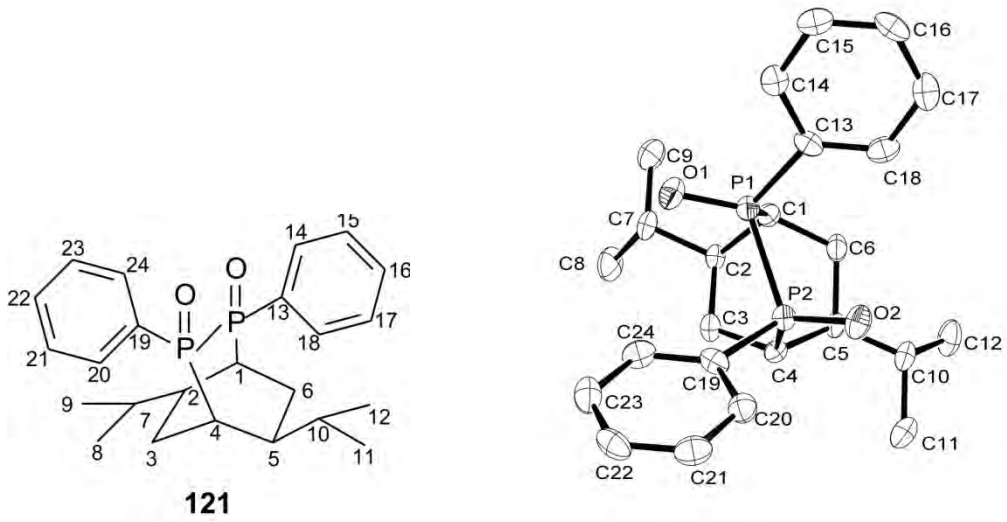


Figure 4.9 The oxidised phosphine **121** (XRD hydrogen atoms are omitted for clarity).

A ^1H and ^{13}C NMR investigation in $CDCl_3$ was done and supports the assigned structure of **121**. The ^1H and ^{13}C NMR data are summarised in **Table 4.7**. A peak at 37.70 ppm is obtained from the ^{31}P recorded at 242 Hz. XRD analysis confirmed the structure.

Table 4.7 ^{1}H-NMR-[a] and ^{13}C-NMR-data[a] of (**121**)

Proton/Carbon	δ_H[b] (ppm)	J_H (Hz)	δ_C[b] (ppm)	J_{PC} (Hz)
1, 4	1.34-1.88 m[c]		41.62 D[d]	
2, 5	2.68-3.11 m[c]		35.05, 35.12, 35.36, 35.43 D[d]	47.39 (10.22)
3, 6	1.88-2.31 m[c]		27.71 T[d]	
7, 10	2.31-2.68 m[c]		31.31 D[d]	
8, 9, 11, 12	0.85, 1.02 dd[c]	6.48, 6.66	21.25, 21.59 Q[d]	
13, 19	-		129.61, 129.68 S[d]	
14, 18, 20, 24	7.94-8.35 dt[c]		128.75, 128.79, 128.83 D[d]	5.64
15, 17, 21, 23	7.37-7.53 m[c]		132.15, 132.19, 132.22 D[d]	4.91
16, 22	7.53-7.94 m[c]		132.34 D[d]	

[a] ^{1}H-Spectrum: 600 MHz, ^{13}C-Spectrum: 150 MHz.
[b] Solvent $CDCl_3$. Capital letters refer to splitting patterns resulting from directly bonded protons and small case letters indicates couplings over more than one bond. S/s = Singlet, D/d = Doublet, T/t = Triplet, Q = Quartet, m = multiplet.
[c] Protons could not be differentiated.
[d] Equivalent carbons that cannot be differentiated.

4.3.6 Metathesis reactions

The reported ratios (**§ 3.8**) of *cis*- to *trans*-7-tetradecene formed at room temperature from the metathesis of 1-octene with **A1** to **A3** were determined.

General procedures for all metathesis reactions

In a 5 mL vial was placed a 1:9000 amount of precatalyst to 1-octene. Nonane (0.2 mL) was used as the internal standard. The precatalyst was weighed directly into the vial, thereafter it was covered with a blanket of argon gas and sealed. The nonane was added to the vial and lastly the 1-octene (4 mL). Immediately after the 1-octene addition, GC-analysis was started. The reaction was performed at room temperature and the vial was not stirred. After every analysis, the vial was shaken for 10 seconds to help mix the solution.

