Synthesis, X-ray crystal structures and Horner–Wittig addition reactions of some protected β-aminophosphine oxides

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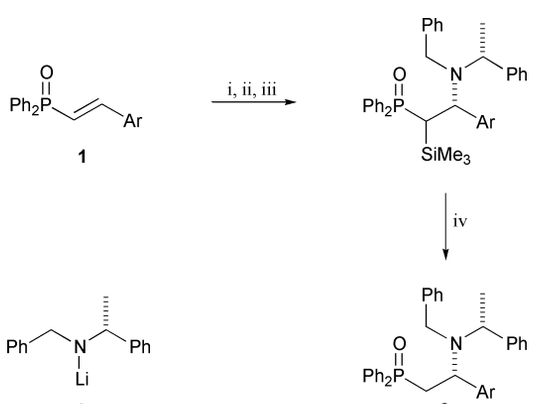
Several protected β-aminophosphine oxides have been synthesised and investigated in the Horner–Wittig addition reaction. Crystal structures of an enantiomerically pure β-amino phosphine oxide and a Horner–Wittig addition product are presented. Horner–Wittig reactions were typically poorly stereoselective, although the ratio of diastereoisomers can be influenced by the addition of lithium bromide.

Introduction

The diphenylphosphinoyl (Ph_2PO) group has been used to control relative and absolute stereochemistry and also the double bond geometry through the Horner–Wittig reaction.[1] This methodology has been used in the synthesis of a range of molecules with 1,4[2,3] and 1,5[4,5] related stereogenic centres across a double bond of fixed geometry. As part of our investigations into the synthetic utility of the diphenylphosphinoyl group, we have been investigating the possible synthesis of enantiomerically enriched allylic amines containing a double bond of fixed geometry.

We have previously reported[6,7] the synthesis of β-aminophosphine oxides in up to 99% ee using the asymmetric conjugate addition reaction developed by Davies.[8] The chiral lithium amide **2** adds selectively, in the presence of trimethylsilyl chloride, to the vinylic phosphine oxides **1** giving β-aminophosphine oxides **3** after proto-desilylation (Scheme 1). The

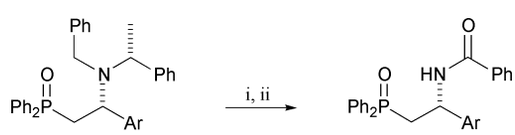


Scheme 1 *Reagents*: i, Me_3SiCl, THF, −78 °C; ii, **2**; iii, H_2O; iv, TBAF, THF.

stereochemistry of the newly created stereogenic centre was tentatively assigned by NMR experiments on a mandelic acid derivative. We now confirm the stereochemistry of the conjugate addition reaction by X-ray crystallography, report the rapid synthesis of racemic β-aminophosphine oxides and the addition of their dilithiated derivatives to aldehydes and ketones (the Horner–Wittig reaction).

Results and discussion

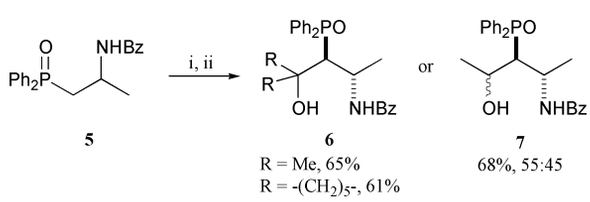
Attempts to crystallise aminophosphine oxides **3**, bearing a known stereogenic centre failed. However, the corresponding amides (such as **4**) solidify more rapidly and several different amides were synthesised (Scheme 2, Table 1) and crystallised.



Scheme 2 *Reagents and conditions*: i, Pd/C, H_2, CH_3CO_2H: ii, PhCOCl, pyridine, CH_2Cl_2.

The absolute stereochemistry of amide **4b** (Ar = 4-MeOPh) was determined from its crystal structure by the method of Flack.[9] There are two molecules in the asymmetric unit (Fig. 1). Two phenyl rings of one molecule are each disordered over two sites. However, both molecules clearly show the stereochemistry to be (*R*), as shown in Scheme 2. Having unambiguously determined the stereochemistry of these protected β-aminophosphine oxides, we set about investigating their reactions with aldehydes and ketones.

We have previously investigated Horner–Wittig addition reactions of β-amino- and β-amido phosphine oxides.[10] Reaction of the dilithiated derivative of the amide **5** with ketones gave the *anti* diastereoisomer **6** in acceptable yield. Reaction with an aldehyde gave a mixture of diastereoisomers **7**, differing only in the relative stereochemistry between the alcohol and phosphorus centers (Scheme 3). We decided to investigate



Scheme 3 *Reagents and conditions*: i, *n*-BuLi, THF, LiBr, −78 °C then RR′CO: ii, NH_4Cl (aq.).

whether the protecting group on nitrogen affected the diastereoselectivity and so we wanted to synthesise differently protected β-aminophosphine oxides.

Table 1 Synthesis of the amides **3** and **4**

Ar	Starting material	Yield of **3** (%)[6,7]	Selectivity	Yield of **4** (%)
Ph	**1a**	65	98 : 2	50
4-$MeOC_6H_4$	**1b**	76	>99 : 1	59
2-Furyl	**1c**	34	>99 : 1	–

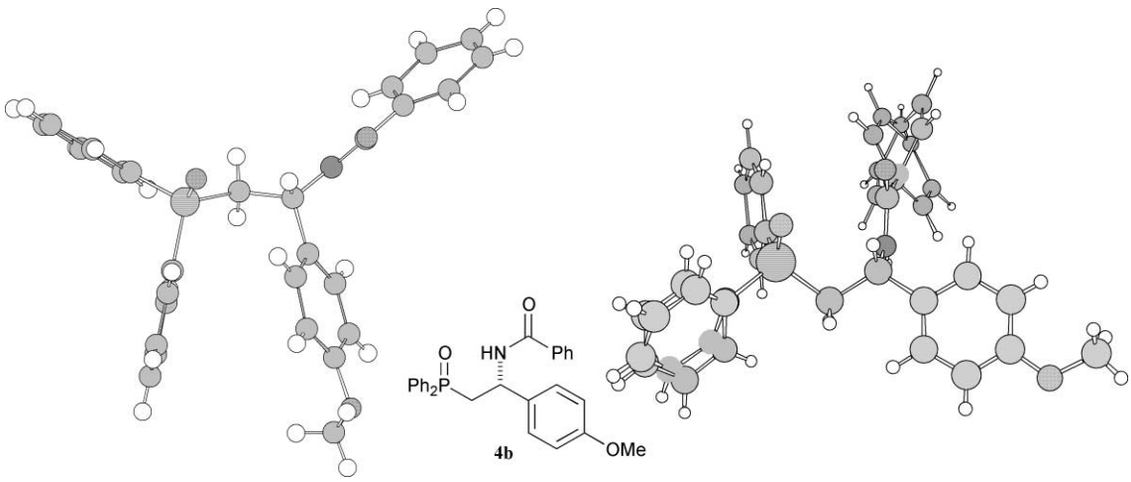
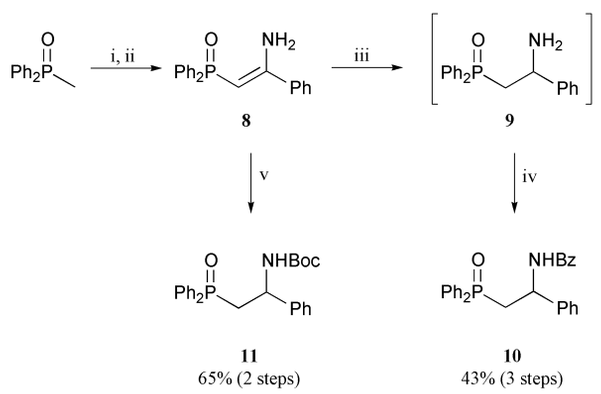


