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Nucleophilic displacement routes to P-chiral phosphines; the introduction of sterically encumbered groups

John M. Brown *, J. Christopher P. Laing

Dyson Perrins Laboratory, Oxford University, South Parks Rd., Oxford OX1 3QY, UK

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Abstract

Methods for the asymmetric synthesis of P-chiral monophosphines carrying a bulky residue have been appraised. Reaction of 2-adamantylmagnesium bromide with *P*-chlorooxazaphospholidine **1** gives two diastereomeric products after oxidation with t-BuOOH; the S_P isomer was characterised by X-ray and the R_P isomer through a detailed NMR analysis. Although ring opening of either isomer **2** or **3** on reaction with *o*-anisylmagnesium bromide occurred satisfactorily, continuation of the desired reaction sequence through acid-catalysed methanolysis of the phosphinamide **4** and further with PhMgBr led to diminution of the enantiomeric purity in each step because of the more forcing conditions brought about by the steric demands of the 2-adamantyl residue. Similar difficulties were experienced when following the P-borane route of Jugé and Genet, where the 2-adamantyl group was introduced in the initial step. More success was achieved by the borane route when the bulky residue was introduced last by reaction of RLi with the phosphinite complex **13**. In this way the ferrocenyl, 1-adamantyl and t-butylphosphines carrying both phenyl and *o*-anisyl residues, were formed as borane complexes. Deboronation proceeded smoothly in the first two cases to give the tertiary phosphines in greater than 92% *e.e.*

Keywords: Phosphorus; Chirality; Oxazaphospholidine; X-ray; Stereoselectivity

1. Introduction

The systematic synthesis of enantiomerically pure P-chiral phosphines for asymmetric catalysis has been vigorously pursued, and hence employing PCl_3 as the formal starting material with three sequential nucleophilic displacements to introduce alkyl or aryl groups is an attractive option [1]. Our own work involved the arylation of *P*-chlorooxazaphospholidine **1** with isolation of the initial product as the P-oxide. Stereoselective ring opening with retention of configuration was followed by an established two-stage double inversion process which permitted the third substituent to be introduced with overall retention of configuration. In order to generate the desired phosphine it was then necessary to reduce the resulting tertiary phosphine oxide with $HSiCl_3$, a procedure known to result in some loss of configurational purity [2]. The most successful application of the ephedrine-based approach to phosphorus chirality was developed by Jugé and Genet [3], who successfully adapted the chemistry of phosphine boranes [4] to asymmetric displacement reactions, since deboronation can be achieved without significant loss of configuration. This permitted the development of a superior synthesis of the Monsanto ligand DIPAMP, utilised in commercial practice [5]. A direct comparison between the phosphine oxide and phosphine borane routes in a synthesis of unsymmetrical P-chiral diphosphines unequivocally favoured the latter [6].

In all of the synthetic work described to date which builds on the original applications of ephedrine-derived oxazaphospholidines as a template [7], there has been only modest structural alteration of the substituents at phosphorus. Since catalytic selectivity normally depends on selective complexation of the reactant(s) by a metal–ligand combination, wider variation is desirable. The present paper describes an evaluation of possible routes to P-chiral phosphines bearing sterically demanding residues.

2. Discussion

2.1. Attempted synthesis of 2-adamantyldiaryl phosphines

Reaction of 2-adamantylmagnesium bromide with halide **1** affords both R_P and S_P diastereoisomers of

* Corresponding author.

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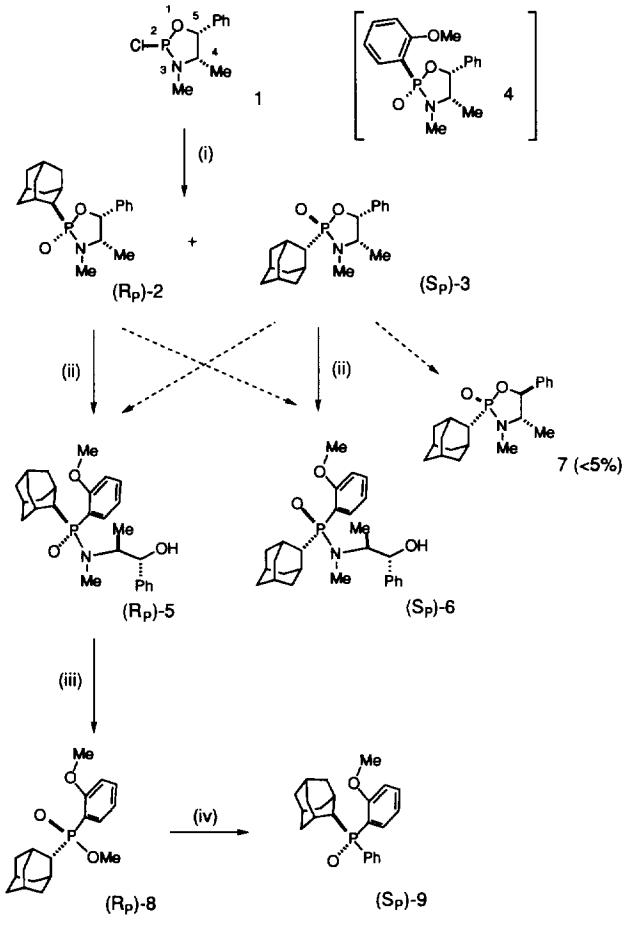
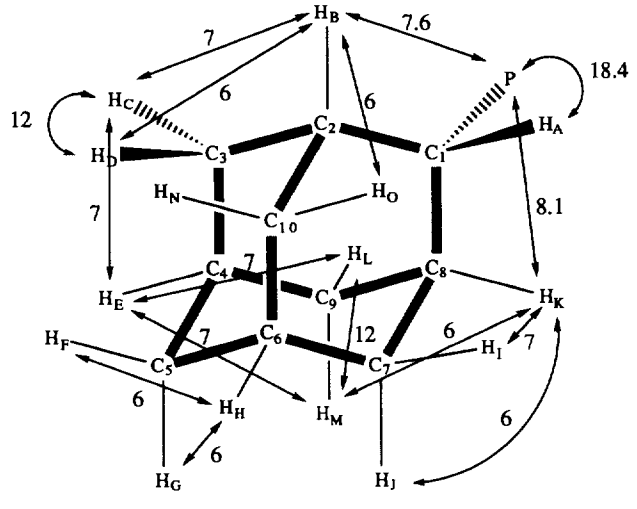


Scheme 1. Synthesis of 2-adamantylphosphine oxides; (i) 2-adamantylMgBr, THF, −78°C to rt, 4h, then t-BuO_2H, *iso*-octane, 2h, 46% **2**, 38% **3** isolated under these conditions, but the proportion of **2** increased up to 80% on standing, and **3** is the major product at short reaction time; (ii) *o*-anisylMgBr, THF, 60°C, 10days; under these conditions the R_P-diastereomer **2** reacts in 42% yield with 95% *d.e.* and the S_P-diastereomer **3** reacts in 48% yield and 55% *d.e.* in refluxing Et_2O isomer **3** reacts in 44% yield and 95% *d.e.*; (iii) 0.18M HCl in MeOH, 55°C, 4days, 54%; (iv) PhLi, 1.8M in C_6H_{12}–Et_2O, rt, 12h, 85%.

(4*S*,5*R*)-2-(2-adamantyl)-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine-2-oxide, **2** and **3**, after oxidation with t-butyl hydroperoxide. It proved possible to obtain the anticipated product of configurational inversion S_P-**3** by performing the reaction under kinetic control (Scheme 1). Since this is the less stable of the two diastereomers in other cases, and they interconvert under the reaction conditions [2], the alternative R_P-**2** isomer was formed in 60% *d.e.* on protracted reaction, as expected. The diastereoisomers were separated by column chromatography using ethyl acetate as the eluent, although fractional crystallisation from ethyl acetate leads to pure *R*-diastereoisomer. The structures of both R_P and S_P-isomers were established by spectroscopic methods and the configuration of compound **3** confirmed by X-ray structure determination [8].

2.2. X-ray and NMR spectroscopic analysis

For many oxazaphospholidine-2-oxides the comparison of ^1H and ^{13}C NMR spectra provides information about configuration at phosphorus which is confirmed by X-ray structure analysis [2]. For the adamantyl fragment of compound **2**, a full analysis of geminal and vicinal coupling constants was possible because the spectrum is well dispersed and the accessibility of three-bond H–P couplings through heteronuclear correlation provides a locus for complete assignment. Of interest is the stereospecificity of the ^3J P–C couplings, large only for C7 and C10 which are antiperiplanar to phosphorus. The results are shown in Fig. 1. Despite the considerable amount of spectroscopic information it was not possible to define the configuration with certainty, hence an X-ray structure was determined for **3**, which



^1H NMR	ppm	^1H NMR	ppm
H_A	2.397	H_N	1.916
H_B	2.475	H_O	1.819
H_C	2.249	^{13}C NMR	ppm
H_D	1.697	C_1	44.86*
H_E	1.911	C_2	28.44
H_F	1.780	C_3	33.39
H_G	1.780	C_4	27.32
H_H	1.958	C_5	37.43
H_I	1.777	C_6	27.87
H_J	1.899	C_7	39.71**
H_K	2.227	C_8	28.44
H_L	2.280	C_9	32.93
H_M	1.613	C_{10}	39.41**

* J(C-P) 122 Hz; ** J(C-P) 16 Hz

Fig. 1. Analysis of the NMR spectra of the adamantyl region of compound **2**, with assignments and parameters obtained from COSY, NOESY and $^1H/^{13}C$ correlation spectra.

