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New Ligands for Asymmetric Palladium Catalysed Allylic Substitution Reactions. X-ray Crystal Structures of Two Enantiomerically Pure Dihydrobenzazaphosphole-Borane Complexes.

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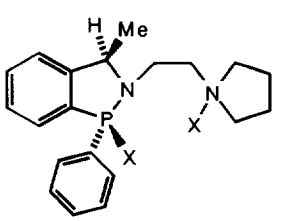
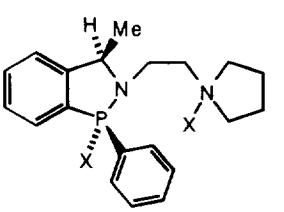
Abstract; The synthesis, application and X-ray crystal structures of two enantiomerically pure dihydrobenzazaphosphole-borane complexes, precursors of ligands for highly enantioselective palladium catalysed allylic substitution reactions, are described. The structures provide the basis for an explanation of the observed stereochemistry.

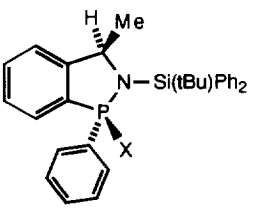
Recently we reported[1,2] a new class of chiral ligands for asymmetric palladium catalysed allylic substitution reactions.[3-6] These are based on a chiral heterocyclic ring system of which representative examples are the mixed phosphorus/nitrogen donors **1** and **2**, and a monodentate phosphorus-based ligand, **3**. These ligands are capable of generating high enantiomeric excesses in the reaction between *rac*-(E)-1,3-diphenylprop-2-enyl-1-acetate **4** and dimethyl malonate, to give **5**, (Scheme 1, Table 1).[5,6]



1 (X=lone pair)
6 ($X=BH_3$)

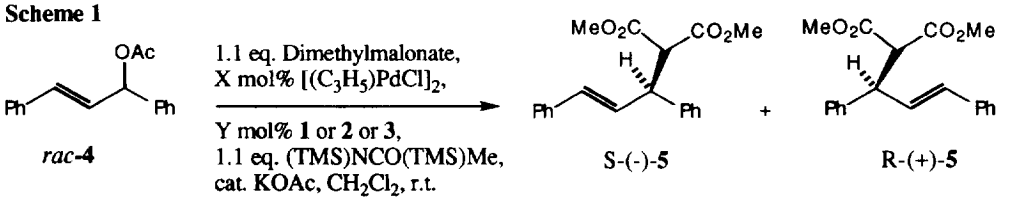


2 (X=lone pair)
7 ($X=BH_3$)



3 (X=lone pair)
8 ($X=BH_3$)

Scheme 1



rac-**4**

S-(-)-**5**

R-(+)-**5**

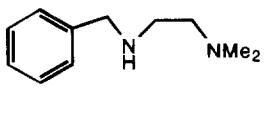
Table 1 Conversion of **4** into **5** by palladium catalysed allylic substitution.

Ligand	X [1]	Y	Deboration method [2]	Time [3]	Yield	R/S	Enantiomeric Excess
1	4	10	M	50 min.	86%	R	60%
2	4	10	M	3 hr	35%	S	33%
1	4	10	D	2 hr	99%	S	62%
3	4	20	M	o/n	56%	S	91.5%
3	4	20	D	o/n	31%	S	89%
3	1	5	M	o/n	84%	S	84% [4]
3	1	5	D	o/n	56%	S	85% [4]
17	1	5	M	2 hr	95%	-	0%
17	1	5	D	2 hr	99%	-	0%

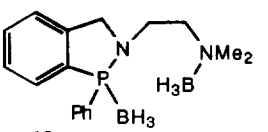
[1] X refers to mol% Pd, i.e. if X=4, 2 mol% of $[(C_3H_5)PdCl]_2$ was used.
[2] M=morpholine, D=DABCO. [3] Time required for full consumption of **4** by tlc.
[4] = No freeze/thaw cycle used in preparation of catalyst.

Ligands **1**, **2** and **3** were generated by *in-situ* removal of borane from the corresponding complexes **6**, **7** and **8** by an amine.[7] The protection of a phosphorus donor ligand in this manner, which has considerable literature precedent, prevents oxidation or decomposition during subsequent synthetic manipulations. An *ortho*- lithiation strategy was employed for the synthesis of each of these ligands, which was first demonstated by the conversion of diamine **9** to benzazaphosphole **10**. The lithiation step for **9** has been described[8] and trapping of the resultant dianion with dichlorophenylphosphine followed by borane, which was a novel process, worked well (71% yield). In common with **6** - **8**, **10** was stable to chromatography on silica gel and could be handled both as a solid and in solution without using special anaerobic handling techniques. The precursor to **6** and **7**, diamine **13**, was prepared by the sequential reaction of R-α-methylbenzylamine with α-bromoacetyl bromide (to give **11**; 75%), pyrrolidine (to give **12**; 86%) and lithium aluminium hydride (43%). Treatment of **13** in the same way as described for **9** led to the formation of **6** and **7** in 74% yield. The product was a ca. 1:1 mixture of diastereoisomers which were easily separated by flash chromatography.