Fig. 1 Chem3D® representation of the two molecules (one disordered) of the amide **4b** in the X-ray crystal structure.

The conjugate addition protocol described above (Scheme 1) is an excellent method for the synthesis of enantiomerically pure protected β-aminophosphine oxides. Its one drawback is that high dilution is required for the conjugate addition step. In order to investigate Horner–Wittig addition reactions we developed a rapid synthesis of three different *racemic* β-aminophosphine oxides **10**–**12**. Addition of lithiated methyldiphenylphosphine oxide to benzonitrile gave the enamine **8** (Scheme 4). Attempted reduction with either sodium borohydride or



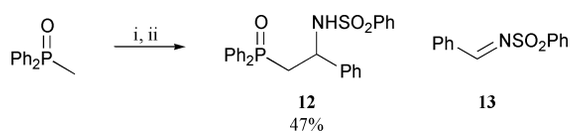
Scheme 4 *Reagents and conditions*: i, *n*-BuLi, THF, −78 °C then PhCN; ii, MeOH; iii, EtOH, Pd/C, H_2; iv, CH_2Cl_2, Et_3N, PhCOCl; v, EtOH, Pd/C, H_2, Boc_2O.

lithium aluminium hydride failed, returning the enamine **8**. The reduction could be achieved by hydrogenation with palladium on charcoal at atmospheric pressure. In fact, the amine **9** can be formed in a one-pot procedure from methyldiphenylphosphine oxide in sufficient purity for immediate protection. The benzamide **10** was synthesised in three steps in 43% yield. Direct Boc protection of the amine **9** was found to be low yielding; good yields could be obtained by hydrogenation of the enamine **8** in the presence of Boc anhydride. The sulfonamide **12** was prepared in moderate yield through the addition of lithiated methyldiphenylphosphine oxide to the imine **13** (Scheme 5).

Initially the Horner–Wittig addition was investigated with the three protected amines **10**–**12**. If suitable reaction conditions and *N*-protecting group could be found, the Horner–

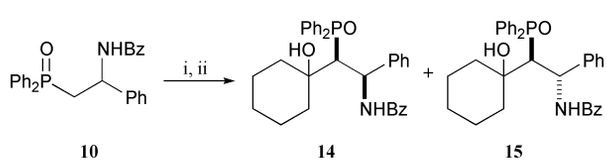
Table 2 Effect of lithium bromide on the product ratio **14** : **15**

Amount of LiBr (eq.)	Ratio **14** : **15**
0.5	1 : 0.6
2	1 : 0.7
4	1 : 1
20	1 : 1.8
Saturated solution	1 : 4.5



Scheme 5 *Reagents and conditions*: i, *n*-BuLi, THF, −78 °C then **13**: ii, NH_4Cl (aq.).

Wittig addition could be repeated with enantiomerically pure β-aminophosphine oxides derived from the conjugate addition reaction (Scheme 1). Horner–Wittig addition reactions of the amide **10** were initially difficult. The amide is insoluble in THF at −78 °C and reaction at 0 °C produced a complex mixture of products. Addition of lithium bromide increases the solubility of the amide **10** and modest yields of the diastereomeric phosphine oxides **14** and **15** were obtained (Scheme 6). The low yield



Scheme 6 *Reagents and conditions*: i, *n*-BuLi, THF, LiBr, −78 °C then cyclohexanone: ii, NH_4Cl (aq.).

may be due to competing deprotonation of cyclohexanone as some starting material was recovered. Although the two diastereoisomers could not be separated by column chromatography, one isomer could be obtained by careful crystallisation. X-Ray diffraction showed it to be the *syn* diastereoisomer **14** (Fig. 2). The ratio of the diastereoisomers **14** and **15** could be influenced by the amount of lithium bromide added (Table 2).

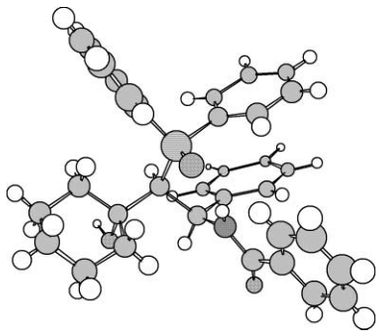
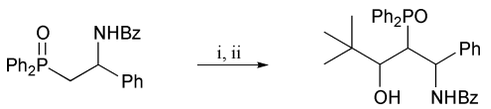


Fig. 2 Chem3D® representation of the X-ray crystal structure of the hydroxyphosphine oxide **14**.

Small amounts of lithium bromide favoured the *syn* isomer **14**. When THF saturated with lithium bromide was used, the reaction was modestly selective for the *anti* isomer **15**, although the yield was low due to precipitation of lithium bromide on cooling. The Horner–Wittig reaction with pivalaldehyde gave a good yield of the hydroxyphosphine oxide **16**, but three of the four possible diastereoisomers were observed (by NMR spectroscopy) in a 2 : 1.3 : 1 ratio (Scheme 7). One diastereoisomer could be isolated in low yield by chromatography.

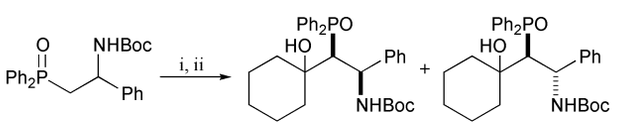


10 **16**

58%, 2.0:1.3:1

Scheme 7 *Reagents and conditions*: i, *n*-BuLi, THF, LiBr, −78 °C then pivalaldehyde: ii, NH_4Cl (aq.).

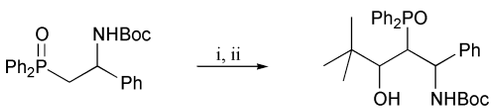
Horner–Wittig addition reactions of the *N*-Boc protected amine **11** were attempted with cyclohexanone and pivalaldehyde (Schemes 8 and 9). In both cases mixtures of diastereo-



11 **17** **18**

30%, 2.6:1

Scheme 8 *Reagents and conditions*: i, *n*-BuLi, THF, LiBr, −78 °C then cyclohexanone; ii, NH_4Cl (aq.).