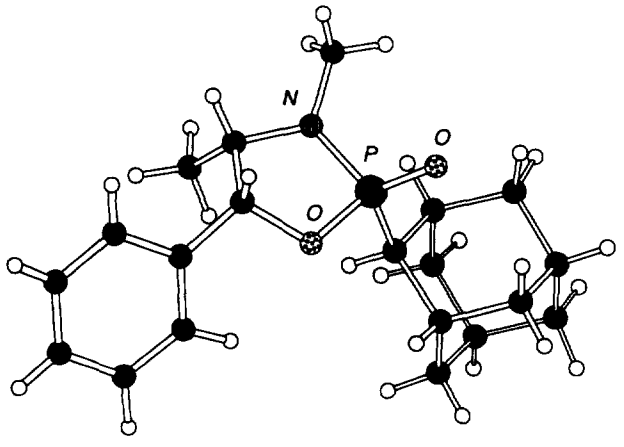


Fig. 2. Structure of compound **3** by X-ray analysis, performed by Dr. C. Schwalbe and Mr. P. Cope, Aston University. Full details will be published separately.

readily gave high quality crystals. The structure is shown in Fig. 2, confirming that the configuration followed simple precedents.

2.3. Ring opening of the oxazaphospholidine

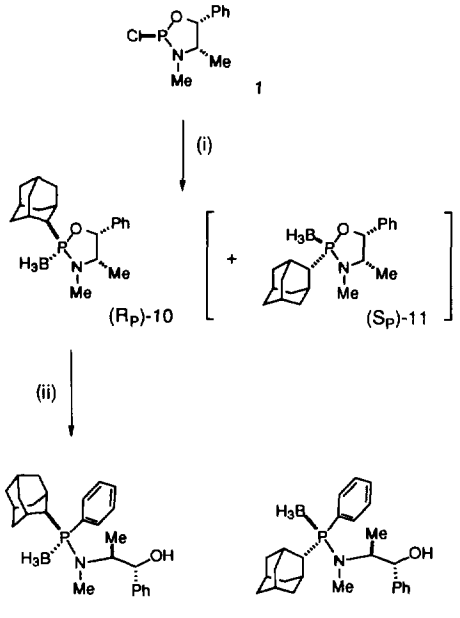
Reaction of 2-adamantylmagnesium bromide with (2*R*,4*S*,5*R*)-2-methoxyphenyl-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine-2-oxide **4** was unsuccessful under a variety of reaction conditions, but the reverse reaction of diastereomerically pure **2** and **3** with 2-methoxyphenylmagnesium bromide led to the ring-opened addition product. The R_P diastereoisomer **2** consistently reacted with greater diastereoselectivity, giving compound **5** in 95% *d.e.*, and the major product formed from isomer **3** in 55% *d.e.* was the analogous S_P diastereomer **6**. By analogy with previous work [2], it was assumed that the major product was most likely formed with retention of configuration at phosphorus. This had previously been explained in terms of nucleophilic attack trans to the endocyclic nitrogen, as the sterically least demanding option. In addition, an unusual side product **7** is obtained in up to 5% yield from the S_P isomer **3**, with a characteristically larger 3,4 vicinal ^1H coupling constant in the oxazaphospholidine, and presumably formed by a deprotonation–reprotonation sequence. Interestingly, this side product is extremely resistant to further reaction, being unchanged after several days at reflux in THF with an excess of reagent. In all of these reactions the yields were moderate and the conditions rather forcing. The reaction scheme was further marginalised by the difficulties experienced in the ring-opening step, where high yields under forcing conditions are associated with significant loss of enantiomeric purity, whilst under milder conditions the enantiomeric purity is 88% or less but the yield is only 50%. Although the product **8** reacted with PhMgBr or PhLi to give the desired phosphine oxide **9** in high yield, albeit slowly, the product shows significant additional racemisation in that step (Scheme 1). It was decided that the sequence was not a favourable route to the desired phosphines. Altering the order of addition was ineffective since 2-adamantylmagnesium bromide did not react with the preformed 2-aryl oxazaphospholidinone. Attention then turned to the phosphine borane route developed by Jugé and Genet.

2.4. Attempted synthesis of 2-adamantyldiaryl phosphine boranes

The initial step of this reaction sequence proceeded as above, with the workup procedure adapted such that the phosphine borane rather than the oxide was formed. The R_P diastereomer **10** was isolated pure, whereas the S_P isomer **11** was never obtained in better than 85% purity, the contaminant being the R_P isomer. This stable phosphine borane **10** reacted cleanly with PhMgBr, although the corresponding reaction with *o*-anisylmagnesium bromide was unsuccessful. The crude mixture of diastereomers of compound **12** in 3:1 ratio was reacted with acidic methanol, but this does not effect cleavage of the P–N bond (Scheme 2). As before, a difficulty was encountered which militated against persisting with the approach as a route to P-chiral phosphines.

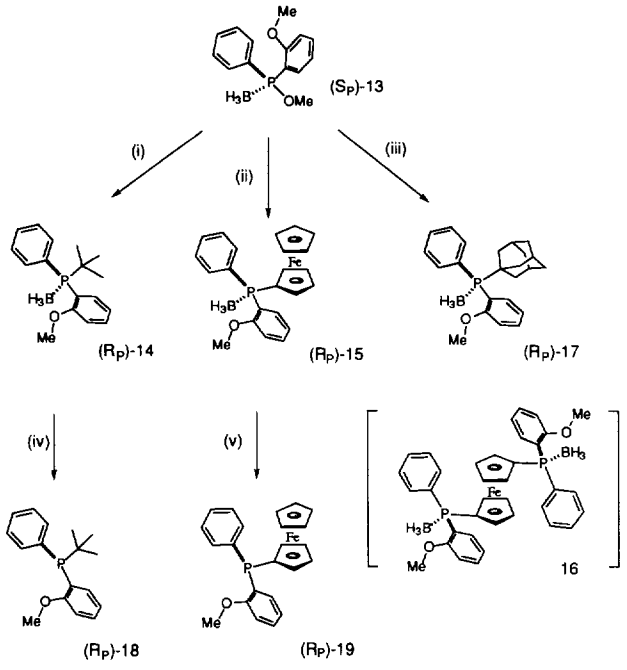
2.5. Approaches via the preformed phosphonate 13

The difficulties encountered in synthesis of 2-adamantylphosphines, via routes in which the bulky



12 (3:1 mixture of diastereomers)

Scheme 2. 2-Adamantylphosphine borane chemistry; (i) 2-adamantylMgBr, THF, −78°C to rt, 4 h, then 13 h stirring, $H_3B \cdot SMe_2$, 48 h (ii) PhLi, THF.



Scheme 3. (I) t-BuLi, Et_2O–hexane, −60 to 0°C, 6h, 51%; (ii) ferrocenylLi, THF, rt, 12h, 67% **15** plus 3% **16**; (iii) 1-adamantylLi, Et_2O, reflux, 56h, 37%; (iv) $HNEt_2$, 50°C, 12h, 98%; (v) $HNEt_2$, 46°C, 8h, 98%.

group was introduced early, encouraged an alternative approach. Following the ground-breaking work of Jugé and Genet, the phosphinite–borane complex **13**, a direct intermediate in their synthesis of DIPAMP, was synthesised. The reactions of this borane with several bulky organolithium reagents were investigated. In all cases the reaction was successful (Scheme 3) and the trisubstituted phosphine borane was isolated and characterised. Good results were obtained using t-BuLi, which is available commercially, and this reaction was carried out on a preparative scale. The product **14** is the precursor of an enantiomerically pure tertiary phosphine. A related product containing a t-butyl group had previously been prepared by Corey et al. using an asymmetric synthesis [9], but from a less readily accessible initial precursor than the oxazaphospholidines. The ferrocenyl compound **15** was synthesised from ferrocenyllithium, itself prepared in two ways. Kagan and coworkers' route from ferrocene and t-butyl lithium [10] proved more convenient than the route from chloromercuriferrocene [11], but in our hands the former may contain traces of 1,1'-dilithioferrocene, since a small amount of the interesting diphosphine diborane **16** was isolated. From 1-adamantyllithium [12], the yield of **17** was quite modest because protracted reaction times were necessary to drive the reaction to completion. In the first two cases, deboronation was achieved simply by warming the phosphine borane with an excess of diethylamine, giving the products **18** and **19** respectively. In order to determine the enantiomeric purity of the products, reoxidation to the phosphine oxide was followed by analysis of the ^1H NMR spectrum in the presence of Kagan's reagent [13]. It was found that the t-butylphosphine **14** had been formed in greater than 97% enantiomeric purity, and the ferrocenylphosphine **15** was formed in greater than 92% enantiomeric purity.

Applications of the new ligands in asymmetric catalysis will be reported separately, but enantiomer excesses of up to 52% in the asymmetric hydrogenation of enamides have been observed [14].

3. Conclusions

In principle, the ephedrine/PCl_3 route to P-chiral mono- and diphosphines gives access to a variety of structures. In practice, each P–C bond forming step is constrained by the steric bulk of the carbanionic reagent, and when forcing conditions are required the stereospecificity of the step is compromised. The experience gained here, and related observations [14], indicate that the most successful strategy involves delaying the introduction of the most spatially demanding residue until the final stage, when acceptable yields and good stereocontrol pertain. As has been observed before, the P-borane route of Jugé and Genet is generally superior to the P-oxide route, and permits simple recovery of the desired ligand, normally from an air-stable crystalline precursor.