For reasons that have been discussed in previous publications,[1,9] the monodentate ligand precursor complex **8** was prepared in a two-step procedure.[1] The first stage required *ortho*- lithiation of *t*-butyldiphenylsilyl protected R-α-methylbenzyamine **14** followed by trapping with phenylphosphinic dichloride to give benzazaphosphole oxide **15**, predominantly (>20:1) as the *trans*- diastereoisomer.[10] In this case however considerable modification of the reported process was required before a good yield was obtained.[11] In particular it was essential that only a small amount of ether was employed together with tetramethylethylene diamine to activate the *n*-butyllithium base. Use of more than the minimal quantity resulted in much lower yields, presumably due to reaction of solvent with the base. The second step involved reduction of **15** to **3** using trichlorosilane/triethylamine[12] followed by trapping of the reduction product with borane to give **8**. The product of this reaction was demonstrated, by X-ray crystallographic analysis, to be that of retention of configuration at the phosphorus atom. We had previously[9] assigned *cis*- stereochemistry to **8** on the basis of the known inversion of configuration which results from the analogous reductive conversion of enantiomerically pure phosphine oxides.[12]



9



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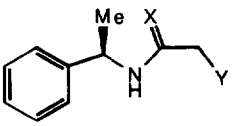
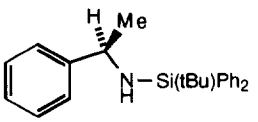


11 (X=O, Y=Br)
12 (X=O, Y=$N(CH_2)_4$)
13 (X=H_2, Y=$N(CH_2)_4$)



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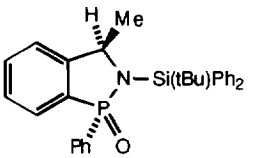

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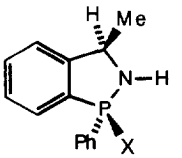

16 X=BH_3
17 X=lone pair

We chose the reaction of *rac*-(E)-1,3-diphenylprop-2-enyl-1-acetate **4** with dimethyl malonate, to give **5**, as a convenient model reaction for the evaluation of ligands **1-3** (Scheme 1). Removal of the borane immediately prior to the allylic substitution reaction could be achieved using either morpholine or DABCO.[7] A dichloromethane solution of $[(C_3H_5)PdCl]_2$ was then transferred to the deprotected catalyst and heated at 50°C for two hours.[3] The reaction was cooled to room temperature prior to addition of **4** and the other reagents then degassed using three freeze/thaw cycles.[3] Small amounts of amine-borane complex will inevitably be transferred into the palladium catalysed reaction however at the lower level (5 mol%) of catalyst they do not appear to cause any appreciable side-reactions such as allylic reduction. The enantiomeric excess (e.e.) of the product **5** was assessed by 400 MHz ^{1}H-NMR spectroscopy using the chiral shift reagent Eu(hfc)$_3$ and the absolute configuration was determined by comparison of its sign of rotation with that reported for authentic material (Table).[3] A number of unexpected results were observed during our studies of the allylic substitution reaction (see Table 1). Firstly the amine used for deboration of **6** or **7**, either morpholine or DABCO, had an effect on the absolute configuration of the product. Secondly the highest level of enantiomeric excess was achieved using the monomeric phosphine **3**, in which case the configuration of the product was irrespective of the base used to remove the borane. In order to explain these observations we obtained X-ray crystal structure solutions of ligand precursors **6** and **8**, which are described in this paper for the first time.

Of the bidentate ligand precursors the more polar, **6**, was purified by flash chromatography followed by recrystallisation from dichloromethane/hexane. The X-ray crystal structure is illustrated in Figure 1. This clearly shows that the phenyl group on phosphorus is *trans*- to the methyl group on the heterocyclic ring. Two molecules of borane are appended, one on the pyrrolidine ring nitrogen atom and one, as predicted, on the phosphorus atom. An X-ray crystal structure solution of **8** (Figure 2), which was also recrystallised from dichloromethane/hexane, revealed that the stereochemical relationship between phenyl and methyl in the heterocyclic ring was also *trans*. In common with **6**, the borane molecule is located on the phosphorus atom. Selected structural data for each compound is given in Table 2.

In the structures of **6** and **8** the heterocyclic rings are essentially flat (sum of angles about nitrogen in each case is ca. 360°) and a borane molecule is located on the phosphorus atom of the heterocyclic ring rather than nitrogen. Whilst in the case of **8** steric factors may influence this selectivity, there is no steric benefit for boration of phosphorus rather than nitrogen in **6**. These observations confirm that phosphorus is the superior donor in this system.[13] In view of this it is likely that **1** and **2** are chelated to the palladium atom through the phosphorus and remote nitrogen atoms and **3** by phosphorus alone. Another interesting observation is the similarity between the angles of the planes of the exocyclic phenyl ring and the heterocyclic ring in each structure. The planes of the phenyl rings are essentially perpendicular to each other in each system.