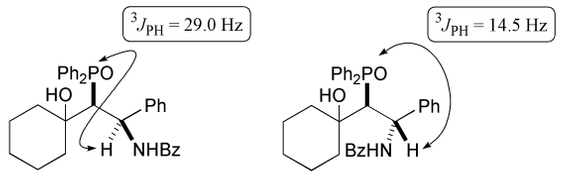


11 **19**

20%, 5.4:2.7:1

Scheme 9 *Reagents and conditions*: i, *n*-BuLi, THF, LiBr, −78 °C then pivalaldehyde; ii, NH_4Cl (aq.).

isomers were obtained. The relative stereochemistry in Scheme 8 was assigned by comparison of the $^3J_{P–CHN}$ coupling constants. Since our initial discovery[11] that the $^3J_{PH}$ coupling constants in β-hydroxyphosphine oxides depend on the relative stereochemistry, all our subsequent work in this area has shown that, within any one class of compounds, this rule is observed. Thus with some confidence we can assign the major diastereoisomer **17** as the *syn* isomer as it has $^3J_{P–CHN} = 29$ Hz, exactly the same value as the *syn* diastereoisomer **14** (Fig. 3). Due to overlapping signals it is not possible to assign any stereochemistry to any of the pivalaldehyde products **19**. Attempts to perform the Horner–Wittig addition on the sulfonamide **12** with cyclohexanone or pivalaldehyde all failed. Decomposition occurred after lithiation, even at −78 °C and the decomposition products could not be identified. Due to the poor



14 **15**

Fig. 3 The relationship between relative stereochemistry and $^3J_{PH}$.

diastereoselectivity of the Horner–Wittig addition reaction, the elimination to form allylic amines was not performed.

In conclusion, although the Horner–Wittig reaction was only poorly selective, we have developed a rapid synthesis of racemic protected β-aminophosphine oxides. We have also confirmed our previous tentative assignment of the stereochemistry in the asymmetric conjugate addition reaction by X-ray crystallography and obtained a crystal structure of a Horner–Wittig addition product.

Experimental

All solvents were distilled before use. THF was freshly distilled from lithium aluminium hydride with triphenylmethane as the indicator. Dichloromethane was distilled from calcium hydride and methanol from calcium methoxide. Pyridine was dried by stirring over and distilling from calcium hydride and was stored over 4 Å molecular sieves. Triethylamine was dried in the same way but stored over calcium hydride. *n*-Butyllithium was titrated against diphenylacetic acid before use. All non-aqueous reactions were carried out under argon using oven and vacuum dried glassware. Column chromatography was performed with Merck Kieselgel 60 (230–400 mesh). Thin layer chromatography was carried out on pre-coated plates (Merck Kieselgel $60F_{254}$).

Proton and carbon NMR spectra were recorded on Bruker DPX250, DPX400, DRX400, DRX500 Fourier Transform spectrometers using an internal deuterium lock. Chemical shifts are quoted in parts per million (ppm) downfield from tetramethylsilane. The symbol "*" after a proton NMR signal indicates that the signal disappears after a D_2O shake. Carbon NMR were recorded with broadband proton decoupling, the symbol "+" after a carbon NMR chemical shift indicates an odd number of attached protons, whereas the symbol "−" indicates an even number, as determined by APT or DEPT analysis. Coupling constants for proton and carbon NMR signals are quoted in Hz, rounded to the nearest 0.5 Hz and are reported as observed.

Electron Impact (EI) mass spectra were recorded on a Kratos double focusing magnetic sector instrument using a DS503 data system for high-resolution analysis or a MSI double focusing magnetic sector Concept IH instrument. Electrospray (ESI) mass spectra were recorded using a Bruker Bio-Apex II FT-ICR instrument or a Micromass Q-Tof machine. Liquid secondary ion mass spectra (LSIMS) were recorded on a MSI double focusing Concept IH instrument. Microanalyses were carried out by the staff of the University Chemical Laboratory using a Leeman Labs CE440 Elemental Analyzer (C, H and N) and LBK Biochrom Ultrospec 4050 (P). Melting points were measured on a Stuart Scientific SMP1 melting point apparatus and are uncorrected. Infra-red spectra were recorded using a Perkin Elmer 1600 (FT-IR) spectrometer and optical rotations were recorded on a Perkin Elmer 241 polarimeter using the sodium D line (589 nm) at room temperature and are given in units of 10^{-1} deg dm^2 g^{-1}.

(*R*)-1-Benzylamido-2-diphenylphosphinoyl-1-(*p*-methoxyphenyl)-ethane 4b

By the method of Bartels,[7] palladium on charcoal (10%, 1.35 g, 1.2 mmol) was added to a solution of (1*R*,1′*R*)-*N*-benzyl-*N*-

[1′-methylbenzyl]-2-diphenylphosphinoyl-1-(*p*-methoxyphenyl)ethylamine[7] **3b** (2.23 g, 4.1 mmol) in glacial acetic acid (35 cm^3). The reaction mixture was shaken in a Parr hydrogenator under hydrogen (4 atm) at 50 °C for 20 hours. The cooled reaction mixture was filtered through Celite, washed with methanol and evaporated under reduced pressure. The residue was basified by addition of saturated sodium bicarbonate solution until the pH was greater than 8. The aqueous layer was extracted with dichloromethane (4 × 100 cm^3), the combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The crude free amine was used without further purification.

The crude amine was dissolved in dry dichloromethane (20 cm^3) and cooled to 0 °C. Pyridine (400 µl, 4.5 mmol) and benzoyl chloride (625 µl, 4.9 mmol) were added and the reaction mixture was stirred for 2 hours. The reaction mixture was quenched with hydrochloric acid (3 M, 30 cm^3), extracted with dichloromethane (3 × 50 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to yield a crude product. The residue was chromatographed (SiO_2, EtOAc–hexane, 1 : 1) to give the *amide* **4b** (0.915 g, 49%) as needles, mp 207–208 °C (from dichloromethane–hexane); R_f(EtOAc) 0.39; $[a]_D$ +19.1 (*c* 1.0 in $CHCl_3$); δ_H(500 MHz; $CDCl_3$) 8.91* (1H, d, *J* 5.5, NH), 7.98 (2H, d, *J* 7.5, Ph), 7.71–7.35 (13H, m, Ph), 7.17 (2H, d, *J* 8.0, *meta*-C_6H_4OMe), 6.65 (2H, d, *J* 8.0, *ortho*-C_6H_4OMe), 5.45–5.39 (1H, m, C*H*N), 3.69 (3H, s, OMe), 2.90–2.80 (2H, m, PCH_2); δ_C(100 MHz; $CDCl_3$) 166.3$^-$ (CO), 158.6$^-$ (*C*OMe), 133.9$^-$ and 133–127 (Ph and C_6H_4OMe), 113.8$^+$ (*ortho*-C_6H_4OMe), 55.2$^+$ (OMe), 50.4$^+$ (d, *J* 5.5, CNH), 35.9$^-$ (d, *J* 67.0, PCH_2); *m*/*z* (EI) 455 (82, M^+), 333 (87, M − NCOPh), 202 (100%, Ph_2POH) (Found: M^+ 455.1690. $C_{28}H_{26}NO_3P$ requires *M*, 455.1650).