4. Experimental

Elemental analyses were carried out by Mrs. V. Lamburn in the Dyson Perrins Laboratory, using a Carlo Erba 1106 elemental analyser.

^1H NMR spectra were recorded on a Varian Gemini 200 (200 MHz), a Bruker AC 200 (200 MHz), a Bruker AM 250 (250 MHz), a Bruker WH 300 (300 MHz) or a Bruker AM 500 (500 MHz) spectrometer. NOESY and COSY experiments were carried out by Mrs. E. McGuinness and Dr. T. Claridge using a Bruker AMX 500 (500 MHz) spectrometer. ^{13}C NMR spectra were recorded on a Varian Gemini 200 (50.33 MHz), a Bruker AM 250 (62.83 MHz) and a Bruker AMX 500 (125.8 MHz) spectrometer. ^{31}P NMR spectra were recorded on a Bruker AM 250 (101.23 MHz) spectrometer. $^1H\{^{31}P\}$ NMR spectra were recorded on a Bruker AMX 500 (500 MHz) spectrometer with a home-built heteronuclear decoupler trolley, using selective continuous wave phosphorus irradiation. ^{11}B NMR spectra were recorded on a Bruker AM 250 (80.2 MHz) spectrometer. IR spectra were recorded on a Perkin Elmer 1750 Fourier Transform spectrometer. Mass spectra were recorded by Mr. R. Proctor on an Varian MAT CH7, VG Micromass 16F or ZAB-1H 16F spectrometer. Elec-

trospray and fast atom bombardment mass spectra were measured by Dr. R.T. Aplin on either a VG BIO Q Platform single quadrupole mass spectrometer or a VG BIO Q triple quadrupole atmospheric pressure mass spectrometer equipped with a VG electrospray interface. All optical rotations were recorded on a thermostatted Perkin Elmer 241 polarimeter, using the 589.3 nm D-line of sodium. Melting points were recorded on a Reichert–Koffler block and are uncorrected. All manipulations of oxygen- and water-sensitive materials were carried out under a dry argon atmosphere, using standard vacuum line and Schlenk techniques. Solvents were deoxygenated by repeated freeze–thaw cycles, in which the solvent was frozen in liquid nitrogen, allowed to warm in vacuo and flushed with argon. Solid reagents were degassed as necessary by evacuation and flushing with argon at room temperature. Transfers and filtrations were carried out using stainless steel cannula wire.

4.1. (2R,4S,5R)- and (2S,4S,5R)-3,4-dimethyl-2-adamantyl-5-phenyl-1,3,2-oxazaphospholidine-2-oxide, 2 and 3

2-Adamantylmagnesium bromide (140 ml, 0.21 M in ether) was added to a stirred THF solution (20 ml) of (2*R*,4*S*,5*R*)-2-chloro-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine (8.01 g, 35 mmol) at −78 °C. The stirred reaction mixture was allowed to warm up to room temperature (rt) over a period of 4 h and was then oxidised by the addition of t-butyl hydroperoxide (12.8 ml, 3 M in octane). After a further 2 h, the reaction was quenched with water (30 ml) and the organics were extracted into ether (3 × 60 ml) and dried ($MgSO_4$). Solvent was removed under reduced pressure to afford a mixture of two diastereoisomers in 87% yield. The diastereoisomers were then separated by column chromatography (flash silica, ethyl acetate, $R_f = 0.5$ (2*R*) and $R_f = 0.2$ (2*S*)).

(2*S*,4*S*,5*R*)-3,4-Dimethyl-2-adamantyl-5-phenyl-1,3,2-oxazaphospholidine-2-oxide (4.59 g, 38%) was obtained as white crystals: m.p. 220–222 °C, Found: C, 69.50; H, 8.24; N, 3.82. $C_{20}H_{28}NO_2P$ requires C, 69.53; H, 8.17; N, 4.07%. $[\alpha]_D^{23}$ −37.7 (*c* 0.975, $CHCl_3$). For ^1H,^{13}C NMR of the adamantyl fragment see Fig. 1; δ_H (500 MHz, $CDCl_3$) 7.42–7.36 (4H, m, *ortho / meta* H), 7.32 (1H, dd, $J_{meta} = J_{meta'}$ 6.9, *para* H), 5.41 (1H, dd, J_{H4} 6.2, J_P 3.7, CHPh), 3.62 (1H, ddq, J_{H5} 6.2, J_{CH3} 6.5, J_P 15.8, C*H*CH_3), 2.71 (3H, d, J_P 9.5, NCH_3) 0.84 (3H, d, J_{H4} 6.5, $CHCH_3$); δ_C (125 MHz, $CDCl_3$) 136.59 (d, J_P 6.1, Ph-*ipso* C), 128.30 (Ph-*ortho* C), 128.01 (Ph-*para* C), 126.18 (Ph-*meta* C), 81.94 (*C*HPh), 58.68 (d, J_P 8, N*C*HCH_3), 29.02 (d, J_P 4, NCH_3), 13.98 (CH*C*H_3); δ_P (101.3 MHz, $CDCl_3$) 47.12. ν_{max} cm^{-1} (KBr): 3066, 3035 (Ar–H st.), 2913 (CH_2 st), 2852 (NCH_3, C–H st), 2654, 2360, 2342, 1950, 1882, 1673, 1606 (Ph–H vib.), 1548, 1493 (Ph–H, vib.), 1470 (CH_2, C–H deformations), 1452 (CH_2, C–H deformations), 1381 (CH_3 symmetrical deformations), 1359, 1334, 1311, 1297 (P=O), 1236, 1213, 1178, 1128, 1112, 1102, 1086, 1062, 1031 (P–Oalkyl), 970, 912, 881, 848, 837, 758 (Ph–H oop bend), 710 (Ph–H oop bend) and 560. *m / z* (CI^+, NH_3) 346 (M + 1, 100%), 347 (20), 228 (10), 148 ($NCHCH_3CHPhO$, 10) and 135 (Ad, 5).

(2*R*,4*S*,5*R*)-3,4-Dimethyl-2-adamantyl-5-phenyl-1,3,2-oxazaphospholidine-2-oxide (5.61 g, 46%) was obtained as white crystals: m.p. 190–192 °C. Found: C, 69.58; H, 8.46; N, 4.08. $C_{20}H_{28}NO_2P$ requires C, 69.53; H, 8.17; N, 4.07%. $[\alpha]_D^{23}$ −70.9 (*c* 1.11, $CHCl_3$). δ_H (500 MHz, $CDCl_3$) 7.42–7.24 (5H, m, Ar H), 5.82 (1H, d, ^3J 6.1, C*H*Ph), 3.64 (1H, ddq, J_{CH3} 6.6, C*H*CH_3), 2.83 (3H, d, J_P 8.8, NC*H*$_3$), 2.44–2.34 (5H, br m, Ad–H_A,H_B,H_C,H_K,H_L), 1.99–1.67 (10H, br m, Ad–H_D,H_E,H_F,H_G,H_H,H_I,H_J,H_M,H_N,H_O) and 0.71 (3H, d, CHC*H*$_3$); δ_C (62.9 MHz, $CDCl_3$) 136.4 (Ph-*ipso* C), 128.3 (Ph-*ortho* C), 127.9 (Ph-*para* C), 125.6 (Ph-*meta* C), 79.7 (*C*HPh), 61.2 (d, J_P 6.1, *C*HCH_3), 46.1 (d, J_P 124, Ad-C_1), 39.7 (d, J_P 7.3 Ad-$C_{7/10}$), 39.5 (d, J_P 7.4, Ad-$H_{7/10}$), 37.4 (Ad-C_5), 33.3 (Ad-C_3), 30.8 (d, J_P 5.7, Ad-C_9), 28.7 (NCH_3), 28.4 (d, J_P 3.5, Ad-C_2,C_8), 27.9 (Ad-C_6), 27.3 (Ad-C_4) and 14.6 (CH*C*H_3); δ_P (101.3 MHz, $CDCl_3$) 46.1; ν_{max} cm^{-1} (KBr): 2900, 2864, 3849, 1607, 1497, 1453, 1380, 1356, 1330, 1246, 1221, 1212, 1191, 1112, 1100, 1082, 1062, 1035, 982, 957, 912, 582, 854, 839, 810 and 704. *m / z* (CI^+, NH_3) 346 (M + 1, 100%), 347 (20), 148 ($NCHCH_3CHPhO$, 15), 135 (Ad, 10) and 58 (35).

4.2. (R_P)- and (S_P)-N-methyl-N-(1S,2S)(1-methyl-2-hydroxy-2-phenyl)ethyl-P-(2-methoxyphenyl)-P-(2-adamantyl)phosphinamide, 5 and 6

2-Methoxyphenylmagnesium bromide (40 ml, 1.6 M in THF) was added to a THF solution of (2*R*,4*S*,5*R*)-3,4-dimethyl-2-adamantyl-5-phenyl-1,3,2-oxazaphospholidin-2-oxide (4.50 g, 13.0 mmol) at rt. The reaction mixture was heated to 60 °C and stirred for 10 days. Water (50 ml) was added and the organic material extracted with ether (3 × 70 ml) to yield a viscous oil. This material was purified by flash chromatography (flash silica, ethyl acetate–pentane: 1/1) to yield a diastereomeric mixture. These were separated by fractional crystallisation (EtOAc, −20 °C).