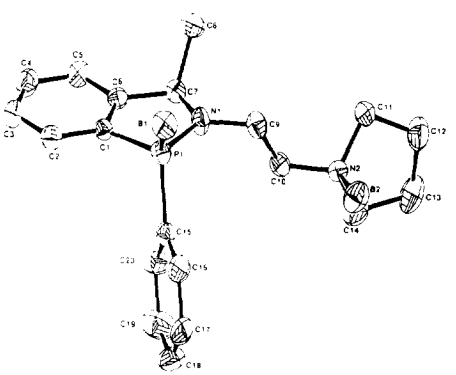

Figure 1 Structure of **6**

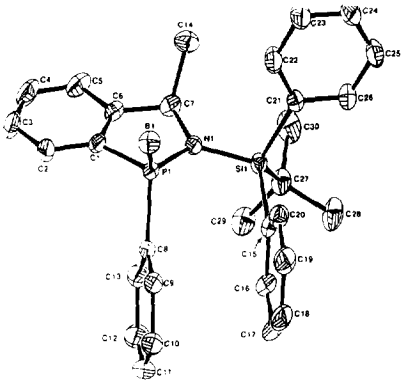

Figure 2 Structure of **8**

Table 2 Selected X-ray crystallographic data

Compound **6** (Figure 1)		Compound **8** (Figure 2)	
Bond lengths/Å		Bond lengths/Å	
B1-P1	1.879(10)	B1-P1	1.925(6)
N1-P1	1.669(6)	N1-P1	1.690(5)
B2-N2	1.631(10)	N1-Si1	1.775(5)
Bond angles /°		Bond angles /°	
N1-P1-B1	118.3(4)	N1-P1-B1	120.5(3)
C1-P1-B1	115.3(4)	C1-P1-B1	111.5(3)
C1-P1-N1	92.0(3)	C1-P1-N1	93.8(3)
C15-P1-B1	112.2(5)	C8-P1-B1	113.6(3)
C15-P1-N1	109.8(3)	C8-P1-N1	109.6(2)
C15-P1-C1	107.3(3)	C8-P1-C1	105.2(3)
C7-N1-P1	117.3(4)	C7-N1-P1	112.3(3)
C9-N1-P1	121.1(4)	Si1-N1-P1	125.3(3)
C9-N1-C7	121.5(5)	Si1-N1-C7	122.4(3)

Whilst caution should be exercised in the use of ground state structures to predict directing effects in chemical reactions, the X-ray structures permit some discussions regarding the mechanism of asymmetric induction in the palladium catalysed reaction. In the case of ligand **1**/morpholine deboration we predict that the chelation motif shown in Figure 3 is relevant. If it is assumed that the conformation of the ligand is similar to that of the X-ray structure then the exocyclic phenyl ring would be predicted to possess a larger steric blocking effect than the other aromatic ring. If the allylic cation orients itself such that the unfavourable interactions with this phenyl ring are minimised (Figure 3) and nucleophilic attack occurs at the terminus *trans-* to the phosphorus (the better π–acceptor)[14] then the configuration of product predicted will match that observed (R). In the case of ligand **1**/DABCO deboration, the superior coordinating ability of the excess amine will permit it to displace the pyrrolidine from the palladium atom. In turn the ligand may adopt, either for steric or stereoelectronic reasons, an alternative conformation as shown in Figure 4. In this case it is the group on nitrogen which imposes a steric obstacle to the allyl group, which would be predicted to be located as shown. Nucleophilic attack in this case will occur again *trans-* to the phosphorus, but now give the opposite configuration of major product (S). Ligand **3**, acting as a monodentate fashion, adopts a similar conformation to **1**/DABCO however the very large silyl group serves to further ensure that the allyl group adopts only the predicted conformation (Figure 5). Consequently the same configuration of product would be predicted as in the **1**/DABCO combination. In all the above arguments it has been assumed that only one phosphorus ligand is attached to the palladium atom for steric reasons.

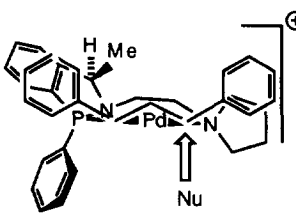

Figure 3
Gives R-(+) enantiomer

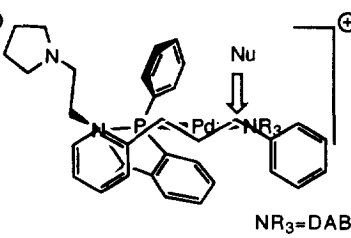

Figure 4
Gives S-(-) enantiomer

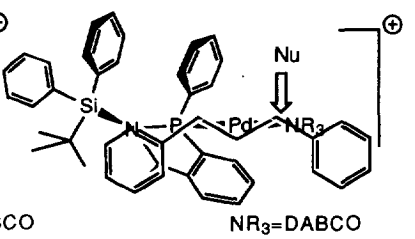

Figure 5
Gives S-(-) enantiomer

In order to test the importance of a large group on the nitrogen atom for enantioselectivity we used the unsubstituted compound **16** (formed by TBAF desilylation of **8**)[9] in the allylic substitution reaction. The resulting product was essentially racemic, which suggests that the group on nitrogen plays a key role in the control of asymmetric induction. This may be the result of either control of the conformation of the ligand or, as suggested by the reactive complexes proposed in this paper, control of the geometry of the allylic group on the palladium atom in the cationic intermediate.