1-Amino-2-diphenylphosphinoyl-1-phenylethene 8

n-Butyllithium (1.4 M in hexane, 36.4 cm^3, 51 mmol) was added to a solution of methyldiphenylphosphine oxide (10 g, 46 mmol) in dry THF (200 cm^3) at −78 °C and the reaction mixture stirred for 30 minutes. Benzonitrile (5.25 g, 5.3 cm^3, 51 mmol) was added and the reaction mixture was stirred for 30 minutes at −78 °C and allowed to warm to room temperature over 1 hour. The reaction was quenched with dry methanol (3 cm^3) and sodium borohydride (2.63 g, 69 mmol) was added in 3 portions over 15 minutes. The reaction mixture was stirred for 18 hours and was quenched by the slow addition of acetic acid (2 cm^3). Water (100 cm^3) was added and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 100 cm^3). The combined organic extracts were washed with brine (100 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product. The 400 MHz ^{1}H NMR spectrum of this residue showed the enamine **8** as previously reported.[12]

(*RS*)-2-Amino-1-diphenylphosphinoyl-2-phenylethane 9

Palladium on charcoal (10%, 3.0 g, 2.8 mmol) was added to the crude enamine **8** (9.1 g, approx. 28 mmol) in absolute ethanol (100 cm^3). The reaction mixture was stirred under a balloon of hydrogen gas for 20 hours, filtered through Celite, washed with ethanol and evaporated under reduced pressure. The residue was dissolved in dichloromethane (100 cm^3) and extracted into hydrochloric acid (3 M, 2 × 70 cm^3). The aqueous layer was basified with sodium hydroxide pellets until the pH was greater than 10 and extracted with dichloromethane (3 × 100 cm^3). The combined organic extracts were washed with brine (200 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a residue. The residue was chromatographed (SiO_2, EtOAc–methanol, 1 : 0 to 19 : 1) to give the aminophosphine oxide **9** (3.5 g, 39%) which has been synthesised previously, but not isolated[6,7] as an amorphous white solid; R_f(EtOAc) 0.05; δ_H (400 MHz; $CDCl_3$) 7.80–7.70 (4H, m, Ph_2PO), 7.54–7.42 (6H, m, Ph_2PO and Ph), 7.33–7.17 (5H, m, Ph_2PO and Ph), 4.46 (1H, td, *J* 10.0 and 2.5, PhC*H*N), 2.68 (1H, ddd, *J* 15.0, 11.5 and 10.0, PCH_AH_B), 2.57 (1H, ddd, *J* 15.0, 8.0 and 2.5, PCH_AH_B) and 1.90* (2H, br s, NH_2); δ_C(100 MHz; $CDCl_3$) 146.7$^-$ (*ipso*-Ph), 134.7$^-$ (d, *J* 98.0, *ipso*-Ph_2PO), 133.2$^-$ (d, *J* 95.5, *ipso*-Ph_2PO), 132.4$^+$ (*para*-Ph_2PO), 132.4$^+$ (*para*-Ph_2PO), 131.6$^+$ (d, *J* 9.0, *ortho*-Ph_2PO), 131.2$^+$ (d, *J* 9.5, *ortho*-Ph_2PO), 129.4$^+$ (d, *J* 12.5, *meta*-Ph_2PO), 129.3$^+$ (d, *J* 12.0, *meta*-Ph_2PO), 129.3$^+$, 128.1$^+$ and 126.8$^+$ (Ph), 51.9$^+$ (CHN) and 40.6$^-$ (d, *J* 68.5, PCH_2); *m*/*z* (LSIMS) 322 (100%, MH^+), and 289 (43, M − O − NH_2) (Found: MH^+, 322.1369. $C_{20}H_{21}NOP$ requires *M*, 322.1360).

(*RS*)-1-Benzylamido-2-diphenylphosphinoyl-1-phenylethane 10

In a method analogous to that of Oh,[13] *n*-butyllithium (2.0 M in hexane, 12.7 cm^3, 25 mmol) was added to a solution of methyldiphenylphosphine oxide (5 g, 23 mmol) in dry THF (100 cm^3) at 0 °C and the reaction mixture stirred for 30 minutes. Benzonitrile (2.86 g, 2.9 cm^3, 28 mmol) was added and the reaction mixture was stirred for 30 minutes at 0 °C and allowed to warm to room temperature over 1 hour. The reaction was quenched with dry methanol (10 cm^3) and the solvent removed under reduced pressure. The residue was dissolved in absolute ethanol (80 cm^3) and palladium on charcoal (10%, 2.40 g, 2.3 mmol) was added. The reaction mixture was vigorously stirred under a balloon of hydrogen gas for 18 hours, filtered through Celite, washed with ethanol and evaporated under reduced pressure to give the crude aminophosphine oxide **9** which was used without further purification.

The residue was dissolved in dry dichloromethane (60 cm^3) and triethylamine (4.7 g, 6.5 cm^3, 46 mmol) and benzoyl chloride (4.88 g, 4.1 cm^3, 35 mmol) were added. The reaction mixture was stirred for 2 hours and quenched with water (30 cm^3). The layers were separated. The aqueous layer was extracted with dichloromethane (3 × 30 cm^3), the combined organic extracts were washed with brine (100 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product. The residue was chromatographed (SiO_2, EtOAc–hexane, 2 : 1 to 1 : 0) to give the amide **10** (4.28 g, 43%), which was spectroscopically identical to the enantiomerically enriched amide reported previously.[6,7]

