# Synthesis of dihydrobenzazaphosphole ligands *via* an intramolecular cyclisation reaction

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A novel intramolecular cyclisation reaction of 1,3,2-oxazaphospholidines has been employed for the diastereoselective synthesis of chiral, non-racemic dihydrobenzazaphosphole ligands. The new ligands have been employed in enantioselective palladium-catalysed allylic substitution reactions.

## Introduction

Enantiomerically pure bidentate phosphorus-donor ligands are pivotal materials in asymmetric catalysis.<sup>1</sup> Whilst  $C_2$  symmetric ligands such as Chiraphos 1, BINAP and DiPAMP have the advantage of simplicity of structure, mixed-donor unsymmetric ligands have the advantage of versatility in terms of electronic and steric structure. An electronic change can have a dramatic effect; for example the enantioselectivity of asymmetric hydrogenation (Scheme 1) may increase markedly when the ligand



**2** or **3**.

containing one electron-rich diphosphine (2) is employed in place of the electronically balanced donor (3).<sup>2</sup> In the allylic substitution reaction in Scheme 2 a product of 93% ee is



Scheme 2 Reagents and conditions: i) 1 mol%  $[Pd_2(dba)_3]$ ,  $CH_2(CO_2Me)_2$ , BSA, NaOAc, ligand 4 or 5.

obtained using non-identical donor ligand 4. However, when the ligand is replaced with a like-donor analogue 5, a dramatic fall in asymmetric induction is observed.<sup>3</sup>



As a part of a programme of ongoing investigations into new chiral ligands containing P–N bonded architechtures,<sup>4-9</sup> we wished to prepare a series of enantiomerically pure dihydrobenzazaphosphole ligands based on the general structure 6.<sup>4-7</sup>

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We anticipated that such ligands would benefit from simple modification towards a number of mono- and bidentate derivatives which could be 'fine-tuned' towards certain reactions by variation of the functional group X and the exocyclic phosphorus donor group.



Previous work in our group<sup>5</sup> had led to the synthesis of ligand *trans*- and *cis*-7 via the reaction of an ortho-lithiated  $\alpha$ -methylbenzylamine derivative with dichlorophenylphosphine. The borane adduct was formed to prevent degradation, and the ca. 1 : 1 product mixture was resolved by flash chromatography. The same approach was adopted for the synthesis of the analogous ligand **8**. The ortho-lithiation and subsequent quenching was again found to produce an inseparable 1 : 1 ratio of diastereoisomers (Scheme 3). In contrast, using diastereo-



Scheme 3 Reagents and conditions: i) nBuLi, TMEDA, PhPCl<sub>2</sub>,  $BH_3$ ·SMe<sub>2</sub>

isomerically pure phosphine oxide as an intermediate,<sup>4</sup> the cyclisation was diastereoselective. After a simple reduction and boration, a single diastereoisomer of *trans*- $\mathbf{8}$  was isolated (Scheme 4).



Scheme 4 Reagents and conditions: i) nBuLi, TMEDA, PhP(O)Cl<sub>2</sub>, ii) Et<sub>3</sub>N, HSiCl<sub>3</sub>, BH<sub>3</sub>·SMe<sub>2</sub>.

We have also reported a synthesis of the  $C_2$ -symmetric diphosphine ligand 9. Several attempts at deprotonation to

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incorporate the ethylene bridge between two molecules of desilylated *trans*-**8** were made but these consistently failed. An alternative approach was therefore devised whereby a lithium–bromide exchange and intramolecular cyclisation, followed by subsequent quenching with dichlorophenylphosphine and trapping with borane (Scheme 5), was employed.<sup>7</sup> The final step



Scheme 5 Reagents and conditions: i) 4.05 eq. nBuL, ii) PhPCl<sub>2</sub>, iii) BH<sub>3</sub>·SMe<sub>2</sub>.

proceeded without stereoselectivity so that a statistical mixture of *trans,trans-9*, *cis,cis-9* and *cis,trans-9* compounds was produced. The *trans,trans-9* was separated from the other diastereoisomers in a yield of 14%.

# **Results and discussion**

We anticipated that the cyclisation reaction depicted in Scheme 5 could be employed in the synthesis of ligands 6 through the use of an enantiomerically pure amino alcohol. Our initial attempted approach to the synthesis of ephedrine-derived monodentate (10) and bidentate (11) ligands is illustrated in Scheme 6.

The alkylation of (1S,2R)-norephedrine with 2-bromobenzyl bromide gave a good yield (84%) of the monoalkylated product, **12**. Unfortunately the oxazaphospholidines (*trans*-**13** and *cis*-**13**) were formed in the next step with little diastereo-isomeric control (*ca.* 2 : 1). Even after repeated column chromatography only 31% of the major diastereoisomer (assumed to



trans-11 not formed

Scheme 6 Reagents and conditions: i) NEt<sub>3</sub>, PhPCl<sub>2</sub>, ii) BH<sub>3</sub>·SMe<sub>2</sub>, iii) 2 eq. tBuLi, iv) Et<sub>3</sub>N, Ph<sub>2</sub>PCl.

be *trans* on the basis of steric effects) and 14% of the minor diastereoisomer (assumed to be *cis*) was isolated.

The pivotal step, the intramolecular cyclisation, was attempted using Bu<sup>t</sup>Li at -78 °C. It was found to be extremely clean and high yielding with apparent formation of a diastereoisomerically pure product **10** in each case. The configuration at the phosphorus atom was not determined but according to existing precedent, the intermolecular reaction of closely related oxazaphospholidine–borane complexes with alkyllithium reagents is known to proceed with *retention* of configuration at phosphorus.<sup>10a-c</sup> However this is believed to arise from a mode of attack which is *cis* to the P–O bond which is unavailable to **13**.<sup>10b</sup> We have therefore assumed a reaction with *inversion* of configuration at phosphorus in our application, a mode which has precedent in other systems.<sup>4</sup> Unfortunately numerous attempts at the phosphinylation of the free hydroxy group, in an attempt to form *trans*-**11**, failed and only unreacted starting material was recovered.

We suspected that the reaction had failed because the phenyl ring adjacent to the hydroxy group was hindering the incoming diphenylphosphine. An attempt was made to phosphinylate benzyl alcohol and a white crystalline solid corresponding to the product **14** was formed in 64% yield. Consequently, it was concluded that the phenyl group was sterically preventing phosphorylation.