In summary therefore we have described the synthesis and use of a new class of chiral ligand to asymmetric synthesis. Several phosphorus donor ligands containing P-N bonds have been reported, and this class of reagent is growing in importance due to their general ease of synthesis and availablility.[13] However the reagents described herein possess an unusually well defined steric environment[13a] due to the rigidity of the heterocyclic ring, and have great potential for use as reagents in asymmetric synthesis. Further results of our

studies in this area will be reported in due course. The X-ray crystal structures reported in this paper represent two of a very small number of solutions of this class of compound.[15]

Acknowledgments

We thank the SERC and SmithKline Beecham Pharmaceuticals for a CASE award (to GB), Dr. J. Ballantine of the SERC Mass Spectrometry Service at Swansea for HRMS-FAB spectra on several compounds and Dr David Guest of SmithKline Beecham Pharmaceuticals for HPLC studies on **6** and **7**.

Experimental

All air and moisture sensitive reactions were performed under an atmosphere of dry nitrogen or argon in thoroughly dried glassware. TMEDA, morpholine and Et_3N were distilled from CaH_2 before use. Dichloromethane (DCM) was distilled from P_2O_5 and stored over 3A molecular sieves. MeOH was distilled from, and stored over, 3A molecular sieves. Acetonitrile was freshly distilled from P_2O_5. DABCO was recrystallised from hexane and stored under Ar. Petrol refers to the fraction boiling in the range 60-80°C. Bromoacetylbromide, pyrrolidine, petrol, and dichlorophenylphosphine were all distilled before use. THF, Et_2O and hexane were all freshly distilled from sodium or potassium-benzophenone ketyl. Ethyl acetate was distilled from K_2CO_3. ^{1}H-NMR spectra were recorded in $CDCl_3$ solution on a Jeol GX270FT spectrometer at 270MHz, unless otherwise stated. ^{13}C-NMR spectra were recorded on a Jeol GX270FT instrument operating at 67.8MHz unless otherwise stated. Mass spectra were recorded on a VG analytical 7070E instrument. Infra-red spectra were recorded on a Perkin-Elmer 1310FT spectrometer. Microanalysis was performed at Bath University.

[(2-dimethylamino)-ethyl]-dihydrobenzazaphosphole diborane complex 10

To a solution of N-benzyl-N',N'-dimethylethylenediamine **9** (10.0g, 56.09mmol, 1eq.) and TMEDA (7.17g, 61.70mmol, 1.1eq.) in dry Et_2O (2ml) cooled to -70°C was added dropwise n-BuLi (51.42ml, 123.40mmol, 2.4M, 2.2eq.). The resulting solution was allowed to reach room temperature and stirred at room temperature overnight. The bright orange solution was diluted with dry Et_2O (100ml), cooled to -70°C and dichloropenylphosphine (15.06g, 84.14mmol, 1.5eq.) was added dropwise. The resulting yellow suspension was stirred at -70°C for 1 hour and at room temperature for 2 hours. Borane-dimethyl sulphide complex (17.90g, 235.58mmol, 4.2eq.) was added dropwise and the resulting thick yellow suspension was stirred at room temperature for 1 hour. It was then poured into saturated $NaHCO_3$ (250ml), extracted with DCM (4 x 100ml), dried with Na_2SO_4, filtered and concentrated under reduced pressure. Flash chromatography (gradient elution: 0-25% EtOAc in petrol) gave **10** as a colourless gum, which later solidified (12.47g, 71%). mp. 108-110°C (from EtOAc); (Found: C, 65.4; H, 8.91; N, 9.04. $C_{17}H_{27}N_2BP$ requires: C, 65.44; H, 8.72; N, 8.98%); υ_{max} (nujol)/cm^{-1} 3209.9, 2940.2, 2357.6, 2072.2, 1988.3, 1895.8, 1818.2, 1705.9, 1589.6, 1455.6; δ_H 0.88-1.60(3H, br m, BH_3), 2.57(3H, s, $N(Me)_2$), 2.62(3H, s, $N(Me)_2$), 2.90 (2H, m, C_3-CH_2), 3.5(2H, m, C_2-CH_2), 4.60(2H, m, C_1-CH_2), 7.2-7.6(9H, m, Ph-H); δ_C 41.1, 51.3, 52.8, 57.0, 62.0, 123.2, 128.4, 131.3; m/z 218(21%), 110(21), 86(65), 84(100), 43(29), 28(38)

[N-bromoacetyl]-(R)-(α)-methylbenzylamine 11:
To a stirred solution of (R)-(α)-methylbenzylamine (40.0g, 330.09mmol, 1eq.) and Et_3N (35.07g, 346.59mmol, 1.05eq.) dissolved in dry DCM (500ml) at -70°C was added dropwise a solution of bromoacetylbromide (66.63g, 330.09mmol, 1eq.) in dry DCM (100ml). The temperature was kept below -65°C throughout the addition. The resultant solution was stirred at -70°C for 5 minutes and quenched by rapid addition of 2M HCl (100ml) by syringe. The organic phase was washed with 2M HCl (500ml), sat. Na_2CO_3 (500ml), dried with $MgSO_4$, filtered and concentrated under reduced pressure. The white solid product was immediately recrystallised from DCM/hexane to give **11** as a white crystalline solid (59.79g, 75%). mp. 104°C (from DCM/hexane); $[\alpha]_D^{17}$ = +19.6° (c 0.598, DCM); (Found: C, 49.7; H, 4.98; N, 5.72. $C_{10}H_{12}NOBr$ requires: C, 49.60; H, 5.00; N, 5.79%); υ_{max} (nujol)/cm^{-1} 3263.0, 1646.4; δ_H 1.52(3H, d, J = 7.0Hz, C_1-Me), 3.83(2H, AB system, J = 15.4Hz, C_3-CH_2), 5.09(1H, p, J = 7.3Hz, C_1-H), 6.85(1H, br s, NH), 7.32(5H, m, Ph-H); δ_C 21.54, 29.13, 49.46, 125.95, 127.47, 128.64, 142.49, 164.48; m/z 162(100%), 106(54)