(S_P)-*N*-Methyl-(1*S*,2*S*)-(1-methyl-2-hydroxy-2-phenyl)-ethyl-P-(2-methoxyphenyl)-P-(2-adamantyl) phosphinamide was obtained as a white powder (240 mg, 4%); m.p. 162–164 °C. Found: C, 71.28; H, 8.22; N, 3.15. $C_{27}H_{36}NO_3P$ requires C, 71.49; H, 7.99; N, 3.10%. $[\alpha]_D^{23}$ −18.8 (*c* 0.515, CH_2Cl_2). δ_H (500 MHz, $CDCl_3$) 8.05 (1H, ddd, J_{H4} 1.8, J_{H5} 7.5, J_P 11.9, *o*-An-H6), 7.46 (1H, ddd, J_{H3} 8.2, J_{H5} 7.9, J_{H6} 1.8, *o*-An-H4), 7.42 (2H, d, J_{meta} 7.2, Ph-*ortho* H), 7.31

(2H, dd, J_{para} 7.2, J_{ortho} 7.3, Ph-*meta* H), 7.25 (1H, dd, J_{meta} 7.2, $J_{meta'}$ 7.2, Ph-*para* H), 7.07 (1H, ddd, J_{H4} 7.9, J_{H6} 7.5, J_P 0.6, *o*-An-H5), 6.87 (1H, dd, J_{H4} 8.2, J_P 5.2, *o*-An-H3), 6.44 (1H, d, J_{H5} 6.3, PhCHO*H*), 4.46 (1H, dd, J_{H4} 2.4, J_{OH} 6.3, PhCH), 3.79 (3H, s, OCH_3), 3.76 (1H, ddq, J_{H5} 2.4, J_{Me} 7.2, J_P 9.6, C*H*CH3) 3.00 (1H, br d, J_P 12.7, Ad-$H_{A/B/K}$), 2.604 (1H, d, J_P 11.3, Ad-$H_{A/B/K}$), 2.39 (2H, br m, Ad-$H_{A/B/K/C/L}$), 2.00 (3H, d, J_P 9.4, NCH_3), 1.99-1.92 (3H, br m, Ad-$H_{C/L}$ and 2$H_{E/H/I/J/N/O/P}$), 1.81–1.71 (5H, m, Ad-$H_{F/F/G/I/J/N/O/P}$), 1.65–1.60 (2H, br m, Ad-H_D, and Ad-$H_{F/G}$), 1.42 (1H, br d, J_{HL} 12.5, Ad-H_M) and 0.96 (3H, d, J_{H4} 7.2, CHCH_3); δ_C (62.8 MHz, $CDCl_3$) 159.7 (*o*-An-C_2), 142.1 (Ph-*ipso* C), 136.4 (d, J_P 5.1, *o*-An-C_6), 133.0 (*o*-An-C_4), 127.5 (Ph-*meta* C), 127.2 (Ph-*ortho* C), 126.9 (Ph-*para* C), 120.9 (d, J_P 9.1, *o*-An-C_5), 120.8 (d, J_P 107, *o*-An-C_1), 109.9 (d, J_P 6.2, *o*-An-C_3), 76.4 (PhCH), 55.0 (d, J_P 7.5, *C*HCH$_3$), 40.4 (d, J_P 16.6, Ad-$C_{7/10}$), 39.8 (d, J_P 14.5, Ad-$C_{7/10}$), 39.2 (d, J_P 66.6, Ad-C_1) 37.5 (Ad-C_5), 32.9 (Ad-$C_{3/9}$), 32.2 (d, J_P 5.7, Ad-$C_{3/9}$), 30.3 (d, J_P 3.1, NCH_3), 28.4 (d, J_P 9.3, Ad-$C_{2/8}$), 28.2 (d, J_P 8.4, Ad-$C_{2/8}$), 27.1 (Ad-C_4, Ad-C_4) and 14.8 (CH*C*H$_3$); δ_P (101.3 MHz, $CDCl_3$) 43.74. ν_{max} cm^{-1} (KBr): 3294 (O–H st.), 3063, 3027, 2904 (Ad–C–H st.), 2848 (OCH_3), 1590 (Ar–H vib), 1576 (Ar–H vib), 1477 (Ad–C–H deformations), 1451 (Ad–C–H deformations), 1431, 1273 (P=O), 1242, 1186, 1134, 1078, 1045, 1022, 835, 800, 759 (Ar–H bend), 701 (Ph–H bend), 682 and 541. *m/z* (CI^+, NH_3) 454 (M + 1, 100%), 455 (M + 2, 25), 346 (M − *o*-An/PhCHOH, 55), 289 (M − ephedrine, 15%) and 135 (Ad, 15).

(R_P)-*N*-Methyl-(1*S*,2*S*)-(1-methyl-2-hydroxy-2-phenyl)ethyl-P-(2-methoxyphenyl)-P-(2-adamantyl)-phosphinamide was obtained as a white powder (3.77 g, 68%); m.p. 214–216 °C. Found: C, 71.49; H, 8.41; N, 3.06. $C_{27}H_{36}NO_3P$ requires C, 71.49; H, 7.99; N, 3.10%. $[\alpha]_D^{21}$ −23.6 (*c* 0.53, CH_2Cl_2). δ_H (500 MHz, $CDCl_3$) 8.10 (1H, ddd, J_{H6} 1.8, J_{H5} 7.5, J_P 12.4, *o*-An-H6), 7.48 (1H, ddd, J_{H3} 8.3, J_{H5} 7.3, J_{H6} 1.8, *o*-An-H4), 7.31 (2H, d, J_{meta} 7.3, Ph-*ortho* H), 7.22 (2H, dd, J_{para} 7.2, J_{ortho} 7.3, Ph-*meta* H), 7.16 (1H, dd, J_{meta} 7.2, $J_{meta'}$ 7.2, Ph-*para* H), 7.11 (1H, dd, J_{H4} 7.3, J_{H6} 7.5 *o*-An-H5), 6.90 (1H, dd, J_{H4} 8.3, J_P 5.3, *o*-An-H3), 6.07 (1H, d, J_{H4} 1.7, PhCHO*H*), 4.88 (1H, s, PhCH), 3.86 (3H, s, OCH_3), 3.54 (1H, ddq, J_{OH} 1.7, J_{Me} 7.2, J_P 14.4, C*H*CH3), 2.81 (1H, br d, J_P 12.6, Ad-$H_{A/B/K}$), 2.69 (1H, d, J_P 12.0, Ad-$H_{A/B/K}$), 2.61 (3H, d, J_P 8.8, NCH_3), 2.41–2.39 (2H, m, Ad-$H_{A/B/K/C/L}$), 1.99–1.93 (3H, br m, Ad-$H_{C/L}$ and 2$H_{E/H/I/J/N/O/P}$), 1.83–1.70 (4H, m, Ad-$H_{F/I/J/N/O/P}$), 1.67–1.65 (3H, m, Ad-$H_{D/F/G}$) and 1.42 (1H, br d, J_{HL} 12.3, Ad-H_M) and 1.02 (3H, d, J_{H4} 7.2, CHCH_3); δ_C (62.8 MHz, $CDCl_3$) 159.6 (*o*-An-C_2), 142.8 (Ph-*ipso* C), 135.3 (d, J_P 5.2, *o*-An-C_6), 132.9 (*o*-An-C_4), 127.8 (Ph-*meta* C), 126.7 (Ph-*para* C), 126.4 (Ph-*ortho* C), 121.2 (d, J_P 9.0, *o*-An-C_5), 110.2 (d, J_P 7.3, *o*-An-C_3), 63.6 (PhCH), 55.2 (*C*HCH$_3$), 41.7 (d, J_P 88.8, Ad-C_1), 40.5 (d, J_P 16.5, Ad-$C_{7/10}$), 40.3 (d, J_P 14.7, Ad-$C_{7/10}$), 37.6 (Ad-C_5), 34.8 (d, J_P 3.5, NCH_3), 33.2 (Ad-$C_{3/9}$), 32.4 (Ad-$C_{3/9}$), 28.3 (Ad-$C_{2/6/8}$), 28.3 (Ad-$C_{2/6/8}$), 28.1 (Ad-$C_{2/6/8}$), 27.2 (Ad-C_4) and 12.2 (CH*C*H$_3$); δ_P (101.3 MHz, $CDCl_3$) 43.86. ν_{max} cm^{-1} (KBr): 3213 (O–H st.), 3062, 3028 (Ad–C–H st.), 2967, 2903, 2850 (OCH_3), 2673, 1933, 1815, 1589 (Ar–H vib), 1575 (Ar–H vib), 1474 (Ad–C–H deformations), 1429, 1387, 1370, 1343, 1268 (P=O), 1240, 1211, 1199, 1163, 1132, 1091, 1077, 1063, 1042, 1020, 994, 938, 769 (Ar–H bend), 757 (Ar–H bend), 712 (Ph–H bend), 700 (Ph–H bend), 682 (Ph–H bend), 566, 534 and 490. *m/z* (CI^+, NH_3) 454 (M + 1, 100%), 455 (M + 2, 25), 346 (M − *o*-An/PhCHOH, 40), 289 (M − ephedrine, 10) and 135 (Ad, 5).