It seemed to us that an appropriate alternative  $\beta$ -amino alcohol would be (S)-valinol. Using the same methodology as that used for (1S,2R)-norephedrine, ligands 15 and 16 were



Scheme 7 Reagents and conditions: i) TMEDA, PhPCl<sub>2</sub>, ii) BH<sub>3</sub>·SMe<sub>2</sub>, iii) 2 eq. tBuLi, iv) Ph<sub>2</sub>PCl, v) TBDMSCl, imidazole, DMF.

both prepared successfully (Scheme 7). From the alkylation of (S)-(+)-valinol using 2-bromobenzyl bromide, using potassium carbonate as the base, **17** was isolated in moderate yield (58%) as a colourless oil. Fortunately, the formation of the oxazaphospholidine, **18**, proceeded selectively to give essentially one diastereoisomer of product. An X-ray structure of **18** was obtained to confirm that there was a *trans* relationship between the isopropyl and the phenyl groups (see Electronic Supplementary Information †).

From the oxazaphospholidine, **18**, intramolecular cyclisation gave the monodentate ligand, **15**, in a very good yield (87%). The stereochemistry was not confirmed but again, according to the arguments outlined above, inversion at phosphorus was assumed to have taken place. The corresponding bidentate ligand, **19**, was made directly from the oxazaphospholidine, **18**, without the isolation of **15**. As predicted no hindrance problems were encountered in the functionalisation of the hydroxy group. Additionally, the TBDMS protected monodentate ligand, **16** was made without difficulty from the corresponding alcohol **15**.

Ligands **15** and **16** were protected from oxidation by coordination to borane. This enabled them to be handled in the air and purified on silica gel. Two methods for deboration were selected which both employed the use of amines morpholine and 1,4-diazabicyclo[2.2.2]octane (DABCO) respectively.<sup>4-7</sup>

A convenient asymmetric reaction which was selected in order to test the efficiency of the ligands in asymmetric catalysis is the allylic substitution of 1,3-diphenyl-3-acetoxyprop-1-ene (20) and dimethyl malonate (Scheme 8) to give adduct 21. This



Scheme 8 Reagents and conditions: i)  $Y \mod [C_3H_5)PdCl]_2$ , CH<sub>2</sub>(CO<sub>2</sub>Me)<sub>2</sub>, DCM, BSA, NaOAc,  $X \mod \%$  deborated ligand 15, 16, 19.

reaction was selected on the basis of its widespread use as a prototype transformation in the literature.<sup>11</sup> Furthermore, the simple method of calculating the enantiomeric excess by paramagnetic shift reagent, Eu(hfc)<sub>3</sub>, was appealing.<sup>6</sup>

A number of reaction conditions were employed for the substitution reaction with the anion of dimethyl malonate.



Fig. 1 Pd complex of decomplexed 15 and 16 (allylic group omitted for clarity).



Fig. 2 Pd complex of decomplexed 19 (allylic group omitted for clarity).

Changing to a more polar solvent, such as DMSO, led to shorter reaction times but lower enantioselectivities. Solvents such as dichloromethane or ether, were unsuitable because of the lack of solubility of the sodium salt of dimethyl malonate. However, using  $(Me_3Si)_2NAc$  (BSA) to deprotonate *in situ* circumvented these difficulties to give a quantitative yield of product, **21**, in a shorter reaction time with no loss of asymmetric induction. To avoid any possible complications, the BSA method was adopted in all cases (Table 1).

Using the monodentate ligands **15** and **16** a number of promising results for the asymmetric allylic substitution reaction (Scheme 8) were achieved. All the observed asymmetric inductions were moderate. The highest ee of 63% (*S*) was achieved using 10 mol% of ligand **15** and 2 mol% of  $[(C_3H_5)PdCl]_2$ . The yields were generally moderate to good. The ratio of ligand to palladium was critical. If this fell below 2 mol% of palladium dimer (to 10 mol% of ligand) no product was seen by TLC after 5 days, presumably because of the low concentration of active palladium–ligand complex present.

Deborated ligand 17 was also employed in the prototype allylic substitution reaction. The ligand derived from the DABCO method of deboration gave a product of lower ee (26%, R) than that from the corresponding morpholine procedure. The highest induction of 59% (R) was obtained using 5 mol% of the bidentate ligand and 2 mol% of palladium dimer.

The stereochemical control may arise from an initial coordination of ligands **15** and **16** to palladium to form an intermediate palladium(0) species (Fig. 1). Due to their steric bulk we believe that only one phosphorus donor ligand is present in the complex. The other coordination site in the square planar array will be occupied by another ligand such as a tertiary amine (residual from the deprotection) or a chloride ion.

In the case of the diphosphine **19**, we believe that it is reasonable to assume that the ligand is acting in a bidentate manner (Fig. 2), since the product was formed with the opposite sense of induction. This reversal could only have arisen from a significant change in the conformation of the ligand in the active complex due to the presence of an additional chelating group. It should be noted that whilst the conformations of the aryl groups in the benzazaphosphole part of the molecule are predictable, those of the aryl rings on the other part of the ligand are unknown.

In summary, we have demonstrated that the intramolecular cyclisation of a diastereoisomerically pure 1,3,2-oxazaphospholidine may be used for the synthesis of dihydrobenzazaphosphole ligands. Such ligands may be employed in either monodonor or bidentate form in asymmetric reactions such as palladium-catalysed allylic substitution.

<sup>&</sup>lt;sup>†</sup> CCDC reference number 167765. See http://www.rsc.org/suppdata/ p1/b1/b105495n/ for crystallographic files in .cif or other electronic format.

Ligand	X (ligand mol%)	Y (Pd dimer mol%)	Deboration method	Yield/%	Ee/%(R/S)
 15	5	2	Morpholine	69	42 (S)
15	10	4	Morpholine	45	44(S)
15	10	3	DABCO	57	54(S)
15	10	2	DABCO	45	63(S)
15	10	1	DABCO	0	
15	10	1.5	Morpholine	0	_
16	5	2	Morpholine	17	59 ( <i>R</i> )
16	10	4	DABCO	35	29(R)
16	5	2	DABCO	26	26(R)
19	5	2	Morpholine	77	42(S)