[N-(2-pyrrolidyl)-acetyl]-(R)-(α)-methylbenzylamine 12:
To a stirred solution/suspension of [N-bromoacetyl]-(R)-(α)-methylbenzylamine (72.36g, 298.86mmol, 1eq.) and Et_3N (30.24g, 298.86mmol, 1eq.) in dry DCM (300ml) at 0°C was added dropwise pyrrolidine (22.32g, 313.80mmol, 1.05eq.). The resultant solution was stirred at room temperature for 1 hour, poured into H_2O (300ml) and extracted with 15% HCl (3 x 250ml). The acid extract was basified with 30% NaOH to pH >12, extracted with DCM (4 x 250ml), dried with Na_2SO_4, filtered and concentrated under reduced pressure. The resulting solid was triturated with Et_2O and filtered off to give **12** as an off-white solid (59.89g, 86%).
mp. 109-110°C (from DCM/hexane); $[\alpha]_D^{20}$ = + 3.97° (c 2.08, DCM); (Found: C, 72.3; H, 8.92; N, 12.3. $C_{14}H_{20}N_2O$ requires: C, 72.37; H, 8.68; N, 12.06%); υ_{max} (nujol)/cm^{-1} 3323.4, 1646.9; δ_H 1.50(3H, d, J = 7.0Hz, C_1-Me), 1.78(4H, m, C_5, C_6-CH_2), 2.58(4H, m, C_4, C_7-CH_2), 3.15 (2H, AB system, J = 17.1Hz, C_3-CH_2), 5.18(1H, p, J = 7.0Hz, C_1-H), 7.32(5H, m, Ph-H), 7.37(1H, br s, NH); δ_C 21.70, 23.68, 47.65, 54.23, 59.10, 125.78, 126.89, 128.31, 143.14, 169.57; m/z 84(100%)

[N-(2-pyrrolidyl)-ethyl]-(R)-(α)-methylbenzylamine 13: To a vigorously stirred suspension of $LiAlH_4$ (19.51g, 515.58mmol, 2eq.) in dry THF (500ml) was added dropwise a solution of [N-(2-pyrrolidyl)-acetyl]-(R)-(α)-methylbenzylamine **12** (59.89g, 257.74mmol, 1eq.) in dry THF (100ml). The resultant suspension was heated at reflux overnight, allowed to cool and 20ml H_2O was added dropwise, followed by 20ml 15% NaOH and 60ml H_2O. The resultant solution was filtered, concentrated under reduced pressure, redissolved in Et_2O (500ml), dried with Na_2SO_4, filtered and concentrated under reduced pressure. The slightly green oil produced was dissolved in dry Et_2O (300ml) and saturated with HCl gas, solvent was removed under reduced pressure and the solid residue was recrystallised from ^iPrOH to give an off-white solid. This solid was dissolved in H_2O (100ml) and basified with 30% NaOH, extracted with Et_2O (4 x 100ml), dried with Na_2SO_4, filtered and concentrated under reduced pressure. Distillation gave **13** as a colourless oil (24.31g, 43%). bp. 98-100°C / 0.2mmHg; $[\alpha]_D^{20}$ = + 41.2° (c 2.021, DCM); (Found: C, 77.0; H, 10.4; N, 13.0. $C_{14}H_{22}N_2$ requires: C, 77.0; H, 10.2; N, 12.8%); υ_{max} (neat)/cm^{-1} 3310.1, 1681.9; δ_H 1.36(3H, d, J = 6.6Hz, C_1-Me), 1.73(4H, s, C_5, C_6-CH_2), 2.41(4H, m, C_4, C_7-CH_2),

2.57(4H, m, C_2, C_3-CH_2), 3.74(1H, q, J = 6.6Hz, C_1-H), 7.30(5H, m, Ph-H); δ_C 23.06, 24.07, 46.12, 53.71, 55.66, 58.19, 126.14, 126.33, 127.92, 145.54; m/z 219(78%), 105(18), 84(100)