(*RS*)-2-(*tert*-Butyloxycarbonylamino)-1-diphenylphosphinoyl-2-phenylethane 11

n-Butyllithium (2.5 M in hexane, 4.1 cm^3, 10.2 mmol) was added to a solution of methyldiphenylphosphine oxide (2 g, 9.3 mmol) in dry THF (40 cm^3) at 0 °C and the reaction mixture stirred for 30 minutes. Benzonitrile (1.14 g, 1.2 cm^3, 11.1 mmol) was added and the reaction mixture was stirred for 30 minutes at 0 °C and allowed to warm to room temperature over 1 hour. The reaction was quenched with dry methanol (5 cm^3) and the solvent was removed under reduced pressure. The residue was dissolved in absolute ethanol (30 cm^3) and palladium on charcoal (10%, 980 mg, 0.92 mmol), and di-*tert*-butyl dicarbonate (3.04 g, 13.9 mmol) were added. The reaction mixture was vigorously stirred under an atmosphere of hydrogen gas for 18 hours, filtered through Celite, washed with ethanol and evaporated under reduced pressure to give a crude product. The residue was chromatographed (SiO_2, EtOAc–hexane, 2 : 1 to 1 : 0) to give the *Boc-protected amine* **11** (2.55 g, 65%) as prisms, mp 211–213 °C (from EtOAc–hexane); R_f(EtOAc) 0.27; $\nu_{max}(CHCl_3)/cm^{-1}$ 1708 (C=O), 1438 (P–Ph), 1174 (P=O); δ_H(400 MHz; $CDCl_3$) 7.73–7.65 (2H, m, Ph_2PO), 7.60–7.04 (13H, m, Ph_2PO and Ph), 6.51* (1H, br s, NH), 5.03–4.93 (1H, m, CHN), 2.82–2.66 (2H, m, PCH_2), 1.35 (9H, s, Me_3); δ_C(100 MHz; $CDCl_3$) 155.5$^-$ (CO), 142.8$^-$ (*ipso*-Ph), 133.1$^-$ (d, *J* 99.0, *ipso*-Ph_2PO), 133.0$^-$ (d, *J* 99.0, *ipso*-Ph_2PO), 132.6$^+$ (*para*-Ph_2PO), 132.3$^+$ (*para*-Ph_2PO), 129.1$^+$ (d, *J* 11.5, *meta*-Ph_2PO), 128.9$^+$ (d, *J* 12.0, *meta*-Ph_2PO), 128.8$^+$, 127.6$^+$ and

126.3$^+$ (Ph), 79.7$^-$ (O*C*Me$_3$), 51.8$^+$ (CHN), 37.0$^-$ (d, *J* 68.0, PCH$_2$) and 28.7$^+$ (C*Me*$_3$); *m*/*z* (LSIMS) 422 (90%, MH$^+$), 366 (38, M − CMe$_3$), 322 (100, M − COOCMe$_3$), 307 (50, M − NHCOOCMe$_3$) (Found: MH$^+$, 422.1866. $C_{25}H_{29}NO_3P$ requires *M*, 422.1885) (Found: C, 71.2; H, 6.75; N, 3.4; P, 7.4. $C_{25}H_{28}NO_3P$ requires C, 71.2; H, 6.7; N, 3.3; P, 7.4%).

(*RS*)-1-Phenylsulfonylamido-2-diphenylphosphinoyl-1-phenylethane 12

n-Butyllithium (1.4 M in hexane, 5.5 cm^3, 7.6 mmol) was added to a stirred solution of methyldiphenylphosphine oxide (1.5 g, 6.9 mmol) in dry THF (20 cm^3) at −78 °C. The orange solution was stirred for 30 minutes and the *N*-benzylidene benzenesulfonamide[14] **13** (2.04 g, 8.3 mmol) was added. The reaction mixture was stirred at −78 °C for 30 minutes and allowed to warm to room temperature over 1 hour. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (20 cm^3). The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 30 cm^3). The combined organic extracts were washed with brine (50 cm^3), dried (MgSO$_4$) and evaporated under reduced pressure to yield the crude β-hydroxyphosphine oxide. The residue was chromatographed (SiO$_2$, EtOAc–hexane, 1 : 1 to 1 : 0) to give the *phosphine oxide* **12** (1.49 g, 47%) as needles, mp 220–222 °C (from EtOAc–hexane); R_f(EtOAc) 0.44; ν_{max}(solid state)/cm^{-1} 3100–3000 (br, NH), 1439 (P–Ph), 1325 (SO$_2$), 1176 (SO$_2$) and 1151 (P=O); δ_H(400 MHz; CDCl$_3$) 7.66 (2H, br d, *J* 7.0, PhSO$_2$N), 7.51–7.23 (13H, m, Ph and Ph$_2$PO), 7.10–7.04 (5H, m, PhSO$_2$N and Ph), 4.60–4.51 (1H, m, CHN), 2.70 (1H, ddd, *J* 15.5, 11.5 and 9.0, PC*H*$_A$H$_B$), 2.49 (1H, ddd, *J* 15.5, 8.0 and 4.0, PCH$_A$*H*$_B$), no NH peak observed; δ_C(100 MHz; CDCl$_3$) 140.4$^-$ (d, *J* 9.5, *ipso*-PhCHN), 140.1$^-$ (*ipso*-PhSO$_2$N), 132.1$^-$ (d, *J* 100.0, *ipso*-Ph$_2$PO), 132.0$^+$ (Ph), 131.9$^+$ (2 × *para*-Ph$_2$PO), 131.1$^-$ (d, *J* 99.0, *ipso*-Ph$_2$PO), 130.5$^+$ (d, *J* 9.5, *ortho*-Ph$_2$PO), 130.2$^+$ (d, *J* 9.5, *ortho*-Ph$_2$PO), 128.7$^+$ (d, *J* 12.0, *meta*-Ph$_2$PO), 128.6$^+$ (d, *J* 10.5, *ortho*-Ph$_2$PO), 128.5$^+$, 128.2$^+$, 127.6$^+$, 127.3$^+$ and 126.5$^+$ (Ph), 54.5$^+$ (d, *J* 4.0, CHN) and 36.7$^-$ (d, *J* 66.5, PCH$_2$); *m*/*z* (ESI) 484 (100%, MNa$^+$) (Found: MNa$^+$, 484.1101. $C_{26}H_{24}NaO_3PS$ requires *M*, 484.1112) (Found: C, 67.5; H, 5.25; N, 3.0; P, 6.7. $C_{26}H_{24}NO_3PS$ requires C, 67.7; H, 5.2; N, 3.0; P, 6.7%).

General procedure for Horner–Wittig additions of protected β-aminophosphine oxides

n-Butyllithium (2.0 to 2.2 eq.) was added to a stirred solution of the phosphine oxide (1 mmol) and dry lithium bromide (0 to 20 eq.) in dry THF (30 cm^3) at −78 °C. The orange solution was stirred for 30 minutes and the electrophile (1.5 eq.) was added. The reaction mixture was stirred at −78 °C for one hour and quenched by the addition of saturated aqueous ammonium chloride solution (20 cm^3). The layers were separated and the aqueous layer was washed with dichloromethane (3 × 30 cm^3). The combined organic extracts were washed with brine (50 cm^3), dried (MgSO$_4$) and evaporated under reduced pressure to yield the crude β-hydroxyphosphine oxide.