### Experimental

### General

All air and moisture sensitive reactions were performed under an atmosphere of dry nitrogen or argon in thoroughly dried glassware. CH<sub>2</sub>Cl<sub>2</sub> was distilled from phosphorus pentoxide. DMF was fractionally distilled and stored over 3 Å molecular sieves. Ether, which refers to diethyl ether, and THF were pre-dried over sodium wire and then distilled from sodiumbenzophenone ketyl in an inert atmosphere. Petroleum ether, which refers to the fraction boiling in the range 60-80 °C, was distilled before use. Toluene was pre-dried over sodium wire and then distilled from sodium in an inert atmosphere. PhP(Cl)<sub>2</sub>, Ph<sub>2</sub>P(Cl) and PhP(O)Cl<sub>2</sub> were distilled before use. Morpholine, NEt<sub>3</sub>, pyridine and TMEDA were distilled from CaH<sub>2</sub>. Alkyllithium reagents were titrated using the method of Juaristi et al.<sup>12</sup> Reactions were monitored by TLC on Whatman aluminium backed  $UV_{254}$  silica gel plates. The chromatograms were viewed under UV light and visualised using potassium permanganate, PMA or iodine-silica. Flash column chromatography was carried out under medium pressure on 60 Å silica gel. Melting points are uncorrected. Optical rotations were recorded on a Perkin-Elmer 141 Polarimeter and are quoted in  $10^{-1} \text{ deg cm}^2 \text{ g}^{-1}$ . IR spectra were recorded on either a Perkin-Elmer 1600 Series FT IR instrument or a Perkin-Elmer 1310FT spectrometer. <sup>1</sup>H NMR spectra were recorded on a Bruker ACF250FT spectrometer at 250 MHz. <sup>13</sup>C NMR spectra were recorded on a JEOL JNM-GX270FT operating at 67.8 MHz, JEOL JNM-EX400 operating at 100.4 MHz, Bruker ACF-250FT operating at 62.9 MHz or a Bruker ACP 400 operating at 100.6 MHz. Both <sup>1</sup>H and <sup>13</sup>C spectra were recorded at rt. DEPT techniques were commonly used to aid interpretation of <sup>13</sup>C spectra, for which C-P couplings are quoted. In some cases distinct P-coupled <sup>13</sup>C peaks could not be assigned with confidence and in these cases the observed peaks are listed. <sup>31</sup>P spectra were proton-decoupled. Mass spectra were recorded on a VG analytical 7070E instrument. For FAB spectra, NBA was used as a matrix. EI spectra were recorded with an ionising potential of 70eV.

# (1S,2R)-N-(2-Bromobenzyl)norephedrine 12

Potassium carbonate (1.87 g, 13.50 mmol) was added to a solution of (1*S*,2*R*)-(+)-norephedrine (1.00 g, 6.61 mmol) in DMF (30 cm<sup>3</sup>). At 0 °C 2-bromobenzyl bromide (1.32 g, 5.29 mmol) was added in one portion. The solution was stirred at 0 °C for 60 minutes and gradually allowed to warm to rt, where it was stirred for a further 3 h. The mixture was diluted with ether (100 cm<sup>3</sup>). The organic layer was then washed with brine (2 × 50 cm<sup>3</sup>), dried over sodium sulfate, filtered and concentrated *in vacuo*. The resulting residue was purified by column chromatography on silica. Elution with petrol–EtOAc (4 : 1) gave the product **12** (1.42 g, 84%) as a waxy colourless oil, bp 166–168 °C (0.3 mmHg);  $[a]_{D}^{18}$  +21.8 (*c* 0.79, CH<sub>2</sub>Cl<sub>2</sub>) (Found: C, 59.9; H, 5.7; N, 4.4. C<sub>16</sub>H<sub>18</sub>NOBr requires: C, 60.0; H, 5.7; N, 4.4%);  $\nu_{max}(film)/cm^{-1}$  3404 (NH), 3061 (OH), 3028, 2968, 2926, 2870, 1668, 1492, 1468;  $\delta_{H}$  (270 MHz, CDCl<sub>3</sub>) 0.86 (3H, d,

*J* 6.4, CHC*H*<sub>3</sub>), 2.93–3.02 (1H, m, CH<sub>3</sub>C*H*NH), 3.96 (2H, s, ArC*H*<sub>2</sub>NH), 4.84 (1H, d, *J* 3.8, ArC*H*OH), 7.15 (1H, dt, *J* 7.6, 1.9, Ar-*H*), 7.22–7.40 (7H, m, Ar-*H*), 7.57 (1H, dd, *J* 7.6, 1.2, Ar-*H*);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 14.58 (CH<sub>3</sub>), 51.15 (CH<sub>2</sub>), 57.49 (CH), 73.03 (CH), 124.05, 125.99, 126.95, 127.44, 127.97, 128.75, 130.32, 132.85, 138.84, 141.22; *m/z* (CI) 321 ([M(<sup>79</sup>Br)<sup>+</sup> + 1], 35%), 320 (100%), 214 (78).