[N-(2-pyrrolidyl)-ethyl]-(R)-benzazaphosphole diborane complex (*trans* 6 and *cis*-7):
To a solution of [N-(2-pyrrolidyl)-ethyl]-(R)-(α)-methylbenzylamine **13** (0.5g, 2.29mmol, 1eq.) and TMEDA (0.29g, 2.52mmol, 1.1eq.) in dry Et_2O (0.5ml) cooled to -70°C was added dropwise n-BuLi (2.10ml, 5.04mmol, 2.4M, 2.2eq.). The resulting solution was allowed to reach room temperature and stirred at room temperature overnight. The bright orange solution was diluted with dry Et_2O (10ml), cooled to -70°C and dichlorophenylphosphine (0.61g, 3.44mmol, 1.5eq.) was added dropwise. The resulting yellow suspension was stirred at -70°C for 1 hour and then at room temperature for 2 hours. Borane-dimethyl sulphide complex (0.73g, 9.62mmol, 4.2eq.) was added dropwise and the resulting thick yellow suspension was stirred at room temperature for 1 hour. It was then poured into saturated $NaHCO_3$ (50ml), extracted with DCM (4 x 50ml), dried with Na_2SO_4, filtered and concentrated under reduced pressure. Flash chromatography (gradient elution: 0-25% EtOAc in petrol) gave a colourless gum (0.60g, 74%). Further flash chromatrography (gradient elution: 15-30% EtOAc in petrol) gave the less polar diastereomer, *cis*-**7**, as a colourless gum (36% yield) and the more polar diastereomer, *trans*-**6**, as a white crystalline solid (38% yield). The more polar diastereomer, *trans*-**6**, was recrystallised from DCM / hexane. Data for *trans*-**6**: mp. 120-121°C; $[\alpha]_D^{20}$ = -210.1° (c 1.16, DCM); υ_{max} (nujol)/cm^{-1} 2613.7 w, 2366.9 s, 2238.0 s, 1459.1 s, 1184.7 s; δ_H 0.2-2.2 (6H, br m, BH_3), 1.59 (3H, d, J = 6.2Hz, C_1-Me), 1.83(2H, br m, C_5, C_6-CH_2), 2.10 (2H, br m, C_5, C_6-CH_2), 2.75(2H, br m, C_3, C_4, C_7-CH_2), 3.13(2H, br m, C_3, C_4, C_7-CH_2), 3.35(1H, br m, C_2-CH_2), 3.65(1H, br m, C_2-CH_2), 4.81(1H, q, J = 6.2Hz, C_1-H), 7.42(9H, m, Ph-H); δ_C 21.44, 21.51, 22.27, 22.67, 39.69, 60.88, 62.44, 62.83, 63.87, 123.27, 123.37, 128.35, 128.53, 128.70, 128.83, 131.62, 131.66, 131.69, 131.83, 131.88, 131.91, 148.07, 148.16; δ_P 75.3(d, J = 81.0Hz); δ_B -10, -35 / -36; m/z 337(100%), 325(18), 84(18). Data for *cis*-**7**: $[\alpha]_D^{22}$ = +160.5° (c 1.26, DCM); υ_{max} (nujol)/cm^{-1} 2613.7 w, 2366.9 s, 2238.0 s, 1459.1 s, 1184.7 s; δ_H 0.2-2.2 (6H, br m, BH_3), 1.61 (3H, d, J = 6.4Hz, C_1-Me), 1.85(2H, br m, C_5, C_6-CH_2), 2.09 (2H, br m, C_5, C_6-CH_2), 2.75(1H, br m, C_3, C_4, C_7-CH_2), 2.96(1H, br m, C_3, C_4, C_7-CH_2), 3.14(2H, br m, C_3, C_4, C_7-CH_2), 3.45(1H, br m, C_2-CH_2), 3.80(1H, br m, C_2-CH_2), 4.71(1H, q, J = 6.4Hz, C_1-H), 7.0-8.0(9H, m, Ph-H); δ_C 21.15, 22.02, 22.35, 38.99, 39.14, 60.59, 60.95, 61.63, 62.60, 123.12, 123.22, 127.83, 128.05, 128.31, 128.44, 130.88, 131.04, 131.17, 131.36, 147.51, 147.64

X-ray crystallographic data for trans-6;
A crystal of approximate dimensions 0.4 x 0.2 x 0.2 mm was used for data collection. *Crystal data:* $C_{20}H_{31}N_2B_2P$, M = 352.1 orthorhombic, a =9.604(1), b = 10.496(2), c = 21.259(3)Å, U = 2143.0 $Å^3$, space group $P2_12_12_1$, Z = 4, D_C = 1.09 gcm^{-3}, μ(Mo-$K\alpha$) = 1.30 cm^{-1}, F(000) = 760. Data were measured at room temperature on a CAD4 automatic four-circle diffractometer in the range $2 \leq \theta \leq 24^o$. 1946 reflections were collected of which 1115 were unique with $I > 2\sigma(I)$. Data were corrrected for Lorentz and polarisation effects but not for absorption. Structure solution was by direct methods and refinement using the SHELX[16] suite of programs. In the final least squares cycle all atoms were allowed to vibrate anisotropically. Hydrogen atoms were included at calculated positions except in the instance of the borane residues, where the protons

(H1-H6) were located in an advanced Difference Fourier and positionally refined. Final residuals after 10 cycles of least squares were R =0.0432, R_w = 0.0345 for a weighting scheme of w =2.5889/[σ^2(F) + 0.000106(F)^2]. The max. and min. residual densities were 0.06 and -0.07 eÅ^{-3} respectively. The absolute configuration of the molecule was assigned on the basis of the chiral centre at C7, which was known to be R configuration. Full details have been deposited at the Cambridge Crystallographic Database.