4.3. (+)-(*R*)-Methyl(2-methoxyphenyl)(2-adamantyl)phosphinate, 8

(R_P)-*N*-Methyl-(1*S*,2*S*)(1-methyl-2-hydroxy-2-phenyl)ethyl-P-(2-methoxyphenyl)-P-(2-adamantyl) phosphinamide (316 mg, 0.70 mmol) was dissolved in acidic methanol (20 ml, 0.18 M HCl in MeOH) and stirred at 55 °C for 4 days. Solvent was removed in vacuo to yield a viscous oil which was dissolved in ethyl acetate. (−)-Ephedrine precipitated out and the title compound was purified by column chromatography (EtOAc, R_f = 0.6).

(+)-(*R*)-Methyl-(2-methoxyphenyl)-(2-adamantyl)phosphinate was obtained as white crystals (120 mg, 54%): m.p. 106–108 °C. Found: C, 67.59; H, 7.72. $C_{18}H_{25}O_3P$ requires C, 67.49; H, 7.86%. δ_H (500 MHz, $CDCl_3$) 8.00 (1H, ddd, J_{H4} 1.9, J_{H5} 7.5, J_P 12.3, *o*-An-H6), 7.52 (1H, ddd, J_{H3} 8.3, J_{H5} 8.3, J_{H6} 1.9, *o*-An-H4), 7.09 (1H, dddd, J_{H4} 8.3, J_{H6} 7.5, J_P 2.1, J_{H3} 0.7, *o*-An-H5), 6.93 (1H, dd, J_{H4} 8.3, J_P 5.3, *o*-An-H3), 3.88 (3H, s, OMe), 3.54 (3H, d, J_P 11.1, $POCH_3$), 2.66 (1H, br m, J_{HD} 12.6, *J* 2.4, Ad-H_C), 2.54 (1H, br d, J_P 16.0, Ad-H_A), 2.47 (1H, br m, Ad-H_B), 2.30 (1H, ddd, J_{HM} 12.6, J_{HF} 2.4, J_{HI} 2.4, Ad-H_L), 1.92–1.87 (3H, br m, Ad-H_H,H_E and $H_{I/J}$), 1.81–1.70 (5H, br m, Ad-H_F, H_G, H_K, K_O and $H_{I/J}$), 1.68–1.62 (2H, br m, Ad-H_D, H_N) and 1.47 (1H, br d, J_{HL} 12.6, Ad-H_M); δ_C (62.9 MHz, $CDCl_3$) 160.5 (*o*-An-C_2), 136.6 (d, J_P 5.9, *o*-An-C_6), 134.0 (*o*-An-C_4), 120.8 (d, J_P 11.1, *o*-An-C_5), 117.7 (d, J_P 112.9, *o*-An-C_1), 110.6 (d, J_P 7.4, *o*-An-C_3), 55.5 (OCH_3), 50.7 (d, J_P 7.4, $POCH_3$), 44.4 (d, J_P 101.7, Ad-C_1), 39.9 (Ad-C_7), 39.7 (d, J_P 3.5, Ad-H_{10}), 37.5 (Ad-C_5), 33.2 (Ad-C_3), 32.8 (Ad-C_9), 28.1 (Ad-$C_{6/4}$), 27.8 (Ad-C_2, Ad-C_8) and 27.3 (Ad-$C_{6/4}$); δ_P (101.3 MHz, $CDCl_3$) 47.2. ν_{max} cm^{-1} (KBr): 3008, 2905 (CH_2 st), 2848 (An–OCH_3, C–H st), 2360, 1593 (Ar–H vib.), 1479, 1471 (CH_2, C–H deformations), 1451 (CH_2,

C–H deformations), 1432, 1275 (P=O), 1249, 1222, 1206, 1185, 1157, 1135, 1083, 1049 (P–OMe), 1030, 840, 804, 774, 691, 573 and 495. m/z (CI^+, NH_3) 321 (M + 1, 100%), 322 (20) and 289 (M − OMe, 15).

4.4. (S)-2-Adamantyl(2-methoxyphenyl)phenylphosphine oxide, 9

Phenyllithium (19 ml, 1.8 M in cyclohexane–ether: 70/30) was added to (+)-(*R*)-methyl adamantyl-2-methoxyphenylphosphinate (220 mg, 0.68 mmol) at rt and the solution was heated to 30 °C and stirred overnight. The reaction was quenched by the addition of water (20 ml) and the organics extracted into ether (3 × 25 ml). The ethereal layer was dried ($MgSO_4$) and the solvent removed under reduced pressure to afford a thick dark yellow oil which solidified on standing. This material was purified by flash chromatography (flash silica, ethyl acetate–hexane: 1/1) to yield, after solvent removal, a pale yellow oil which forms a white solid on standing (214 mg, 85%); m.p. 157–159 °C. Found: C, 74.92; H, 7.39. $C_{23}H_{27}O_2P$ requires C, 75.39; H. 7.43%. δ_H (500 MHz, $CDCl_3$) 8.16 (1H, ddd, J_{H4} 1.8, J_{H5} 7.6, J_P 12.4, *o*-An-H6), 7.94 (2H, ddd, J_{meta} 7.7, J_{para} 1.4, J_P 10.6, Ph-*ortho* H), 7.47 (1H, ddd, J_{H3} 8.2, J_{H6} 1.8, J_{H5} 7.4, *o*-An-H4), 7.439–7.401 (3H, m, Ph-*meta*/*para* H), 7.12 (1H, dd, J_{H4} 7.4, J_{H6} 7.5, *o*-An-H5), 6.87 (1H, dd, J_{H4} 8.2, J_P 5.1, *o*-An-H3), 3.82 (3H, s, OCH_3) 2.98 (1H, d, J_P 8.3, Ad-$H_{A/B/K}$), 2.79 (1H, d, J_{HM} 12.6, Ad-H_L), 2.42 (1H, d, J_{HD} 12.5, Ad-H_C), 2.25 (1H, br, Ad-$H_{A/B/K}$), 1.97–1.72 (9H, m, Ad-$H_{A/B/K}$, Ad-H_E, H_F, K_G, H_H, H_I, H_J, H_N and H_O), 1.59 (1H, d, J_{HL} 12.5, Ad-H_D) and 1.50 (1H, d, J_{HL} 12.6, Ad-H_M); δ_C (62.8 MHz, $CDCl_3$) 159.0 (*o*-An-C_2), 134.8 (d, J_P 3.8, *o*-An-C_6), 134.3 (d, J_P 94.0, Ph-*ipso* C), 133.6 (*o*-An-C_4), 131.1 (Ph-*ortho*), 130.9 (Ph-*meta* C), 130.7 (Ph-*para* C), 121.2 (d, J_P 10.9, *o*-An-C_5), 121.1 (d, J_P 90.7, *o*-An-C_1), 110.5 (d, J_P 7.1, *o*-An-C_3), 55.1 (OCH_3), 42.5 (d, J_P 71.9, Ad-C_1), 40.2 (Ad-$C_{7/10}$), 40.0 (Ad-$H_{7/10}$), 37.4 (Ad-C_5), 33.1 (Ad-$C_{3/9}$), 33.0 (Ad-$C_{3/9}$), 28.8 (Ad-C_6), 28.2 (Ad-$C_{2/8}$), 28.1 (Ad-$C_{2/8}$), 27.2 (Ad-C_4); δ_P (101.3 MHz, $CDCl_3$) 34.67. ν_{max} cm^{-1} (KBr): 2897, 2851 (OCH_3), 1589, 1577, 1478, 1459, 1432, 1275 (P=O), 1175, 1133, 1106, 1076, 1018, 692 and 563. m/z (Cl^+, NH_3) 367 (M + 1, 100%), 368 (M + 2, 25), 335 (M − OMe + 1, 20), 233 (5), 199 (5) and 91 (5).

4.5. (2R,4S,5R)- and (2S,4S,5R)-3, 4-dimethyl-2-adamantyl-5-phenyl-1,3,2-oxazaphospholidine borane, 10 and 11