### (1*S*,2*R*)-2-Phenyl-3-(2-bromobenzyl)-4-methyl-5-phenyl-1,3,2oxazaphospholidine–borane complex 13

(1S,2R)-N-(2-Bromobenzyl)norephedrine 12 (0.30 g, 0.94 mmol) was dissolved in THF (35 cm<sup>3</sup>). At 0 °C triethylamine (0.32 cm<sup>3</sup>, 2.34 mmol) and dichlorophenylphosphine (0.15 cm<sup>3</sup>, 1.13 mmol) were added dropwise. The resulting mixture was stirred at rt for a further 2 h. At 0 °C borane-methyl sulfide complex solution (0.13 cm<sup>3</sup>, 1.41 mmol) was added dropwise. The solution was stirred at rt for a further 2 h. Saturated sodium hydrogen carbonate solution (50 cm<sup>3</sup>) was then added. The aqueous layer was extracted with  $CH_2Cl_2$  (5 × 50 cm<sup>3</sup>). The combined extracts were dried over sodium sulfate, filtered and concentrated in vacuo. The resulting residue was purified by chromatography on silica. Elution with petrol-EtOAc (10:1) separated the two diastereoisomers of the product. Data for the top spot, assigned trans-13: colourless oil (0.18 g, 43%), bp 93–95 °C;  $[a]_{D}^{20}$  +66.9 (c 0.77, CH<sub>2</sub>Cl<sub>2</sub>);  $v_{max}$ (film)/cm<sup>-1</sup> 3061, 3031, 2977, 2929, 2871, 2385, 2279, 1437; δ<sub>H</sub> (270 MHz, CDCl<sub>3</sub>) 0.2-2.2 (3H, br m, BH<sub>3</sub>), 0.64 (3H, d, J 6.6, CHCH<sub>3</sub>), 3.51-3.61 (1H, m, NCHCH<sub>3</sub>), 4.29-4.48 (2H, m, ArCH<sub>2</sub>N), 5.62 (1H, d, J 5.7, CHCHO), 7.10 (1H, dt, J 7.6, 1.7, Ar-H), 7.23-7.32 (6H, m, Ar-H), 7.43-7.62 (5H, m, Ar-H), 7.82-7.90 (2H, m, Ar-H);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 14.82 (CH<sub>3</sub>), 52.09 ( $J^{PC}$  18, ArCH<sub>2</sub>N), 57.09 ( $J^{PC}$  15, CHN), 83.38 ( $J^{PC}$  4, CHO), 123.58, 123.63, 125.48, 125.72, 125.76, 125.81, 125.98, 126.05, 126.93, 127.26, 127.77, 127.90, 128.02, 128.08, 128.13, 128.23, 128.30, 128.48, 128.48, 128.57, 128.70, 128.85, 128.92, 128.97, 129.01, 129.12, 129.25, 129.60, 130.05, 130.15, 130.42, 130.51, 130.66, 130.75, 130.99, 131.11, 132.01, 132.25, 132.99, 132.54, 132.67, 134.08, 134.57, 135.69, 135.76, 136.47, 136.53, 136.60;  $\delta_{\rm P}$  (160 MHz, CDCl<sub>3</sub>) 137.43; m/z (FAB+) 441 ([M(<sup>79</sup>Br)<sup>+</sup> + 1], 15%), 346 (100%). Found: 439.083046 (M<sup>+</sup>. C<sub>22</sub>H<sub>24</sub>NOBP<sup>79</sup>Br requires 439.087194). Lower spot, assigned cis-13: colourless oil (0.11 g, 27%), bp 93–96 °C;  $[a]_{D}^{18}$  –41.3 (c 0.32, CH<sub>2</sub>Cl<sub>2</sub>);  $v_{max}$ (neat)/cm<sup>-</sup> 3061, 2926, 2388, 1436;  $\delta_{\rm H}$ (270 MHz, CDCl<sub>3</sub>) 0.2–1.8 (3H, br m, BH<sub>3</sub>), 0.86 (3H, d, J 6.6, CHCH<sub>3</sub>), 3.98 (1H, septet, J 6.6, CH<sub>3</sub>CHN), 4.26–4.48 (2H, m, ArCH<sub>2</sub>N), 5.73 (1H, d, J 5.3, ArCHO), 7.04 (1H, dt, J 7.8, 1.7, Ar-H), 7.32-7.51 (1H, m, Ar-H), 7.76–7.83 (2H, m, Ar-H); δ<sub>c</sub> (100 MHz, CDCl<sub>3</sub>) 13.52 (CH<sub>3</sub>), 47.31 (J<sup>PC</sup> 11, ArCH<sub>2</sub>N), 59.12 (J<sup>PC</sup> 16, CHN), 84.12 (J<sup>PC</sup> 7, CHO), 124.07, 125.89, 126.03, 126.34, 126.58, 126.62, 127.62, 127.84, 128.15, 128.19, 128.28, 128.50, 128.63, 128.85, 128.92, 129.05, 129.30, 129.51, 130.86, 131.04, 131.15, 131.37, 131.50, 131.66, 132.69, 132.87, 133.05, 133.80, 134.28, 136.16, 136.22, 136.95, 137.00;  $\delta_{\rm P}$  (160 MHz, CDCl<sub>3</sub>) 135.14; m/z(CI) 441 ( $[M(^{79}Br)^+ + 1]$ , 6%), 439 ( $[M^+ + 1] - H_2$ , 5%), 426 (100%). Found: 439.085500. ([M<sup>+</sup>]. C<sub>22</sub>H<sub>24</sub>NOBP<sup>79</sup>Br requires: 439.087194).

Oxazaphospholidine trans-13 (0.40 g, 0.91 mmol) was dissolved in ether (30 cm<sup>3</sup>). At -78 °C tert-butyllithium was added dropwise. The mixture was stirred a further 30 minutes at -78 °C. Saturated sodium hydrogen carbonate solution (50 cm<sup>3</sup>) was added slowly. The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3  $\times$  100 cm<sup>3</sup>). The organics were combined, dried over sodium sulfate, filtered and concentrated in vacuo. The resulting residue was purified by chromatography on silica. Elution with petrol-EtOAc (10:1) gave the product *trans*-10 (0.20 g, 61%) as a white solid, mp 105–108 °C; [a]<sup>20</sup> –246.2 (c 0.31, CH<sub>2</sub>Cl<sub>2</sub>);  $v_{max}(CDCl_3)/cm^{-1}$  3508, 3060, 2927, 2855, 2374, 2251;  $\delta_{H}$  (270 MHz, CDCl<sub>3</sub>) 0.8-1.8 (3H, br m, BH<sub>3</sub>), 1.24 (3H, d, J 7.0, CHCH3), 2.07 (1H, d, J 3.3, OH), 3.69-3.81 (1H, m, CH3-CHN), 4.58 (1H, dd, J 14.3, 8.7, ArCH<sub>2</sub>N), 4.73 (1H, d, J 14.3, ArCH2N), 4.79-4.82 (1H, m, ArCHOH), 7.21-7.65 (14H, m, ArH);  $\delta_{\rm C}$  (67.8 MHz, CDCl<sub>3</sub>) 12.72 (CH<sub>3</sub>), 53.53 (CH<sub>2</sub>), 57.51 (J<sup>PC</sup> 10, CHN), 77.36 (J<sup>PC</sup> 7, CHO), 122.90, 125.72, 127.24, 127.89, 128.05, 128.22, 128.37, 130.76, 131.16, 131.35, 131.65, 141.99; m/z (CI) 362 ([M<sup>+</sup> + 1], 3%), 360 ([M<sup>+</sup> + 1] - H<sub>2</sub>, 38%), 240 (100%). Found: 360.168900 ( $[M^+ + 1] - H_2$ . C<sub>22</sub>H<sub>24</sub>NOBP requires 360.168849).

