Diastereoselective Synthesis of α,β'-Disubstituted Aminomethyl(2-carboxyethyl)phosphinates as Phosphinyl Dipeptide Isosteres

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Supporting Information-Part I

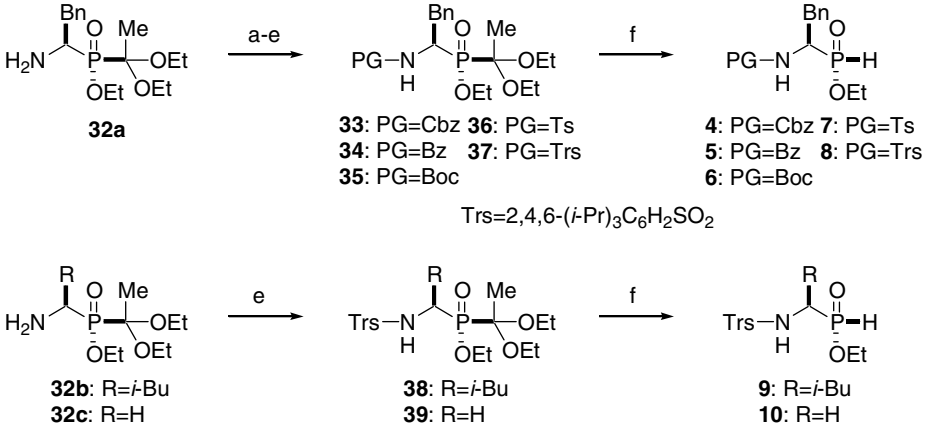
General Information

All melting points were taken on a Yanagimoto micromelting point apparatus and are uncorrected. IR spectra were recorded on a JASCO FTIR-620. Mass spectra were measured on Micromass Autospec by electrospray ionization. Elemental analysis was performed on an Elemental Vavio EL. NMR spectra were obtained on a Bruker DPX400 NMR Spectrometer (^{1}H NMR: 400 MHz, ^{13}C NMR: 100 MHz, and ^{31}P NMR: 162 MHz), Bruker AV-400 NMR Spectrometer (^{1}H NMR: 600 MHz and ^{13}C NMR: 150 MHz) or Varian Mercury-300 NMR Spectrometer (31P NMR: 121 MHz). The chemical shift data for each signal on ^{1}H NMR are given in units of δ relative to TMS (δ=0) for $CDCl_3$ solution. For ^{13}C NMR spectra, the chemical shifts in $CDCl_3$ are recorded relative to the $CDCl_3$ resonance (δ=77.0). The chemical shifts of ^{31}P are recorded relative to external 85% H_3PO_4 (δ=0) with broadband ^{1}H decoupling. Column chromatography was carried out using 63-210 μm silica gel 60N (Kanto Chemical Co., Inc.). Analytical TLC was carried out with Merck plates precoated with silica gel 60 F_{254} (0.25 mm thick). Preparative TLC was performed with Merck plates precoated with silica gel 60 F_{254} plates (2mm thick).

Preparation of α-amino-*H*-phosphinates 4-10

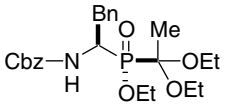
Compounds **4-10** were prepared from **32a-c** as shown in Scheme A. Preparation of **5** and **7** has already been reported.[1,2]

Scheme A



Reagents and conditions: (a) TsCl, Et_3N, DMAP, CH_2Cl_2, 80%; (b) BzCl, Et_3N, CH_2Cl_2, 54%; (c) CbzCl, Et_3N, CH_2Cl_2, 78%; (d) Boc_2O, $NaHCO_3$, dioxane, 65%; (e) TrsCl, Et_3N, DMAP, CH_2Cl_2, **37**: 40%, **38**: 75%, **39**: 46%; (f) TMSCl, EtOH, CH_2Cl_2, **4**: 36%, **5**: 67%, **6**: 67%, **7**: 83%, **8**: 45%, **9**: 30%, **10**: 86%.