***Trans*-(R)-(-)-N-(*Tert*-butyldiphenylsilyl)-dihydrobenzazaphosphole oxide 15:**[9]

TBDPS protected (R)-(α)-methylbenzylamine **14**[10] (2.0g, 5.56mmol, 1eq.) was dissolved in dry Et_2O (0.5ml) and TMEDA (0.71g, 6.12mmol, 1.1eq.) added. The resultant solution was cooled to -70°C and n-BuLi (4.89ml, 12.23mmol, 2.5M, 2.2eq.) added dropwise.[11] The solid precipitate formed was redissolved by gentle heating using a heat-gun. After stirring at room temperature over-night the solution was cooled to -70°C and dry Et_2O (11ml) was added. Phenylphosphinyldichloride (1.19g, 6.12mmol, 1.1eq.) was added slowly dropwise. The resulting slurry was stirred at -70°C for 1 hour and at room temperature for 1 hour. The viscous yellow slurry was poured into saturated $NaHCO_3$ and extracted with DCM (4 x 50ml), dried over Na_2SO_4, filtered and concentrated under reduced pressure. Flash chromatography (gradient elution: 30-50% EtOAc in petrol) gave **15** as a white solid (1.00g, 37%). This material was shown to be identical to an authentic sample of **15** by ^{1}H NMR, polarimetry and TLC.[9]

***Trans*-(R)-(-)-(N-*Tert*-butyldiphenylsilyl)-dihydrobenzazaphosphole borane complex (*trans*-8):**[9]

Triethylamine (1.13g, 11.21mmol, 6eq.) was added, dropwise over 1 minute, to a stirred solution of trichlorosilane (1.27g, 9.34mmol, 5eq.) in dry toluene (7.5ml) cooled in an ice-bath. The resultant solution was heated to 70°C and *trans*-(R)-(-)-N-(*tert*-butyldiphenylsilyl)-dihydrobenzazaphosphole oxide **15** (0.90g, 1.87mmol, 1eq.) was added in one portion. The solution was stirred at 70°C for 3.25 hours, cooled in an ice-bath and borane:dimethyl sulphide complex (1.01g, 13.27mmol, 7.1eq.) added dropwise. This solution was stirred at room temperature for 0.75 hours, poured into saturated $NaHCO_3$, extracted with EtOAc (3 x 50ml), dried with Na_2SO_4, filtered and concentrated under reduced pressure. Flash chromatography (5% EtOAc in petrol) gave **8** as a white solid which was recrystallised from DCM / hexane (0.31g, 35%). mp. 191-193°C (DCM / hexane); $[\alpha]_D^{20}$ = -405.3° (c 0.246, DCM); (Found: C, 74.9; H, 7.46; N, 3.08. $C_{30}H_{35}NSiPB$ requires: C, 75.15; H, 7.36; N, 2.92%); υ_{max} (nujol)/cm^{-1} 2721.4 w, 2418.9 s, 2363.0 s, 2314.5 s, 2239.5 m, 1588.4 w, 1463.8 s, 1427.5 s, 1396.4 w, 1376.0 s; δ_H 0.2-2.0(3H, br m, BH_3), 1.26(9H, s, ^{t}Bu), 1.44(3H, d, J = 6.6Hz, C_1-Me), 5.52(1H, m, C_1-CH), 6.92(4H, m, Ph-H), 7.15-7.6(13H, m, Ph-H), 8.01(3H, m, Ph-H); δ_C 20.11, 27.67, 29.69, 65.52, 122.30, 122.43, 126.90, 127.58, 127.76, 127.89, 128.26, 128.39, 128.46, 128.54, 129.43, 129.50, 130.91, 130.94, 132.16, 132.43, 132.59, 133.46, 135.14, 136.42, 136.79, 137.43, 137.51, 148.47; dP 84.19 (d, J = 70.5Hz); m/z (NOBA matrix) 481.2(7%), 480.2(19), 479.2(37), 478.2(100), 477.2(30).

X-ray crystallographic data for *trans*-8:

A crystal of approximate dimensions 0.4 x 0.2 x 0.2 mm was used for data collection. *Crystal data:* $C_{30}H_{35}NBPSi$, M = 479.5, monoclinic, a =9.016(2), b = 14.218(2), c = 11.413(2)Å, β=109.52(2)°,U =

1378.9 $Å^3$, space group $P2_1$, $Z = 2$, $D_C = 1.16$ gcm^{-3}, μ(Mo-$K\alpha$) = 1.60 cm^{-1}, $F(000) = 512$. Data were measured at room temperature on a CAD4 automatic four-circle diffractometer in the range $2 \leq \theta \leq 24^o$. 2417 reflections were collected of which 1964 were unique with $I > 2\sigma(I)$. Data were corrrected for Lorentz and polarisation effects but not for absorption. The structure was solved by direct methods and refined using the SHELX[16] suite of programs. In the final least squares cycle all atoms were allowed to vibrate anisotropically. Hydrogen atoms were included at calculated positionsexcept in the instance of the borane residue, where the protons (H1-H3) were located in an advanced Difference Fourier and refined at a distance of 1.04 Å from the parent boron atom. Final residuals after 10 cycles of least squares were R =0.0310, R_w = 0.0334 for a weighting scheme of $w = 1.4815/[\sigma^2(F) + 0.001089(F)^2]$. The max. and min. residual densities were 0.07 and -0.05 $eÅ^{-3}$ respectively. The absolute configuration of the molecule was assigned on the basis of the chiral centre at C7, which was known to be R configuration. Full details have been deposited at the Cambridge Crystallographic Database.