2-Adamantylmagnesium bromide (7.5 ml, 0.7 M in THF) was slowly added to a stirred THF solution (20 ml) of (2*R*,4*S*,5*R*)-2-chloro-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine (1.15 g, 5 mmol) at −78 °C. The stirred reaction mixture was allowed to warm up to rt over a period of 4 h and then stirred for a further 13 h. The phosphine was then complexed by the addition of borane · dimethyl sulphide (2.6 ml, 2 M, 5.2 mmol). After a further 48 h, the reaction was quenched with water (30 ml) and the organics extracted into dichloromethane (3 × 30 ml) and dried ($MgSO_4$). Solvent was removed under reduced pressure to afford a mixture of two diastereoisomers in 68% yield. (2*R*,4*S*,5*R*)-3,4-Dimethyl-2-adamantyl-5-phenyl-1,3,2-oxaphospholidine-2-borane was then isolated by fractional crystallisation (ethyl acetate at −20 °C) as white needles (650 mg, 38%): m.p. 152–154 °C. Found: C, 69.88; H, 9.40; N, 3.82. $C_{20}H_{31}BNOP$ requires C, 69.97; H, 9.10; N, 4.10%. $[\alpha]_D^{25}$ −17.3 (*c* 0.15, CH_2Cl_2). δ_H (500 MHz, $CDCl_3$) 7.40–7.35 (4H, m, Ph-*ortho*/*meta* H), 7.32 (1H, m, Ph-*para* H), 5.50 (1H, d, J_{H4} 5.8, CHPh), 3.69 (1H, dq, J_{H5} 5.8, J_{CH3} 6.6, C*H*CH_3), 2.71 (3H, d, J_P 9.7, NCH_3), 2.54 (1H, br, Ad-H_B), 2.37 (1H, br, Ad-H_K), 2.14–2.12 (2H, m, Ad-H_C,H_L), 2.03 (1H, br d, *J*p 5.7, Ad-H_A), 1.97–1.71 (8H, m, Ad-H_E,H_F,H_G,H_H,H_I,H_J,H_N,H_O), 1.62 (1H, br d, J_{HC} 20.9, Ad-H_D), 1.48 (1H, br d, J_{HL} 11.8, Ad-H_M), 0.82–0.35 (3H, br, BH_3) and 0.80 (3H, d, J_{H4} 6.6, CHCH_3); δ_C (50.3 MHz, $CDCl_3$) 136.8 (Ph-*ipso* C), 128.5 (Ph-*ortho* C), 128.2 (Ph-*para* C), 126.4 (Ph-*meta* C), 84.0 (*C*HPh), 59.6 (*C*HCH_3), 49.0 (d, J_P 22.9, Ad-C_1), 39.7 (d, J_P 9.2 Ad-C_7), 39.3 (d, J_P 13.2, Ad-H_{10}), 37.0 (Ad-C_5), 33.3 (Ad-C_3), 33.3 (Ad-C_9), 29.7 (d, J_P 8.0, NCH_3), 27.9 (Ad-$C_{2/6/8}$), 27.7 (Ad-$C_{2/6/8}$), 27.6 (Ad-$C_{2/6/8}$), 27.1 (Ad-C_4) and 12.5 (CH*C*H_3); δ_P (101.3 MHz, $CDCl_3$) 152.8 (q, J_B 76); δ_B (80.2 MHz, $CDCl_3$) −40.0 (dq, J_H 94). ν_{max} cm^{-1} (KBr): 3446, 2976, 2959 (Ad–C–H st.), 2854 (Ad–C–H st.), 2824 (NCH_3 st.), 2400 (BH_3), 2375 (BH_3), 1606 (Ph–H vib.), 1559, 1496, 1451 (CH_2), 1381 (CH_3 sym), 1367, 1355, 1310, 1209, 1175, 1057, 1032 (P–Oalkyl), 964, 759, 737 (Ph–oop bending), 703 and 634. m/z (EI^+) 342 (M − 1, 2%), 329 (35), 194 (100), 176 (25), 147 ($NCHCH_3CHPhO$, 15), 135 (Ad, 15), 91 (25), 79 (15), 67 (10) and 56 (10). (2*S*,4*S*,5*R*)-3,4-Dimethyl-2-adamantyl-5-phenyl-1,3,2-oxaphospholidine-2-borane could not be isolated as a single diastereoisomer, although samples up to 70% *d.e.* were obtained by fractional crystallisation.

4.6. (R)-t-Butyl (2-methoxyphenyl)phenylphosphine borane, 14

t-Butyllithium (Aldrich, 8.8 ml, 1.7 M in hexane, 15 mmol) was slowly added to a stirred ethereal solution of (+)-(*S*)-methyl-(2-methoxyphenyl)phenylphosphinite borane (2.60 g, 10 mmol, 50 ml of ether) at −60 °C. The reaction was slowly warmed to rt over 6 h

and stirred overnight. The reaction was quenched by slow addition of water (20 ml) at 0 °C and the organics extracted into ether (3 × 30 ml) and dried ($MgSO_4$). The solvent was removed in vacuo to yield an off-white powder. This material was purified by column chromatography (flash silica, ethyl acetate–pentane: 1/10) to yield a white powder (1.46 g, 51%); m.p. 85–87 °C. Found: C, 71.48; H, 8.16. $C_{17}H_{24}BOP$ requires C, 71.35; H, 8.45%. $[\alpha]_D^{23}$ +9.3 (*c* 0.505, MeOH). δ_H (500 MHz, $CDCl_3$) 7.987 (1H, ddd, J_{H6} 1.5, J_{H5} 7.7, J_P 12.6, *o*-An-H6), 7.696 (2H, ddd, J_{meta} 6.8, J_{para} 1.6, J_P 8.8, Ph-*ortho* H), 7.500 (1H, dd, J_{H3} 8.3, J_{H5} 7.5, *o*-An-H4), 7.411 (1H, dt, J_{meta} 7.3, J_{ortho} 1.7, Ph-*para* H), 7.374 (2H, ddd, J_{para} 2.1, J_{ortho} 6.8, J_P 7.3, Ph-*meta* H) 7.069 (1H, ddd, J_{H4} 7.5, J_{H6} 7.7, J_P 1.0, *o*-An-H5), 6.912 (1H, dd, J_{H4} 8.3, J_P 3.4, *o*-An-H3), 3.579 (3H, s, OCH_3) and 1.346 (9H, d, J_P 14.4, $C(CH_3)_3$); δ_C (62.8 MHz, $CDCl_3$) 161.0 (*o*-An-C_2), 137.4 (d, J_P 12.1, *o*-An-C_6), 133.2 (*o*-An-C_4), 132.4 (d, J_P 9.1, Ph-*ortho* C), 130.4 (d, J_P 53.5, Ph-*ipso* C), 129.8 (Ph-*para* C), 127.8 (d, J_P 9.1, Ph-*meta* C), 120.8 (d, J_P 10.6, *o*-An-C_5), 116.4 (d, J_P 48.8, *o*-An-C_1), 111.4 (d, J_P 4.5, *o*-An-C_3), 54.7 (OCH_3), 31.5 (d, J_P 32.2 $(CH_3)_3C$) and 28.0 (d, J_P 2.4, $(CH_3)_3C$); δ_P (101.3 MHz, $CDCl_3$) 36.74 (br, J_B 57.3); δ_B (80.21 MHz, $CDCl_3$) −37.8 (dq, J_P 57.3). ν_{max} cm^{-1} (KBr): 3089, 3064, 2960 ($C(CH_3)_3$ C–H st.), 2867 ($C(CH_3)_3$ C–H st.), 2839 (OCH_3), 2354 (BH_3), 1588 (Ar–H vib), 1573, 1471, 1434, 1399 ($C(CH_3)_3$), 1371 ($C(CH_3)_3$), 1274, 1251, 1181, 1163, 1129, 1101, 1020, 802, 759 (Ar–H bend), 741 (Ar–H bend), 697 (Ph–H bend) and 636. *m/z* (EI^+) 285 (M − 1, 15%), 272 (M − BH_3, 100), 273 (M − BH_3, 15), 216 (M − ^tBu − BH_3, 90%), 183 (30), 138 (M − Ph − ^tBu − BH_3, 60), 108 (An, 30), 91 (50), 77 (Ph, 10) and 57 (^tBu, 30).

4.7. (*R*)-t-Butyl-(2-methoxyphenyl)phenylphosphine, *18*

Diethylamine (3ml) was added to (*R*)-t-butyl-(2-methoxyphenyl)phenylphosphine borane (572 mg, 2.0 mmol) and the solution heated to 50 °C for 12 h. The diethylamine was then removed under reduced pressure to yield the crude product which was passed through a short silica column (flash silica, toluene as eluent). Solvent was removed under reduced pressure to yield a thick oil (534 mg, 98%). δ_H (500 MHz, $CDCl_3$) 7.53 (2H, ddd, J_{meta} 5.2, J_{para} 3.5, J_P 9.6, Ph-*ortho* H), 7.45 (1H, ddd, J_{H4} 1.7, J_{H5} 7.5, J_P 3.8, *o*-An-H6), 7.33 (1H, ddd, J_{H3} 8.2, J_{H6} 1.7, J_{H5} 7.4, *o*-An-H4), 7.31–7.29 (3H, m, Ph-*meta*/*para* H), 7.11 (1H, ddd, J_{H4} 7.4, J_{H6} 7.4, J_P 0.8, *o*-An-H5), 6.98 (1H, dd, J_{H4} 8.2, J_P 4.4, *o*-An-H3), 3.737 (3H, s, OCH_3) and 1.23 (9H, d, J_P 12.5, $C(CH_3)_3$); δ_C (125.7 MHz, $CDCl_3$) 162.1 (*o*-An-C_2), 134.7 (*o*-An-C_6), 134.4 (d, J_P 20.0, *o*-An-C_4), 129.9 (Ph-*ortho*), 128.1 (Ph-*para* C), 127.7 (d, J_P 6.3, Ph-*meta* C), 120.4 (*o*-An-C_5), 110.7 (*o*-An-C_3), 55.4 (OCH_3), 30.6 (d, J_P 15.0, $(CH_3)_3C$) and 28.8 (d, J_P 14.4, $(CH_3)_3C$); δ_P (101.3 MHz, Et_2NH) 7.60. *m/z* (EI^+) 273 (M + 1, 15%), 272 (M, 65), 217 (M − ^{t}Bu + H, 10), 216 (M − ^{t}Bu, 100), 183 (40), 138 (M − ^{t}Bu − Ph, 100), 137 (50), 108 (An, 60), 91 (80) and 57 (^{t}Bu, 40).