# (1*S*,2*R*)-*cis*-*N*-[(1-Methyl-2-hydroxy-2-phenyl)ethyl]dihydro-2,1-benzazaphosphole–borane complex 10

Oxazaphospholidine cis-13 (0.30 g, 0.69 mmol) was dissolved in ether (30 cm<sup>3</sup>). At -78 °C tert-butyllithium was added dropwise. The mixture was stirred for a further 30 minutes at -78 °C. Saturated sodium hydrogen carbonate solution (50 cm<sup>3</sup>) was then added slowly. The aqueous layer was extracted with  $CH_2Cl_2$  (3 × 100 cm<sup>3</sup>). The organics were combined, dried over sodium sulfate, filtered and concentrated in vacuo. The resulting residue was purified by chromatography on silica. Elution with petrol-EtOAc (10:1) gave the product cis-10 (0.20 g, 79%) as a white solid, mp 102-105 °C;  $[a]_{D}^{20}$  +240.3 (c 0.67, CH<sub>2</sub>Cl<sub>2</sub>);  $v_{max}$ (CDCl<sub>3</sub>)/cm<sup>-1</sup> 3507, 3061, 2982, 2937, 2905, 2849, 2374, 2244;  $\delta_{\rm H}$  (270 MHz, CDCl<sub>3</sub>) 0.8–1.8 (3H, br m, BH<sub>3</sub>), 1.01 (3H, d, J 6.8, CHCH<sub>3</sub>), 2.32 (1H, d, J 3.4, OH), 3.56-3.64 (1H, m, CH<sub>3</sub>CHN), 4.72 (1H, dd, J14.7, 11.7, ArCH<sub>2</sub>N), 4.82 (1H, d, J14.0, ArCH<sub>2</sub>N), 5.24-5.26 (1H, m, ArCHOH), 7.18–7.58 (14H, m, ArH);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 11.49 (CH<sub>3</sub>), 53.11 (J<sup>PC</sup> 19, ArCH<sub>2</sub>N), 55.82 (J<sup>PC</sup> 9, CHN), 78.59 (J<sup>PC</sup> 4, CHO), 123.58, 123.63, 125.77, 126.09, 126.32, 126.36, 127.51, 127.69, 128.17, 128.30, 128.43, 128.65, 128.76, 128.79, 128.85, 128.99, 129.05, 129.08, 131.24, 131.35, 131.48, 131.52, 131.68, 131.79, 132.03, 132.08, 142.60, 143.93, 144.01;  $\delta_{\mathbf{P}}$  (160 MHz, CDCl<sub>3</sub>) 77.58; m/z (CI) 362 ([M<sup>+</sup> + 1], 3%), 360 ([M<sup>+</sup> + 1] - H<sub>2</sub>, 47%), 240 (57%). Found 360.168900  $([M^+ + 1] - H_2, C_{22}H_{24}NOBP requires 360.168849).$ 

### Benzyloxy(diphenyl)phosphine-borane complex 14

Benzyl alcohol (1.00 cm<sup>3</sup>, 8.85 mmol) was dissolved in THF (150 cm<sup>3</sup>). At -78 °C n-butyllithium (5.5 cm<sup>3</sup>, 8.95 mmol) was added dropwise. The mixture was stirred at -78 °C for 60 minutes and then gradually allowed up to rt and stirred for a further 30 minutes. The temperature was lowered again to -78 °C whereupon chlorodiphenylphosphine (2.4 cm<sup>3</sup>, 13.00 mmol) was added dropwise. It was stirred at -78 °C for 30 minutes and then warmed to rt where it was once again stirred for 30 minutes. At -78 °C borane-methyl sulfide complex solution (1.3 cm<sup>3</sup>, 13.00 mmol) was added dropwise. The mixture was gradually allowed up to rt and stirred overnight. The mixture was concentrated in vacuo. It was diluted in toluene (150 cm<sup>3</sup>), filtered and concentrated in vacuo. The resulting residue was purified by chromatography on silica. Elution with petrol–EtOAc (20 : 1) gave the product 14 (1.74 g, 64%) as a white solid, mp 66-68 °C (Found: C, 74.4; H, 6.7. C<sub>19</sub>H<sub>20</sub>OPB requires: C, 74.5; H, 6.6%);  $\nu_{max}$ (Nujol)/cm<sup>-1</sup> 1820, 1587, 1436, 1309, 1242;  $\delta_{\rm H}$  (270 MHz, CDCl<sub>3</sub>) 0.8–1.7 (3H, br m, BH<sub>3</sub>), 5.00 (2H, d, J 6.8, ArCH<sub>2</sub>O), 7.18–7.77 (15H, m, Ar-H);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 68.77 ( $J^{PC}$  13, CH<sub>2</sub>), 127.87, 128.02, 128.13, 128.25, 128.38, 128.49, 128.57, 128.67, 128.80, 128.91, 129.00, 130.80, 130.98, 131.11, 131.24, 131.34, 131.56, 131.73, 131.89, 132.20, 136.70; *m*/*z* (CI) 307 ([M<sup>+</sup> + 1], 3%), 305 ([M<sup>+</sup> + 1] – H<sub>2</sub>, 45%).

# (S)-(+)-2-Amino-3-methylbutan-1-ol

Sodium borohydride (6.28 g, 0.17 mol) was dissolved in THF (200 cm<sup>3</sup>). L-Valine (10.05 g, 85.47 mmol) was added in one portion. At 0 °C a solution of iodine (19.50 g, 84.98 mmol) in THF (50 cm<sup>3</sup>) was added dropwise over 50 minutes. The mixture was gradually allowed up to rt and stirred until the effervescence had stopped. It was refluxed for a further 24 h. Methanol (100 cm<sup>3</sup>) was added and the solution was stirred at rt for a further 30 minutes. The solvent was removed in vacuo. The resulting white paste was dissolved in 20% potassium hydroxide solution (150 cm<sup>3</sup>) and stirred for a further 24 h. The aqueous layer was extracted with  $CH_2Cl_2$  (5 × 100 cm<sup>3</sup>). The extracts were combined, dried over sodium sulfate, concentrated in vacuo to give an oily residue which was purified by short path distillation [100-106 °C (20 mmHg)] to give the product (4.68 g, 54%) as a colourless solid which displayed identical physical and spectroscopic properties to an authentic sample. Mp 30 °C; δ<sub>H</sub> (270 MHz, CDCl<sub>3</sub>) 0.91 (3H, d, J 3.3, CH<sub>3</sub>CH), 0.93 (3H, d, J 3.3, CH<sub>3</sub>CH), 1.52-1.62 (1H, m, CH<sub>3</sub>CHCH<sub>3</sub>) 2.0-2.2 (2H, broad, NH2), 2.53-2.60 (1H, m, NH2CH), 3.30 (1H, dd, J 10.4, 8.7, CHCH2OH), 3.64 (1H, dd, J 10.4, 3.6, CHCH2OH).