(1*SR*,2*RS*)-2-Benzylamido-1-diphenylphosphinoyl-1-(1′-hydroxycyclohexyl)-2-phenylethane 14. 1-Benzylamido-2-diphenylphosphinoyl-1-phenylethane **10** (300 mg, 0.71 mmol), *n*-butyllithium (1.9 M in hexane, 820 µl, 1.55 mmol), cyclohexanone (100 mg, 110 µl, 1.06 mmol) and lithium bromide (0.50 g, 5.7 mmol) gave a crude product that was chromatographed (SiO$_2$, EtOAc–hexane, 1 : 1) to give the *hydroxyphosphine oxide* **14** (75 mg, 20%) as needles, mp 192–194 °C (from EtOAc–hexane); R_f(EtOAc) 0.55; ν_{max}(CHCl$_3$)/cm^{-1} 3500–3100 (br, OH and HN), 1658 (C=O), 1438 (P–Ph), 1160 (P=O); δ_H(500 MHz; CDCl$_3$) 9.71* (1H, d, *J* 7.5, NH), 8.09 (2H, br dd, *J* 6.5 and 1.5, Ph), 7.80–7.70 (2H, m, Ph), 7.57–6.85 (16H, m, Ph), 6.11 (1H, dd, *J* 29.0 and 7.5, CHN), 3.25 (1H, dd, *J* 10.0 and 2.0, PCH), 2.43* (1H, br s, OH), 2.05–0.90 (10H, m, 5 × CH$_2$); δ_C(125 MHz; CDCl$_3$) 166.3$^-$ (C=O), 140.6$^-$ (Ph), 135.6$^-$ (d, *J* 96.0, *ipso*-Ph$_2$PO), 133.9$^-$ (Ph), 133.8$^-$ (d, *J* 94.0, *ipso*-Ph$_2$PO), 131.6$^+$ (Ph), 131.4$^+$ (*para*-Ph$_2$PO), 130.9$^+$ (d, *J* 9.5, *ortho*-Ph$_2$PO), 130.6$^+$ (*para*-Ph$_2$PO), 130.0$^+$ (*para*-Ph$_2$PO), 128.7$^+$ (Ph), 128.4$^+$ (*meta*-Ph$_2$PO), 128.1$^+$ (*meta*-Ph$_2$PO), 128.0$^+$ (Ph), 126.3$^+$ (Ph), 125.8$^+$ (Ph), 75.2$^-$ (COH), 55.2$^+$ (d, *J* 63.5, PCH), 52.5$^+$ (d, *J* 4.5, CHN), 37.7$^-$ (d, *J* 5.0, CH$_2$), 36.4$^-$, 36.4$^-$, 24.8$^-$, 21.9$^-$ and 21.8$^-$ (CH$_2$); *m*/*z* (ESI) 546 (100%, MNa$^+$) (Found: MNa$^+$, 546.2160. $C_{33}H_{34}NNaO_3P$ requires *M*, 546.2174) (Found: C, 75.4; H, 6.6; N, 2.7; P, 5.9. $C_{33}H_{34}NO_3P$ requires C, 75.7; H, 6.55; N, 2.7; P, 5.9%).

*(1RS,2RS)-2-Benzylamido-1-diphenylphosphinoyl-1-(1′-hydroxycyclohexyl)-2-phenylethane **15**.* Also isolated was the *hydroxyphosphine oxide* **15** (40 mg, 11%) as a 2 : 1 mixture of *anti* and *syn* isomers as a white amorphous solid.

R_f(EtOAc) 0.55; ν_{max}(CHCl$_3$)/cm^{-1} 3500–3100 (br, OH and HN), 1658 (C=O), 1438 (P–Ph), 1160 (P=O); δ_H(500 MHz; CDCl$_3$) 9.65* (1H, d, *J* 6.0, NH), 8.02–7.92 (4H, m, Ph), 7.67–6.83 (16H, m, Ph), 6.28* (1H, br s, OH), 5.16 (1H, dd, *J* 14.5 and 6.0, CHN), 3.29 (1H, dd, *J* 10.0 and 1.5, PCH), 2.00–0.78 (10H, m, 5 × CH$_2$); δ_C(125 MHz; CDCl$_3$) 165.9$^-$ (C=O), 142.2$^-$ (d, *J* 14.5, *ipso*-Ph), 134.9$^-$ (d, *J* 93.0, *ipso*-Ph$_2$PO), 134.3$^-$ (*ipso*-Ph), 132.3$^+$ (*para*-Ph$_2$PO), 132.0$^+$ (*para*-Ph$_2$PO), 131.4$^+$ (Ph), 130.7$^-$ (d, *J* 98.5, *ipso*-Ph$_2$PO), 130.6$^+$ (d, *J* 9.5, *ortho*-Ph$_2$PO), 129.9$^+$ (d, *J* 8.5, *ortho*-Ph$_2$PO), 129.1$^+$ (d, *J* 11.5, *meta*-Ph$_2$PO), 129.0$^+$ (d, *J* 12.0, *meta*-Ph$_2$PO), 128.6$^+$ (Ph), 128.3$^+$ (Ph), 127.2$^+$ (Ph), 126.4$^+$ (Ph), 125.3$^+$ (Ph), 78.9$^-$ (d, *J* 3.0, COH), 53.8$^+$ (CHN), 49.2$^+$ (d, *J* 62.5, PCH), 42.1$^-$, 40.7$^-$, 25.9$^-$, 21.5$^-$ and 21.4$^-$ (CH$_2$).

1-Benzylamido-4,4-dimethyl-2-diphenylphosphinoyl-3-hydroxy-1-phenylpentane 16. 1-Benzylamido-2-diphenylphosphinoyl-1-phenylethane **10** (300 mg, 0.71 mmol), *n*-butyllithium (2.4 M in hexane, 620 µl, 1.5 mmol), pivalaldehyde (91 mg, 120 µl, 1.05 mmol) and lithium bromide (62 mg, 0.71 mmol) gave a crude product that was chromatographed (SiO$_2$, dichloromethane–EtOAc, 2 : 1 to 1 : 1) to give one diastereoisomer of the *hydroxyphosphine oxide* **16** (52 mg, 14%) as plates, mp 221–223 °C (from dichloromethane–hexane); R_f(EtOAc) 0.49; ν_{max}(solid state)/cm^{-1} 3350–3100 (br, OH and NH), 1724 (C=O), 1436 (P–Ph) and 1158 (P=O); δ_H(500 MHz; CDCl$_3$) 8.99* (1H, d, *J* 7.0, NH), 7.99–7.93 (2H, m, Ph$_2$PO), 7.91 (2H, br d, *J* 7.0, Ph), 7.85–7.80 (2H, m, Ph$_2$PO), 7.58–7.40 (9H, m, Ph and Ph$_2$PO), 7.29–7.19 (4H, m, Ph), 7.14 (1H, br t, *J* 7.0, *para*-Ph), 5.72 (1H, ddd, *J* 16.5, 7.0 and 1.0, CHN), 4.23–4.16 (2H, m, C*H*OH and OH), 3.27 (1H, br d, *J* 12.0, PCH) and 0.54 (9H, s, CMe$_3$); δ_C(125 MHz; CDCl$_3$) 165.9$^-$ (C=O), 141.3$^-$ (d, *J* 13.0, *ipso*-PhCHN), 134.5$^-$ (Ph), 132.4$^+$ (*para*-Ph$_2$PO), 132.1$^+$ (*para*-Ph$_2$PO), 131.8$^-$ (d, *J* 94.5, *ipso*-Ph$_2$PO), 131.2$^+$ (d, *J* 6.5, *ortho*-Ph$_2$PO), 131.1$^+$ (Ph), 131.0$^+$ (d, *J* 8.5, *ortho*-Ph$_2$PO), 131.5$^-$ (d, *J* 96.0, *ipso*-Ph$_2$PO), 129.0$^+$ (d, *J* 12.0, *meta*-Ph$_2$PO), 128.9$^+$ (d, *J* 11.5, *meta*-Ph$_2$PO), 128.5$^+$ (Ph), 128.2$^+$ (Ph), 127.2$^+$ (Ph), 126.9$^+$ (Ph), 126.8$^+$ (Ph), 51.9$^+$ (CHN), 44.1$^+$ (d, *J* 65.5, PCH), 35.8$^-$ (d, *J* 10.0, *C*Me$_3$) and 26.5$^+$ (C*Me*$_3$); *m*/*z* (ESI) 534 (100%, MNa$^+$) (Found: MNa$^+$, 534.2183. $C_{32}H_{34}NNaO_3P$ requires *M*, 534.2174).