4.8. (*S*)-t-Butyl(2-methoxyphenyl)phenylphosphine oxide

t-Butyl hydroperoxide (0.2 ml, 3.0 M in *iso*-octane, 0.6 mmol) was slowly added to an ethereal solution of (*R*)-t-butyl(2-methoxyphenyl)phenylphosphine (109 mg, 0.4 mmol) in 10 ml of ether and stirred for 4 h. Water was then added (50 ml) and the organics extracted into ether (3 × 20 ml) and dried ($MgSO_4$). Solvent was removed under reduced pressure to yield an oil which slowly crystallised (113 mg, 98%); m.p. 148–150 °C. $[\alpha]_D^{25}$ +42.6 (*c* 0.94, CH_2Cl_2); δ_H (500 MHz, $CDCl_3$) 8.17 (1H, ddd, J_{H4} 1.8, J_{H5} 7.6, J_P 12.0, *o*-An-H6), 7.94 (2H, ddd, J_{meta} 8.0, J_{para} 1.1, J_P 10.9, Ph-*ortho* H), 7.494 (1H, ddd, J_{H3} 8.3, J_{H6} 1.8, J_{H5} 7.5, *o*-An-H4), 7.41–7.38 (3H, m, Ph-*meta*/*para* H), 7.11 (1H, dd, J_{H4} 7.5, J_{H6} 7.6, *o*-An-H5), 6.92 (1H, dd, J_{H4} 8.3, J_P 5.1, *o*-An-H3), 3.75 (3H, s, OCH_3) and 1.27 (9H, d, J_P 15.4, $C(CH_3)_3$); δ_C (62.8 MHz, $CDCl_3$) 159.6 (*o*-An-C_2), 136.1 (d, J_P 4.8, *o*-An-C_6), 133.5 (*o*-An-C_4), 132.0 (d, J_P 8.4, Ph-*ortho*), 130.9 (d, J_P 3.0, Ph-*para* C), 127.7 (d, J_P 12.3, Ph-*meta* C), 121.1 (d, J_P 10.6, *o*-An-C_5,), 110.8 (d, J_P 6.0, *o*-An-C_3), 54.6 (OCH_3), 34.7 (d, J_P 71.6, $(CH_3)_3C$) and 26.0 ($(CH_3)_3C$); δ_P (101.3 MHz, $CDCl_3$) 43.30. ν_{max} cm^{-1} (KBr): 3452, 2946, 2862 (OCH_3), 2310, 2043, 1589, 1576, 1461 (P–Ph st.), 1392 ($C(CH_3)_3$), 1363 ($C(CH_3)_3$), 1317, 1273 (P=O), 1156, 1137, 1099 and 1072. *m/z* (EI^+) 288 (M, 20%), 289 (M + 1, 20), 232 (M − ^{t}Bu + 1, 100%), 231 (M − ^{t}Bu, 50%), 199 (40), 141, 107 (An, 10), 77 (Ph, 20) and 57 (^{t}Bu, 10).

4.9. (*R*)-Ferrocenyl(2-methoxyphenyl)phenylphosphine borane, *15* (+*16*)

t-Butyllithium (2.95 ml, 1.7 M) was slowly added to a THF (5 ml) solution of ferrocene (1.10 g) at 0 °C. This solution was stood for 25 min at 0 °C and then added to a THF (5 ml) solution of (*S*)-methyl-(2-methoxyphenyl)phenylphosphine borane (1.56 g, 6 mmol). After stirring overnight, the reaction was quenched by the addition of water (15 ml) and the organics extracted with ether (3 × 35 ml) and dried ($MgSO_4$). The solvent was removed in vacuo to yield an orange solid which was purified by column chromatography (flash silica, ethyl acetate–pentane: 1/3) to yield (*R*)-ferrocenyl-(2-methoxyphenyl)-phenyl-phosphine borane (R_f = 1) as the major product (1.66 g,

67%). $[\alpha]_D^{25}$ −93.6 (*c* 0.125, CH_2Cl_2). δ_H (500 MHz, $CDCl_3$) 7.79 (1H, ddd, J_{H4} 1.7, J_{H5} 7.6, J_P 13.4, *o*-An-H6), 7.53 (2H, ddd, J_{meta} 8.0, J_{para} 1.1, J_P 11.5, Ph-*ortho* H), 7.49 (1H, ddd, J_{H3} 8.2, J_{H5} 8.2, J_{H6} 0.9, *o*-An-H4), 7.42–7.33 (3H, m, Ph-*meta*/*para* H), 7.07 (1H, ddd, J_{H4} 8.2, J_{H6} 7.5, J_P 0.8, *o*-An-H5), 6.89 (1H, dd, J_{H4} 8.2, J_P 3.7, *o*-An-H3), 4.69 (1H, s, Fc-*ortho* H), 4.53 (1H, s, Fc-*ortho*-H'), 4.49 (2H, s, Fc-*meta* H), 4.04 (5H, s, Fc'-H), 3.47 (3H, s, OCH_3) and 1.54–0.89 (3H, vbr m, BH_3); δ_C (125.8 MHz, $CDCl_3$) 160.8 (*o*-An-C_2), 135.4 (d, J_P 12.1, *o*-An-C_6), 133.3 (*o*-An-C_4), 132.6 (d, J_P 62.1, Ph-*ipso* C), 131.3 (d, J_P 10.3, Ph-*ortho* C), 129.9 (Ph-*para* C), 127.8 (d, J_P 10.7, Ph-*meta* C), 120.8 (d, J_P 11.1, *o*-An-C_5), 119.6 (d, J_P 58.7, *o*-An-C_1), 111.8 (d, J_P 3.8, *o*-An-C_3), 73.8 (d, J_P 11.3, Fc-*ortho* C), 73.4 (d, J_P 7.9, Fc-*ortho* C'), 71.6 (d, J_P 8.1, Fc-*meta* C), 71.3 (d, J_P 8.5, Fc-*meta* C'), 69.6 ('Fc-C), 68.4 (d, J_P 70.6, Fc-*ipso* C) and 55.2 (OCH_3); δ_P (202.5 MHz, $CDCl_3$) 15.02 (br d, J_B 75.2). ν_{max} cm^{-1} (KBr): 3102, 3065, 2994, 2939, 2836 (OCH_3), 2373 (BH_3), 2342 (BH_3), 2258 (BH_3), 1589 (Ar–H vib), 1573, 1480, 1465, 1430 (P–Ph), 1411, 1278, 1253, 1167, 1108, 1063, 1025, 1013, 829, 763 (Ar–H out of plane bend), 743 (Ar–H bend), 700 (Ph–H bend), 689 (Ph–H bend), 619, 490, 475 and 453. *m*/*z* (EI^+) 414 (M, 10%), 401 (M − BH_3, 30), 400 (M − BH_3, 100), 323 (M − BH_3 − Ph, 5), 293 (M − BH_3 − An, 10), 186 (Fc, 30), 170 (15) and 121 (30). A second component eluted from the column (R_f = 0.6) and was identified as (*R*,*R*)-1,1'-bis(phenyl-(2-methoxyphenyl)phosphino)ferrocene borane (58 mg, 3%); m.p. 78–80 °C. $[\alpha]_D^{25}$ −63 (*c* 0.05, CH_2Cl_2). δ_H (500 MHz, $CDCl_3$) 7.67 (2H, ddd, J_{H4} 1.6, J_{H5} 7.6, J_P 13.4, *o*-An-H6), 7.46 (6H, m, Ph-*ortho*/*para* H), 7.39 (2H, ddd, J_{H3} 8.2, J_{H5} 7.6, J_{H6} 1.8, *o*-An-H4), 7.32 (4H, ddd, J_{para} 7.7, J_{ortho} 7.7, J_P 2.3, Ph-*meta* H), 7.03 (2H, ddd, J_{H4} 7.6, J_{H6} 7.6, J_P 1.1, *o*-An-H5), 6.84 (2H, dd, J_{H4} 8.2.J_P 3.8, *o*-An-H3), 4.45 (2H, s, Fc-*ortho* H), 4.44, 4.42 (2H, dd, $J_{meta'}$ 1.1, J_P 1.1, Fc-*meta* H; 2H, dd, J_P 1.1, Fc-*meta* H'), 4.35 (2H, s, Fc-*ortho* H) and 3.43 (6H, s, OCH_3); δ_C (125.8 MHz, $CDCl_3$) 160.8 (*o*-An-C_2), 135.2 (d, J_P 12.4, *o*-An-C_6), 133.4 (*o*-An-C_4), 132.0 (d, J_P 53.1, Ph-*ipso* C), 131.3 (d, J_P 9.5, Ph-*ortho* C), 130.1 (Ph-*para* C), 127.9 (d, J_P 10.6, Ph-*meta* C), 120.8 (d, J_P 11.6, *o*-An-C_5), 119.1 (d, J_P 59.0, *o*-An-C_1), 111.8 (*o*-An-C_3), 74.6 (Fc-C), 74.6 (Fc-C), 74.5 (Fc-C), 73.9 (Fc-C), 69.8 (d, J_P 68.1, Fc-*ipso* C) and 55.2 (OCH_3); δ_P (202.5 MHz, $CDCl_3$) 14.58 (br d, J_B 35.5). ν_{max} cm^{-1} (KBr): 3421, 2963, 2849 (OCH_3), 2369 (BH_3), 2343 (BH_3), 1718, 1654, 1589 (Ar–H vib), 1574, 1478, 1431, 1262, 1172, 1104, 1060, 1029, 802, 758 (Ar–H oop bend), 741 (Ar–H bend), 698 (Ph–H bend), 637 and 612. *m*/*z* (EI^+) 614 (M − $(BH_3)_2$, 30%), 537 (M − Ph − $(BH_3)_2$, 5), 507 (M − An − $(BH_3)_2$, 5), 470 (10), 400 (M − P − An − Ph − $(BH_3)_2$, 30), 354 (10), 307 (10), 278 (10), 246 (FcP2, 15), 233 (15), 226 (15), 215 (AnPhP, 30), 186 (Fc, 35), 170 (70), 152 (30), 137 (50), 121 (90), 91 (100) amd 77 (Ph, 40).