# (S)-2-[N-(2-Bromobenzyl)amino]-3-methylbutan-1-ol 17

2-Amino-3-methylbutan-1-ol (4.72 g, 45.79 mmol) was dissolved in DMF (200 cm<sup>3</sup>). Potassium carbonate (12.66 g, 91.58 mmol) was added in one portion. At 0 °C 2-bromobenzyl bromide (10.64 g, 42.57 mmol) was added. The mixture was allowed up to rt at which point it was stirred overnight. The solution was extracted with ether  $(5 \times 50 \text{ cm}^3)$ . The extracts were combined, dried over sodium sulfate, filtered and concentrated in vacuo. The oily brown residue was purified by chromatography on silica. Elution with petrol-EtOAc (1:1) gave the product 17 (6.76 g, 58%) as a colourless oil, bp 158 °C (0.3 mmHg);  $[a]_{D}^{17}$  +1.4 (c 1.05, CH<sub>2</sub>Cl<sub>2</sub>) (Found: C, 52.9; H, 6.8; N, 5.1. C<sub>12</sub>H<sub>18</sub>NOBr requires: C, 53.0; H, 6.7; N, 5.1%); v<sub>max</sub>(neat)/ cm<sup>-1</sup> 3356 (NH), 3063 (OH), 2957, 2872, 1568, 1468, 1440; δ<sub>H</sub> (270 MHz, CDCl<sub>3</sub>) 0.90 (3H, d, J 6.8, CHCH<sub>3</sub>), 0.96 (3H, d, J 6.8, CHCH<sub>3</sub>), 1.85 (1H, octet, J 6.8, CH<sub>3</sub>CHCH<sub>3</sub>), 2.0-2.8 (2H, br m, NH, OH), 2.40-2.47 (3H, m, NHCHCH<sub>2</sub>), 3.39 (1H, dd, J 10.7, 6.7, CHCH2OH), 3.65 (1H, dd, J 10.7, 4.1, CHCH2OH), 3.85 (2H, dd, J 21.6, 13.2, ArCH2NH), 7.11 (1H, dt, J 7.6, 1.8, Ar-H), 7.27 (1H, dt, J 6.9, 1.1, Ar-H), 7.37 (1H, dd, J 7.5, 1.7, Ar-H), 7.53 (1H, dd, J 8.0, 1.0, Ar-H); δ<sub>c</sub> (100 MHz, CDCl<sub>3</sub>) 18.42 (CH<sub>3</sub>), 19.39 (CH<sub>3</sub>), 28.72 (CH), 51.42 (CH<sub>2</sub>), 60.36 (CH<sub>2</sub>), 63.71 (CH<sub>2</sub>), 127.40, 128.65, 130.42, 132.74, 139.22; *m*/*z* (CI) 273 ([M<sup>+</sup> + 1], 24%), 242 ([M<sup>+</sup> + 1] -CH<sub>2</sub>OH, 62%).

# *trans-(S)*-2-Phenyl-3-(2-bromobenzyl)-4-isopropyl-1,3,2-oxaza-phospholidine-borane complex 18†

(S)-N-(2-Bromobenzyl)valinol **17** (2.18 g, 8.05 mmol) was dissolved in THF (50 cm<sup>3</sup>). At rt TMEDA (2.6 cm<sup>3</sup>, 17.22 mmol) was added dropwise. At 0 °C dichlorophenyl phosphine (1.2 cm<sup>3</sup>, 8.84 mmol) was added dropwise. The solution was stirred for a further 15 minutes at 0 °C and then allowed up to rt whereupon it was stirred for a further 30 minutes. On recooling to 0 °C, borane–methyl sulfide complex solution (22 cm<sup>3</sup>, 44.00 mmol) was added dropwise. The solution was gradually allowed up to rt where it was stirred overnight. Saturated sodium hydrogen carbonate solution (80 cm<sup>3</sup>) was added cautiously. The aqueous layer was extracted with  $CH_2Cl_2$  (5 × 50 cm<sup>3</sup>). The extracts were combined, dried over sodium sulfate, filtered and concentrated in vacuo. The resulting white solid was purified by chromatography on silica. Elution with petrol-EtOAc (10:1) with 1% NEt<sub>3</sub> gave the product 18 (2.47 g, 78%) as a white solid, mp 96–98 °C;  $[a]_{D}^{15}$  +85.4 (c 0.52, CH<sub>2</sub>Cl<sub>2</sub>) (Found: C, 54.9; H, 6.2; N, 3.5. C<sub>18</sub>H<sub>24</sub>NOBPBr requires: C, 55.1 H, 6.2; N, 3.6%); v<sub>max</sub>(Nujol mull)/cm<sup>-1</sup> 2384, 2338, 1588, 1568, 1438, 1395;  $\delta_{\rm H}$  (270 MHz, CDCl<sub>3</sub>) 0.2–1.8 (3H, br m, BH<sub>3</sub>), 0.85 (3H, d, J 7.0, CHCH<sub>3</sub>), 0.90 (3H, d, J 6.8, CHCH<sub>3</sub>), 1.95-2.06 (1H, m, CH<sub>3</sub>CHCH<sub>3</sub>), 3.69 (1H, dt, J 7.3, 3.7, CHCHN), 4.22-4.41 (4H, m, ArCH2N & CHCH2O), 7.00-7.78 (9H, m, Ar-H); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 14.74 (CH<sub>3</sub>), 19.31 (CH<sub>3</sub>), 27.70 (CH), 46.98 (J<sup>PC</sup> 14, ArCH<sub>2</sub>), 63.98 (CH), 67.71 (J<sup>PC</sup> 11, CH2O), 123.27, 127.23, 128.23, 128.38, 128.88, 130.66, 130.75, 130.84, 132.08, 132.50, 136.67, 136.71; δ<sub>P</sub> (160 MHz, CDCl<sub>3</sub>) 137.15; m/z (CI) 393 ([M(<sup>79</sup>Br)<sup>+</sup> + 1], 8%), 391([M<sup>+</sup> + 1] - H<sub>2</sub>, 15%) 298 (100%).