4.4 Conclusions

Since this was only a preliminary experimental study and not the main aim of the project, the synthesis reactions were stopped at this point. In terms of the three requirements listed at the beginning of this chapter, this synthesis does not seem to be the best route to new ligands. In terms of the low overall yields for **112** (29%), **113** (35%) and **119** (38%) from **31**, **32** and **116** and the preference for dimerisation of the phosphines, this synthesis does seem to fail when it comes to ease of synthesis. The low yields also raise the costs of the ligand. The expensive shipping costs of the commercial anhydrous phosphine should also be taken into consideration. In terms of the environmental impact, this synthesis is also not ideal since large quantities of solvents had to be used to purify the diols as well as the highly toxic nature of the phosphines. While the need for

experimental results is very clear from **Chapter 3**, serious consideration has to be given towards the type of ligands that will be used to try to elucidate the very complex metathesis reaction. If a more expensive ligand only leads to a very small incremental increase in the activity of the precatalysts or none whatsoever, it does once again raise questions about the current approach towards alkene metathesis. For the catalysts to be used on industrial scale, cheap reusable catalysts with a long lifetime have to be found. However, until the mechanism is better understood, this will not happen, except by some fortunate accident.

4.5 Analyses

4.5.1 Infrared spectrometry

IR-spectra were obtained by using a Bruker ALPHA-P ATR (attenuated total reflection). All crystalline samples were applied directly onto the ATR. In the cases of liquids, a small drop was applied directly onto the ATR.

4.5.2 Nuclear magnetic resonance spectroscopy

^{1}H-NMR (600 mHz), ^{13}C-NMR (150 mHz), ^{31}P-NMR (242 mHz), DEPT135 (150 mHz), COSY (600 mHz) and HSQC (600 mHz and 150 mHz) spectra were obtained using a Bruker Ultrashield Plus 600 Avance III spectrometer. NMR samples were prepared by dissolving 20 mg of the sample in a suitable deuterated solvent.

4.5.3 Melting points

Melting points of the products were determined with a Buchi B-540 melting point apparatus.

4.5.4 GC-MS

All reactions were analysed on an Agilent 6890 gas chromatograph equipped with an Agilent 7683 autosampler, HP-5 capillary column and an Agilent 5973 mass selective detector (MSD). The same oven programme was used with either a two-minute solvent delay or no solvent delay. Helium was used as carrier gas with a 1.5 mL.min^{-1} flow rate at 20 °C.

The following general GC settings were used:
Column: HP-5, 30.0 m × 320 µm × 0.25 µm
Split ratio: 50:1
Split flow: 74.9 mL/min

Inlet: 250 °C, 34.3 kPa
Injection volume: 0.2 µl
Detector: 50 – 550 Dalton mass range; scan speed of 2.94 seconds per decade
Oven programming: 120 °C hold for 2 min
120 to 290 °C at 10 °C min^{-1}
290 °C hold for 5 min

4.5.5 GC for metathesis

All reactions were analysed on an Agilent 6850 gas chromatograph equipped with an Agilent 7683 autosampler, HP-1 capillary column and a flame ionisation detector (FID).

The following general GC settings were used:
Column: HP-1, 30.0 m × 320 µm × 0.25 µm,
Detector: FID at 250 °C
H_2 flow rate: 40 mL min^{-1} at 20 °C
Air flow rate: 450 mL min^{-1} at 20 °C
Inlet temperature: 250 °C
N_2 carrier gas flow rate: 78.1 mL min^{-1} at 20 °C
Injection volume: 0.2 µL (auto injection)
Split ratio: 50:1

Oven programming: 60 °C hold for 5 min
60 to 110 °C at 25 °C min^{-1}
110 °C hold for 10 min
110 to 300 °C at 25 °C min^{-1}
300 °C hold for 5 min

4.5.6 XRD

All crystals were mounted on a Mitegen Micromount that was automatically centred on a Bruker SMART X2S benchtop crystallographic system. Intensity measurements were performed using monochromated (doubly curved silicon crystal) Mo-Kα-radiation (0.71073 Å) from a sealed microfocus tube. Generator settings were 50 kV, 1 mA. Data collection temperature was either room temperature or -73 °C. Data were acquired using three sets of Omega scans at different Phi settings. The frame width was 0.5° with an exposure time of 5.0 s.
Detector distance: 40 mm
Detector swing angle (fixed 2 Theta): -20°.

APEX2 software was used for the preliminary determination of the unit cell. The determination of integrated intensities and unit cell refinement were performed using SAINT. Data were corrected for absorption effects with SADABS using the multi-scan technique. The structure was solved with XS and subsequent structure refinements were performed with XL. All structures were automatically solved by the software included in the Bruker SMART X2S benchtop crystallographic system.

4.6 Literature references

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