Trans-(R)-(-)-benzazaphosphole borane complex (_trans_-16):

Trans-(R)-(-)-(N-_Tert_-butyldiphenylsilyl)-dihydrobenzazaphosphole borane complex **8** (0.5g, 1.04mmol, 1eq.) was dissolved in dry THF (10ml) and TBAF (1.04ml, 1.15mmol, 1.1eq.) added. The resultant solution was stirred at room temperature for 2 hours, poured into saturated NH_4Cl and extracted with EtOAc (4 x 50ml). The organic extract was dried with Na_2SO_4, filtered and concentrated under reduced pressure. Flash chromatography (gradient elution: 10-15% EtOAc in petrol) gave **16** as a colourless oil (245mg, 98%). mp. 202-203°C (DCM / hexane); $[\alpha]_D^{20}$ = -62.7° (c 0.95, chloroform); (Found: C, 69.7; H, 7.18; N, 5.68. $C_{14}H_{17}NPB$ requires: C, 69.75; H, 7.11; N, 5.81%); δ_H 0.2-1.8(3H, br q, J = 45Hz, BH_3), 1.59(3H, d, J = 6.4Hz, C_1-Me), 2.42(1H, br d, J = 17.4Hz, NH), 4.98(1H, q, J = 6.4Hz, C_1-CH), 7.3-7.75(9H, m, Ph-H); δ_C 24.28, 59.45, 59.52, 122.96, 123.07, 128.25, 128.35, 128.39, 128.54, 130.57, 130.73, 131.23, 131.72, 135.19, 135.90, 148.65, 148.78; m/z 227(73%), 212(43), 150(100).

Morpholine deboration procedure:

Ligand was dissolved in dry morpholine (1ml) and heated to 70°C for two hours. Excess morpholine was removed by oil pump (0.1mmHg) while the vessel remained in the 70°C heating bath. After 10 minutes the vessel was cooled in an ice-bath and filled with dry argon.

DABCO deboration procedure:

Ligand and 1eq. of DABCO per borane molecule on the ligand were dissolved in dry toluene (1ml) and heated to 40°C for two hours. The solvent was removed by oil pump (0.1mmHg) while the vessel remained in the 40°C heating bath. After 10 minutes the vessel was cooled in an ice-bath and filled with dry argon.

Pd catalysed allylation reaction:[5]

A solution of diallyl palladium chloride dimer in dry DCM (1ml) was added to the vessel containing deborated ligand. The resultant yellow solution was refluxed for two hours, allowed to reach room temperature and sequentially was added 1,3-diphenylpropenyl acetate **4** (0.2g, 0.79mmol, 1eq.) dissolved in dry DCM (1ml), dimethyl malonate (0.12g, 0.87mmol, 1.1eq.), bis-[trimethylsilyl] acetamide (0.18g, 0.87mmol, 1.1eq.) and

KOAc (1mg). The resulting suspension was stirred at room temperature overnight, diluted with Et_2O, washed with ice-cold, saturated NH_4Cl solution (2 x 20ml), dried with Na_2SO_4, filtered and concentrated under reduced pressure. If time allowed it was left under high vacuum (0.1mmHg) overnight to remove excess dimethyl malonate. Flash chromatography (gradient elution: 5-10% EtOAc in petrol) gave the addition product as a slightly yellow oil that solidified on standing. This material gave ^1H NMR data identical to that described in reference 5. Data for **5**, δ_H 3.50(3H, s, CO_2Me), 3.69(3H, s, CO_2Me), 3.96(1H, d, J = 11.0Hz, C_4-CH), 4.27(1H, dd, J = 8.4, 11.0Hz, C_3-CH), 6.33(1H, dd, J = 8.4, 15.8Hz, C_2-CH), 6.48(1H, d, J = 15.8Hz, C_1-CH), 7.15-7.4(10H, m, Ph-H)

NMR enantiomeric excess determination:

A sample of the allylation adduct (5-10mg) was weighed accurately into a screw-top vial. 0.4-0.45 eq. of Eu(HFC)3 was weighed out avoiding undue exposure to atmospheric moisture into another screw-top vial. The original allylation sample was dissolved in 0.6ml of dry $CDCl_3$ and transferred into the vial containing the shift-reagent. After approximately 30 seconds of vigorous shaking the shift-reagent dissolved and the homogeneous yellow solution was transferred into an NMR tube. The ^1H spectrum of the sample shows a doublet and two singlets at approximately 4ppm (depending on the amount of shift-reagent used). The singlets are the signal given by each antipode for one of the methyl groups in the product. The doublet is the unresolved signal for the other methyl group in the product. The integral of the doublet and the sum of the integrals of the two singlets should thus give an approximately similar numerical value. The relative integrals of the two singlets can be used to give the enantiomeric excess of the sample analysed. Using the (+)-antipode of the shift reagent, the singlet with highest ppm value corresponds to the (R)-enantiomer.

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