### (S)-trans-N-[(1-Isopropyl-2-hydroxy)ethyl]dihydrobenzazaphosphole-borane complex 15

Oxazaphospholidine 18 (4.03 g, 1.03 mmol) was dissolved in ether (50 cm<sup>3</sup>). At -78 °C tert-butyllithium (1.21 cm<sup>3</sup>, 2.06 mmol) was added dropwise. The solution was stirred for a further 90 minutes at -78 °C. Saturated sodium hydrogen carbonate solution (100 cm<sup>3</sup>) was added. The aqueous layer was extracted with  $CH_2Cl_2$  (5 × 60 cm<sup>3</sup>). The extracts were combined, dried over sodium sulfate, filtered and concentrated in vacuo. The resulting white solid was purified by chromatography on silica. Elution with petrol-EtOAc (6:1) with 1% NEt<sub>3</sub> gave the product 15 (0.28 g, 87%) as a white solid; mp 55 °C;  $[a]_{D}^{22}$  -206.5 (c 0.96, CH<sub>2</sub>Cl<sub>2</sub>);  $v_{max}$ (CDCl<sub>3</sub>)/cm<sup>-1</sup> 3525, 3057 (OH), 2959, 2366, 1456;  $\delta_{\rm H}$  (270 MHz, CDCl<sub>3</sub>) 0.2–1.8 (3H, br m, BH<sub>3</sub>), 0.41 (3H, d, J 6.8, CH<sub>3</sub>), 0.82 (3H, d, J 6.6, CH<sub>3</sub>), 1.63-1.84 (1H, m, CH<sub>3</sub>CHCH<sub>3</sub>), 2.03 (1H, br s, OH), 3.07-3.19 (1H, m, CHCHN), 3.65-3.72 (1H, m, CHCH2OH), 3.83-3.89 (1H, m, CHCH2OH), 4.45-4.64 (2H, m, ArCH2N), 7.15-7.58 (9H, m, Ar-H); δ<sub>c</sub> (100 MHz, CDCl<sub>3</sub>) 19.91 (CH<sub>3</sub>), 20.50 (CH<sub>3</sub>), 29.00 (CH), 51.07 (CH<sub>2</sub>), 61.58 (CH<sub>2</sub>), 62.39 (CH), 123.20, 123.30, 128.02, 128.13, 128.25, 128.30, 128.38, 128.51, 128.72, 131.18, 131.65, 131.75, 131.91, 143.78, 143.90;  $\delta_{\rm P}$  (160 MHz, CDCl\_3) 79.51;  $m\!/z$  (CI) 314 ([M^+ + 1], 5%), 312  $([M^+ + 1] - H_2, 12\%), 300 ([M^+ + 1] - BH_3, 52\%), 176 (100\%).$ Found: 312.168900 ([M<sup>+</sup> + 1] - H<sub>2</sub>. C<sub>18</sub>H<sub>24</sub>NOBP requires 312.168849).

### (S)-trans-N-[(1-Isopropyl-2-diphenylphosphanyloxy)ethyl]dihydro-2,1-benzazaphosphole-diborane complex 19

Oxazaphospholidine 18 (0.48 g, 1.23 mmol) was dissolved in ether (100 cm<sup>3</sup>). At -78 °C tert-butyllithium (1.54 cm<sup>3</sup>, 2.46 mmol) was added dropwise. It was stirred at -78 °C for 30 minutes. At -78 °C chlorodiphenylphosphine (0.33 cm<sup>3</sup>, 1.85 mmol) was added. The mixture was gradually allowed up to rt whereupon it was stirred overnight. At 0 °C borane-methyl sulfide complex solution (0.20 cm<sup>3</sup>, 1.97 mmol) was added dropwise. The mixture was stirred at 0 °C for 15 minutes and then at rt for 30 minutes. Saturated sodium hydrogen carbonate (100 cm<sup>3</sup>) was added. The aqueous layer was extracted with  $CH_2Cl_2$  (5 × 50 cm<sup>3</sup>). The extracts were combined, dried over sodium sulfate, filtered and concentrated in vacuo. The resulting yellow oil was purified by chromatography on silica. Elution with petrol-EtOAc (20:1) gave the product 19 (0.23 g, 38%) as a white solid, mp 103–105 °C;  $[a]_{D}^{19}$  –179.7 (c 0.30, CH<sub>2</sub>Cl<sub>2</sub>) (Found: C, 70.5; H, 7.2; N, 2.7. C<sub>30</sub>H<sub>37</sub>NOP<sub>2</sub>B<sub>2</sub> requires: C, 70.5 H, 7.3; N, 2.7%); v<sub>max</sub>(Nujol mull)/cm<sup>-1</sup> 3048, 2385, 2344, 2245, 1482, 1436;  $\delta_{\rm H}$  (270 MHz, CDCl<sub>3</sub>) 0.2–1.8 (6H, br m, B*H*<sub>3</sub>), 0.53 (3H, d, *J* 6.8, C*H*<sub>3</sub>), 0.84 (3H, d, *J* 6.8, C*H*<sub>3</sub>), 1.92–2.05 (1H, m, CH<sub>3</sub>C*H*CH<sub>3</sub>), 3.20–3.31 (1H, m, NC*H*CH<sub>2</sub>), 4.17–4.20 (2H, m, CHC*H*<sub>2</sub>O), 4.51–4.62 (2H, m, ArC*H*<sub>2</sub>N), 7.24–7.72 (19H, m, Ar-*H*);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 19.78 (CH<sub>3</sub>), 20.34 (CH<sub>3</sub>), 28.72 (CH), 52.76 (CH<sub>2</sub>), 60.83 (CH), 67.74 (CH<sub>2</sub>), 123.03, 123.12, 128.04, 128.18, 128.33, 128.48, 128.64, 129.92, 130.70, 130.96, 131.12, 131.31, 131.43, 131.49, 131.61, 131.77, 131.90, 134.83, 135.47, 143.85, 143.96;  $\delta_{\rm P}$  (400 MHz, CDCl<sub>3</sub>) 79.99 (d, *J* 63.7), 106.65 (d, *J* 77.1); *m*/*z* (EI) 497 (M<sup>+</sup> – BH<sub>3</sub>, 32%).