*1-Benzylamido-4,4-dimethyl-2-diphenylphosphinoyl-3-hydroxy-1-phenylpentane **16**.* Also isolated was a mixture of two more diastereoisomers of the *hydroxyphosphine oxide* **16** (157 mg, 44%) as a 3 : 2 mixture of diastereoisomers as a white amorphous solid.

R_f(EtOAc) 0.67; ν_{max}(solid state)/cm^{-1} 3300–3100 (br, OH and NH), 1660 (C=O), 1439 (P–Ph) and 1180 (P=O); δ_H(400 MHz; CDCl$_3$) 9.41 (1H$_{major}$, d, *J* 7.0, NH), 8.90 (1H$_{minor}$, d, *J* 6.5, NH), 8.00–6.95 (20H$_{major}$ and 20H$_{minor}$, m, Ph$_2$PO and 2 × Ph), 6.19 (1H$_{major}$, dd, *J* 28.0 and 6.5, CHN), 5.22 (1H$_{minor}$, td, *J* 9.0 and 2.0, CHN), 3.82 (1H$_{minor}$, dd, *J* 23.5 and 11.0, C*H*OH), 3.75 (1H$_{major}$, dd, *J* 14.5 and 4.5, C*H*OH), 3.33 (1H$_{minor}$, br d, *J* 13.5, PCH), 3.28 (1H$_{major}$, br d, *J* 5.5, PCH),

3.13 ($1H_{minor}$, dd, *J* 10.5 and 2.0, OH), 0.98 ($9H_{major}$, s, CMe_3) and 0.59 ($9H_{minor}$, s, CMe_3). No OH_{major} peak observed; δ_C(100 MHz; $CDCl_3$) 166.3^-_{minor} (C=O), 165.6^-_{major} (C=O), 142.2^-_{major} (d, *J* 1.0, *ipso*-PhCHN), 140.3^-_{minor} (d, *J* 12.5, *ipso*-PhCHN), 135–126 (m, Ph_2PO and 2 × Ph), 81.3^+_{major} (d, *J* 4.5, CHOH), 76.1^+_{minor} (d, *J* 1.0, CHOH), 55.6^+_{minor} (CHN), 51.9^+_{major} (d, *J* 5.0, CHN), 44.6^+_{major} (d, *J* 64.5, PCH), 41.7^+_{minor} (d, *J* 62.0, PCH), 37.1^-_{minor} (d, *J* 11.5, CMe_3), 35.9^-_{major} (d, *J* 1.0, CMe_3), 27.0^+_{major} (CMe_3) and 26.7^+_{minor} (CMe_3); *m*/*z* (ESI) 534 (100%, MNa^+) (Found: MNa^+, 534.2161. $C_{32}H_{34}NNaO_3P$ requires *M*, 534.2174).

Horner–Wittig addition of 2-(*tert*-butyloxycarbonylamino)-1-diphenylphosphinoyl-2-phenylethane 11 to cyclohexanone

2-(*tert*-Butyloxycarbonylamino)-1-diphenylphosphinoyl-2-phenylethane **11** (300 mg, 0.71 mmol), *n*-butyllithium (2.4 M in hexane, 630 µl, 1.49 mmol), cyclohexanone (105 mg, 110 µl, 1.06 mmol) and lithium bromide (62 mg, 0.71 mmol) gave a crude product that was chromatographed (SiO_2, EtOAc–dichloromethane, 1 : 1) to give a mixture (2.6 : 1) of the *hydroxyphosphine oxides* **17** and **18** (112 mg, 30%) as a white amorphous solid that we were unable to separate. R_f(EtOAc) 0.68; ν_{max}(solid state)/cm^{-1} 3500–3100 (br, OH and NH), 1666 (C=O), 1438 (P–Ph) and 1159 (P=O); *m*/*z* (ESI) 542 (100%, MNa^+).

(1*SR*,2*RS*)-2-(*tert*-Butyloxycarbonylamino)-1-diphenylphosphinoyl-1-(1′-hydroxycyclohexyl)-2-phenylethane 17. δ_H(500 MHz; $CDCl_3$) 7.64–7.57 (4H, m, Ph_2PO), 7.35–6.68 (11H, m, Ph_2PO and Ph), 5.58 (1H, dd, *J* 29.0 and 8.0, CHN), 3.03 (1H, br t, *J* 10.5, PCH), 1.80–0.97 (10H, m, 5 × CH_2), 1.31 (9H, s, CMe_3). The OH and NH signals were not observed; δ_C(125 MHz; $CDCl_3$) 155.6^- (C=O), 141.3^- (*ipso*-Ph), 135.7^- (d, *J* 95.0, *ipso*-Ph_2PO), 134.1^- (d, *J* 94.5, *ipso*-Ph_2PO), 132–125 (m, Ph_2PO and Ph), 79.2^- (COH), 74.9^- ($OCMe_3$), 58.8^+ (CHN), 53.4^- (d, *J* 86.0, PCH), 43.7^- (CH_2), 36.4^- (CH_2), 29.5^- (CH_2), 28.3^+ (CMe_3), 25.0^- (CH_2) and 21.8^- (CH_2).

(1*SR*,2*SR*)-2-(*tert*-Butyloxycarbonylamino)-1-diphenylphosphinoyl-1-(1′-hydroxycyclohexyl)-2-phenylethane 18. δ_H(500 MHz; $CDCl_3$) 7.88–7.80 (2H, m, Ph_2PO), 7.35–6.68 (13H, m, Ph_2PO and Ph), 4.60 (dd, *J* 14.5 and 6.5, CHN), 3.03 (1H, br t, *J* 10.5, PCH), 1.80–0.97 (10H, m, 5 × CH_2), 1.31 (9H, s, CMe_3). The OH and NH signals were not observed; δ_C(125 MHz; $CDCl_3$) 154.2^- (C=O), 143.3^- (*ipso*-Ph), 135.0^- (d, *J* 92.5, *ipso*-Ph_2PO), 134.1^- (d, *J* 94.5, *ipso*-Ph_2PO), 132–125 (m, Ph_2PO), 78.7^- (COH), 71.8^- ($OCMe_3$), 55.2^- (d, *J* 64.0, PCH), 37.3^- (CH_2), 35.9^- (CH_2), 28.9^- (CH_2), 28.1^+ (CMe_3), 21.4^- (CH_2) and 21.3^- (CH_2). The peak for CHN was not observed.