4.10. (*R*)-Ferrocenyl(2-methoxyphenyl)phenylphosphine, **19**

Diethylamine (5 ml) was added to (*R*)-ferrocenyl-(2-methoxyphenyl)phenylphosphine borane (62 mg, 0.15 mmol) and the solution heated to 46 °C for 8 h. The diethylamine was then removed under reduced pressure to yield the crude product which was passed through a short silica column in C_7H_8. Solvent was removed under reduced pressure to yield an orange solid (59 mg, 98%); m.p. 127–129 °C. δ_H (500 MHz, $CDCl_3$) 7.46 (2H, ddd, $J_{ortho/para}$ 5.8, $J_{ortho/para}$ 8.1, J_P 2.2, Ph-*meta* H), 7.33 (3H, m, Ph-*ortho*/*para* H), 7.30 (1H, ddd, J_{H4} 1.8, J_{H5} 6.4, J_P 8.2, *o*-An-H6), 6.91 (1H, ddd, J_{H3} 8.2, J_{H6} 1.8, J_{H5} 7.3, *o*-An-H4), 6.87 (1H, dd, J_{H4} 7.3, J_{H6} 7.3, *o*-An-H5), 6.83 (1H, dd, J_{H4} 8.2, J_P 4.5, *o*-An-H3), 4.40 (1H, s, Fc-H), 4.34 (1H, s, Fc-H), 4.28 (1H, s, Fc-H), 4.11 (5H, s, Fc'-H), 3.84 (1H, s, Fc-H) and 3.72 (3H, s, OCH_3); δ_C (125.7 MHz, $CDCl_3$) 160.8 (d, J_P 15.6, *o*-An-C_2), 138.1 (d, J_P 8.0, *o*-An-C_6), 133.6 (d, J_P 19.8, *o*-An-C_4), 130.0 (Ph-*para* C), 128.4 (Ph-*ortho* C), 128.1 (d, J_P 11.8, Ph-*ipso* C), 127.9 (d, J_P 6.9, Ph-*meta* C), 120.7 (*o*-An-C_5), 110.2 (*o*-An-C_3), 75.7 (d, J_P 4.8, Fc-*ipso* C), 74.0 (d, J_P 25.1, Fc-C), 72.2 (d, J_P 4.4, Fc-C), 70.9 (d, J_P 6.2, Fc-C), 70.4 (Fc-C), 69.1 (Fc'-C) and 55.6 (OCH_3); δ_P (101.3 MHz, Et_2NH) −26.4. *m*/*z* (EI^+) 400 (M, 100%), 401 (M, 20), 323 (M − Ph, 10), 293 (M − An, 10), 226 (10), 215 (15), 186 (Fc, 40), 170 (25) and 121 (65).

4.11. (*S*)-Ferrocenyl(2-methoxyphenyl)phenylphosphine oxide

t-Butyl hydroperoxide (0.07 ml, 3.0 M in *iso*-octane, 0.2 mmol) was slowly added to a diethylamine solution of (*R*)-ferrocenyl-(2-methoxyphenyl)phenylphosphine (41 mg, 0.1 mmol) and stirred for 4 h. Water was then added (10 ml) and the organics extracted into ether (3 × 20 ml) and dried ($MgSO_4$). Solvent was removed under reduced pressure to yield an oil which slowly crystallised (42 mg, 98%); m.p. 163–165 °C. $[\alpha]_D^{25}$ −51.6 (*c* 0.11, CH_2Cl_2). δ_H (500 MHz, $CDCl_3$) 7.98 (1H, ddd, J_{H4} 1.7, J_{H5} 7.6, J_P 13.4, *o*-An-H6), 7.69 (2H, ddd, J_{meta} 7.0, J_{para} 1.4, J_P 12.7, Ph-*ortho* H), 7.51 (1H, dd, J_{H3} 8.1, J_{H5} 8.1, *o*-An-H4), 7.45 (1H, dt, J_{meta} 7.2, J_{ortho} 1.4, Ph-*para* H), 7.39 (2H, dt, J_{para} 7.2, J_{ortho} 7.0, Ph-*meta* H), 7.12 (1H, ddd, J_{H4} 8.1, J_{H6} 7.4, J_P 1.6, *o*-An-H5), 6.89 (1H, dd, J_{H4} 8.1, J_P 5.3, *o*-An-H3), 4.60 (1H, s, Fc-H), 4.484 (1H, s, Fc-H), 4.45 (2H, d, J_P 4.2, Fc-H), 4.14 (5H, s, Fc'-H) and 3.53 (3H, s, OCH_3); δ_C (125.8 MHz, $CDCl_3$) 160.3 (*o*-An-

C_2), 135.8 (d, J_P 112.0, Ph-*ipso* C), 134.3 (*o*-An-C_6), 133.6 (*o*-An-C_4), 130.9 (Ph-*para* C), 130.8 (Ph-*meta* C), 127.7 (d, J_P 12.5, Ph-*ortho* C), 122.9 (d, J_P 106.9, *o*-An-C_1), 120.7 (d, J_P 11.0, *o*-An-C_5), 111.5 (*o*-An-C_3), 72.8 (d, J_P 12.9, Fc-H), 72.1 (d, J_P 13.1, Fc-H), 71.2 (d, J_P 10.7, Fc-H), 70.9 (d, J_P 10.4, Fc-H), 69.5 (Fc'-C) and 55.2 (OCH_3); δ_P (202.6 MHz, $CDCl_3$) 28.2. ν_{max} cm^{-1} (KBr): 3088, 3066, 2841 (OCH_3), 1654, 1590 (Ar–H vib.), 1578, 1482, 1465, 1439, 1387, 1367, 1313, 1285 (P=O), 1247, 1193, 1161, 1139, 1106, 1020, 823, 767,752,738 (Ar–H oop bend (Ar–H oop bend), 715 and 572. *m/z* (EI^+) 416 (M, 100%), 417 (M, 25), 351 (M − Cp, 20), 335 (10), 273 (10), 215 (15) and 186 (Fc, 10).

4.12. (R)-(1-Adamantyl)(2-methoxyphenyl)phenylphosphine borane, 17

1-Adamantyllithium (20 ml, 0.12 M in ether) was added to (*S*)-methyl (2-methoxyphenyl)phenylphosphinite borane (52 mg, 0.2 mmol) and the solution heated to 40 °C for 56 h, then quenched with water (20 ml), the organics extracted into ether (3 × 20 ml) and dried ($MgSO_4$). The solvent was removed under reduced pressure to afford a white solid which was purified by thin layer chromatography (ethyl acetate–pentane: 1/1, R_f = 0.4) to yield (*R*)-(1-adamantyl)(2-methoxyphenyl)phenylphosphine borane as a sticky white solid (27 mg, 37%). δ_H (500 MHz, $CDCl_3$) 8.01 (1H, ddd, J_{H4} 1.7, J_{H5} 7.7, J_P 12.8, *o*-An-H6), 7.70 (2H, ddd, J_{meta} 8.0, J_{para} 1.2, J_P 9.8, *ortho* H), 7.51 (1H, dddd, J_{H3} 7.3, J_{H6} 1.7, J_{H5} 7.3, *o*-An-H4), 7.42–7.34 (3H, m, *meta/para* H), 7.07 (1H, dddd, J_{H3} 1.1, J_P 1.6, J_{H4} 7.3, J_{H6} 7.7, *o*-An-H5), 6.93 (1H, dd, J_{H4} 8.3, J_P 3.3, *o*-An-H3), 3.61 (3H, s, OMe), 2.05 (6H, br d, J_P 20.0, $PCCH_2$), 2.00 (2H, s, $PCCH_2CH$) and 1.72 (6H, s, $PCCH_2CHCH_2$); δ_C (125.7 MHz, $CDCl_3$) 161.00 (*o*-An-C_2), 137.99 (d, J_P 12.7, *o*-An-C_6), 133.2 (*o*-An-C_4), 132.70 (d, J_P 7.3, Ph-*ortho* C), 129.76 (Ph-*para* C), 127.79 (d, J_P 10.0, Ph-*meta* C) 120.96 (d, J_P 11.2, *o*-An-C_5), 115.52 (d, J_P 48.4, An-C_1), 111.27 (*o*-An-C_3), 54.69 (OCH_3), 38.17 (Ad-C), 36.51 (Ad-C), 34.93 (d, J_P 30.8, $PCCH_2$) and 28.50 (d, *J* 9.5, $PCCH_2$); δ_P (202.5 MHz, $CDCl_3$) 34.60 (br d, J_B 73). *m/z* (EI^+) 363 (M − 1, 5%), 350 (M − BH_3, 20), 215 (M − Ad, 10), 183 (10), 152 (10), 135 (Ad, 100)), 107 (An, 45), 93 (45) and 77 (Ph, 20).

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