### (S)-trans-N-[(1-Isopropyl-2-tert-butyldimethylsilyloxy)ethyl]dihydro-2,1-benzazaphosphole-borane complex 16

Benzazaphosphole 15 (0.49 g, 1.56 mmol) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (30 cm<sup>3</sup>). Imidazole (0.13 g, 1.86 mmol) was added at rt and the temperature was lowered to 0 °C whereupon tertbutylchlorodimethylsilane (0.28 g, 1.86 mmol) in CH2Cl2 (10 cm<sup>3</sup>) was added dropwise. The mixture was allowed to warm to rt where it was stirred for 96 h. The reaction was quenched with saturated ammonium chloride solution (30 cm<sup>3</sup>). The aqueous layer was extracted with  $CH_2Cl_2$  (5 × 30 cm<sup>3</sup>). The extracts were combined, dried with sodium sulfate, filtered and concentrated in vacuo. The resulting oil was purified by chromatography on silica. Elution with petrol-EtOAc (20:1) gave the product 16 (0.56 g, 83%) as a white solid, mp 98-100 °C;  $[a]_{D}^{21}$  –128.8 (c 0.52, CH<sub>2</sub>Cl<sub>2</sub>);  $v_{max}$  (Nujol mull)/cm<sup>-1</sup> 2359, 1640, 1251, 837, 782;  $\delta_{\rm H}$  (250 MHz, CDCl<sub>3</sub>) 0.14 (6H, s, CH<sub>3</sub>SiCH<sub>3</sub>), 0.2-1.0 (3H, br m, BH<sub>3</sub>), 0.53 (3H, d, J 6.7, CH<sub>3</sub>CHCH<sub>3</sub>), 0.92 (9H, s, C(CH<sub>3</sub>)<sub>3</sub>), 0.94 (3H, d, J 7.6, CH<sub>3</sub>CHCH<sub>3</sub>), 2.18-2.22 (1H, m, CH<sub>3</sub>CHCH<sub>3</sub>), 2.82-2.90 (1H, m, NCHCH), 3.95 (1H, dd, J 10.6, 3.3, CHCH<sub>2</sub>O), 4.08 (1H, dd, J 10.6, 2.6, CHCH2O), 4.61 (1H, d, J 14.8, ArCH2N), 5.00 (1H, dd, J 14.8, 8.7, ArCH<sub>2</sub>N), 7.33-7.61 (9H, m, Ar-H); m/z (FAB+) 428 ([M<sup>+</sup> + 1], 6%), 268 (39%). Found: 427.2574 ([M<sup>+</sup>]. C<sub>24</sub>H<sub>39</sub>NPBOSi requires 427.2631).

### 1,3-Diphenyl-3-hydroxyprop-1-ene

Chalcone (10.24 g, 49.2 mmol) was dissolved in methanol (100 cm<sup>3</sup>). At rt cerium(III) chloride heptahydrate (18.3 g, 49.2 mmol) was added in one portion. Then at 0 °C sodium borohydride (2.36 g, 62.4 mmol) was added spatula-wise. After the effervescence had ceased it was gradually allowed up to rt where it was stirred for a further 3 h. Water (50 cm<sup>3</sup>) was added and the aqueous layer was extracted with ether (5 × 50 cm<sup>3</sup>). The extracts were combined, dried over magnesium sulfate, filtered and concentrated *in vacuo*. The resulting oil was purified by chromatography on silica. Elution with petrol–EtOAc (5 : 1) gave the product (9.17 g, 89%) as a yellow oil,  $\delta_{\rm H}$  (270 MHz, CDCl<sub>3</sub>) 2.10 (1H, s, OH), 5.39 (1H, d, J 6.2, ArCHOH), 6.38 (1H, dd, J 15.8, 6.2, CHCHCH), 6.69 (1H, d, J 15.8, ArCHCH), 7.23–7.45 (10H, m, Ar-H).<sup>6</sup>

# (E)-1,3-Diphenyl-3-acetoxyprop-1-ene 20

1,3-Diphenyl-3-hydroxyprop-1-ene (4.45 g, 21.15 mmol) was dissolved in pyridine (10 cm<sup>3</sup>). DMAP (1–2 crystals, catalytic) was added. At 0 °C acetic anhydride (6.0 cm<sup>3</sup>, 63.5 mmol) was added dropwise. The solution was gradually allowed up to rt where it was stirred overnight. Ether (200 cm<sup>3</sup>) was added and the solution washed with saturated copper(II) sulfate solution (5 × 50 cm<sup>3</sup>), saturated sodium hydrogen carbonate solution (2 × 50 cm<sup>3</sup>) and water (2 × 25 cm<sup>3</sup>). The organic layer was dried with magnesium sulfate, filtered and concentrated *in vacuo*. The resulting yellow oil was purified by chromatography on silica. Elution with petrol–EtOAc (20 : 1) gave the product **20** (4.55 g, 85%) as a pale yellow oil,  $\delta_{\rm H}$  (270 MHz, CDCl<sub>3</sub>) 2.10 (3H, s, OCOCH<sub>3</sub>), 6.29–6.38 (1H, m, CHCHCH), 6.44 (1H, d, *J* 7.0, ArCHOCO), 6.63 (1H, d, *J* 15.6, ArCHCH), 7.21–7.42 (10H, m, Ar-H).<sup>6</sup>

#### Pd catalysed allylation reaction of 20 to give 21<sup>6</sup>

The procedure for deboration has been described.<sup>6</sup> A solution of diallylpalladium chloride dimer in dry CH<sub>2</sub>Cl<sub>2</sub> (1 ml) 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 20 (0.2 g, 0.79 mmol, 1 eq.) dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (1 ml), dimethyl malonate (0.12 g, 0.87 mmol, 1.1 eq.), bis[trimethylsilyl]acetamide (0.18 g, 0.87 mmol, 1.1 eq.), ligand 15, 16 or 19 (5 or 10 mol%) and KOAc (1 mg). The resulting suspension was stirred at room temperature overnight, diluted with Et<sub>2</sub>O, washed with ice-cold, saturated NH<sub>4</sub>Cl solution  $(2 \times 20 \text{ ml})$ , dried with Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure. Flash chromatography (gradient elution: 5-10% EtOAc in petrol) gave the addition product 21 as a slightly yellow oil that solidified on standing. This material gave <sup>1</sup>H NMR data identical to that described.<sup>6</sup> Data for **21**,  $\delta_{\rm H}$  3.50 (3H, s, CO<sub>2</sub>Me), 3.69 (3H, s, CO<sub>2</sub>Me), 3.96 (1H, d, J 11.0, CH(CH<sub>3</sub>)<sub>2</sub>), 4.27 (1H, dd, J 8.4, 11.0, CH), 6.33 (1H, dd, J 8.4, 15.8, =CH-), 6.48 (1H, d, J 15.8, =CH-Ph), 7.15-7.40 (10H, m, Ph-H).

# Calculation of ee of the allylic substitution product 21

The allylation adduct (7 mg,  $2.4 \times 10^{-2}$  mmol) was dissolved in chloroform- $d(0.8 \text{ cm}^3)$  in a screw-top vial. (+)-Eu(hfc)<sub>3</sub> (13 mg,  $1.06 \times 10^{-2}$  mmol) was added and the mixture was mixed thoroughly to give a homogeneous bright yellow solution. It was then transferred into an NMR tube. The <sup>1</sup>H spectrum of the sample showed 4 sharp signals—2 singlets and a doublet in the region of 4 ppm. The singlets were the signals given by each antipode for one of the methyl groups of the product. The doublet is the non-baseline resolved signal for the other methyl group. Therefore the integral of the doublet was identical to the sum of the integrals of the 2 singlets. The relative integrals of the 2 singlets were used to give the ee. Using the (+)-antipode of the shift reagent, the singlet with the highest ppm corresponded to the (*R*)-enantiomer.

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