1-(*tert*-Butyloxycarbonylamino)-4,4-dimethyl-2-diphenylphosphinoyl-3-hydroxy-1-phenylpentane 19

2-(*tert*-Butyloxycarbonylamino)-1-diphenylphosphinoyl-2-phenylethane **11** (300 mg, 0.71 mmol), *n*-butyllithium (2.4 M in hexane, 630 µl, 1.49 mmol), pivalaldehyde (92 mg, 117 µl, 1.07 mmol) and lithium bromide (62 mg, 0.71 mmol) gave a crude product that was chromatographed (SiO_2, EtOAc–dichloromethane, 1 : 1) to give 3 diastereoisomers (a : b : c, 5.4 : 2.7 : 1) of the *hydroxyphosphine oxide* **19** (99 mg, 27%) as a white amorphous solid that we were unable to separate; R_f(EtOAc) 0.67; ν_{max}(solid state)/cm^{-1} 3400–3000 (br, OH and NH), 1716 (C=O), 1438 (P–Ph) and 1150 (P=O); δ_H(500 MHz; $CDCl_3$) 7.97–6.81 ($15H_a$, $15H_b$ and $15H_c$, m, Ph_2PO and Ph), 6.48–6.40 ($1H_a$, $1H_b$ and $1H_c$, m, NH), 5.67 ($1H_b$, dd, *J* 27.0 and 8.5, CHN), 5.15 ($1H_c$, br d, *J* 25.0, CHN), 4.78 ($1H_a$, t, *J* 7.5, CHN), 3.65 ($1H_a$, $1H_b$ and $1H_c$, br d, *J* 14.5, C*H*OH), 3.23 ($1H_b$, d, *J* 13.5, PCH), 2.95 ($1H_a$, dd, *J* 10.5 and 0.5, PCH), 2.90–2.83 ($1H_c$, m, PCH), 1.42 ($9H_c$, s, $OCMe_3$), 1.35 ($9H_b$, s, $OCMe_3$), 1.30 ($9H_a$, s, $OCMe_3$), 0.92 ($9H_b$, s, $CHCMe_3$), 0.90 ($9H_c$, s, $CHCMe_3$), 0.51 ($9H_a$, s, $CHCMe_3$), OH signals not observed; δ_C(125 MHz; $CDCl_3$) 155.8^-_c (C=O), 155.6^-_b (C=O), 154.1^-_a (C=O), 141.8^-_c (*ipso*-Ph), 141.4^-_b (*ipso*-Ph), 141.2^-_a (*ipso*-Ph), 134–125 (m, Ph_2PO and Ph), 81.2^+_b (CHOH), 80.4^+_a (CHOH), 80.4^+_c (CHOH), $79.7^-_{b\,+\,c}$ ($OCMe_3$), 78.9^-_a ($OCMe_3$), 58.2^+_b (CHN), 57.5^+_c (CHN), 52.7^+_a (CHN), 45.3^+_c (d, *J* 66.0, PCH), 44.9^+_b (d, *J* 66.5, PCH), 41.7^+_a (d, *J* 62.5, PCH), 37.0^-_a (CMe_3), 37.0^-_b (CMe_3), 36.4^-_c (CMe_3), $28.4^+_{a\,+\,c}$ ($OCMe_3$), 28.2^+_b ($OCMe_3$), 26.9^+_b ($CHCMe_3$), 26.5^+_a ($CHCMe_3$) and 26.1^+_c ($CHCMe_3$); *m*/*z* (ESI) 530 (100%, MNa^+) (Found: MNa^+, 530.2415. $C_{30}H_{38}NNaO_4P$ requires *M*, 530.2436).

Crystal structure determination of amide 4b

Crystal data†. $C_{28}H_{26}NO_3P$, *M* = 455.47, monoclinic, *a* = 10.759(6), *b* = 10.339(6), *c* = 22.581(7) Å, *β* = 103.56(4), *U* = 2242(2) Å^3, *T* = 180(2) K, space group $P2_1$, *Z* = 4, adsorption coefficient 1.228 mm^{-1}, 6545 reflections measured, 6122 unique (R_{int} = 0.0310), which were used in all calculations. Final *R* indicies [$I > 2s(I)$], R_1 = 0.0619, wR_2 = 0.1308, Flack parameter[9] 0.01(4).

Crystal structure determination of amide 14

Crystal data†. $C_{33}H_{34}NO_3P$, *M* = 523.58, monoclinic, *a* = 15.1746(7), *b* = 10.3826(5), *c* = 17.3450(9) Å, *β* = 93.820(3), *U* = 2726.7(2) Å^3, *T* = 180(2) K, space group $P2_1/n$, *Z* = 4, adsorption coefficient 0.136 mm^{-1}, 13304 reflections measured, 4774 unique (R_{int} = 0.0631), which were used in all calculations. Final *R* indicies [$I > 2s(I)$], R_1 = 0.0454, wR_2 = 0.1083.

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† CCDC reference numbers 112685 and 179763. See http://www.rsc.org/suppdata/p1/b2/b201680j/ for crystallographic files in .cif or other electronic format.

References

1 J. Clayden and S. Warren, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 241.
2 J. Clayden, E. W. Collington, E. Egert, A. B. McElroy and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1994, 2801.
3 J. Clayden and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1994, 2811.
4 A. Nelson and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1963.
5 A. Nelson and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1983.
6 B. Bartels, C. G. Martin, A. Nelson, M. G. Russell and S. Warren, *Tetrahedron Lett.*, 1998, **39**, 1637.
7 B. Bartels, J. Clayden, C. G. Martin, A. Nelson, M. G. Russell and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1807.
8 S. G. Davies and O. Ichihara, *Tetrahedron: Asymmetry*, 1991, **2**, 183.
9 H. D. Flack, *Acta Crystallogr., Sect. A Found. Crystallogr.*, 1983, **39**, 876.
10 D. Cavalla, W. B. Cruse and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1883.
11 A. D. Buss, W. B. Cruse, O. Kennard and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1984, 243.
12 J. Barluenga, F. López and F. Palacios, *J. Chem. Res. (M)*, 1985, 2541.
13 W. B. Jang, W. S. Shin, K. Lee and D. Y. Oh, *Synth. Commun.*, 1997, **27**, 4101.
14 R. Albrecht, G. Kresze and B. Mlakar, *Chem. Ber.*, 1964, 483.