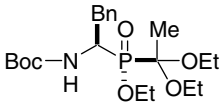
(1*R,*R*$_P$*)-Ethyl 1-{[1-(benzyloxy)carbonyl]amino}-2-phenylethyl (1,1-diethoxyethyl)phosphinate (33)**



To a solution of **32a** (50 mg, 0.15 mmol) in CH_2Cl_2 (0.60 mL) was added CbzCl (0.06 mL, 0.46 mmol), Et_3N (0.06 mL, 0.46 mmol) and stirred for 7 h at room temperature. The mixture was diluted with H_2O and extracted with Et_2O. The combined extracts were washed with brine and dried over $MgSO_4$. Removal of the solvent gave a residue which was purified by column chromatography (hexane/EtOAc=10:1 to 0:1) to give **33** (55 mg, 78 %). White crystals; mp 85-88 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40-7.04 (10H, m), 5.42 (1H, br.d, *J*=10.2 Hz), 5.01 (1H, d, *J*=12.5 Hz), 4.91 (1H, d, *J*=12.5 Hz), 4.47 (1H, ddd, *J*=4.3, 10.7, 21.4 Hz), 4.22 (1H, dq, *J*=7.0, 14.0 Hz), 3.89-3.55 (4H, m), 3.24 (1H, ddd, *J*=4.5, 4.5, 14.3 Hz), 2.91 (1H, ddd, *J*=9.0, 11.0, 15.0 Hz), 1.56 (3H, d, *J*=11.6 Hz), 1.30 (3H, t, *J*=7.0 Hz), 1.21 (3H, t, *J*=7.1 Hz), 1.14 (3H,

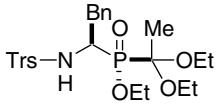
t, *J*=7.1 Hz), 0.88 (3H, t, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.6 (d, J_{CP}=6.2 Hz), 137.2-126.5 (aromatic), 102.3 (d, J_{CP}=138.3 Hz), 62.2 (d, J_{CP}=7.5 Hz), 58.6 (d, J_{CP}=4.9 Hz), 58.0 (d, J_{CP}=7.0 Hz), 49.3 (d, J_{CP}=94.1 Hz), 35.4 (d, J_{CP}=2.3 Hz), 31.6, 22.6, 16.6 (d, J_{CP}=5.2 Hz), 15.4, 15.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 33.15; IR (KBr) 3222, 1708, 1032 cm^{-1}; MS *m/z* 486 (MNa^+); HRMS calcd for $C_{24}H_{34}NO_6NaP$: 486.2021 (MNa^+). Found: 486.1989.

(1*R,*R*$_P$*)-Ethyl 1-[(*tert*-butoxycarbonyl)amino]-2-phenylethyl (1,1-diethoxyethyl)phosphinate (35)**



To a solution of **32a** (1.1 g, 3.36 mmol) in dioxane/H_2O 2:1 (10.2 mL) was added 1 M $NaHCO_3$ solution (3.6 mL, 3.6 mmol), Boc_2O (0.85 mL, 3.74 mmol) at 0 ˚C and stirred for 2 h at room temperature. To the mixture was added saturated citric acid solution and extracted with EtOAc. The combined extracts were washed with brine and dried over K_2CO_3. Removal of the solvent gave a residue which was purified by column chromatography (hexane/EtOAc=10:1 to 1:1) to give **35** (940 mg, 65 %). White crystals; mp 91-93 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.28-7.16 (5H, m), 5.04-5.01 (1H, br.d, *J*=10.2 Hz), 4.40 (1H, ddd, *J*=4.4, 16.3, 21.8 Hz), 4.23 (2H, dq, *J*=7.0, 7.0 Hz), 3.90-3.55 (4H, m), 3.21 (1H, ddd, *J*=4.0, 4.0, 14.0 Hz), 2.86 (1H, ddd, *J*=5.1, 11.0, 7.3 Hz), 1.56 (3H, d, *J*=11.6 Hz), 1.31 (3H, t, *J*=7.1 Hz), 1.26 (9H, s), 1.222 (3H, t, *J*=7.0 Hz), 1.218 (3H, t, *J*=7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 174.7 (d, J_{CP}=6.9 Hz), 137.3-126.3 (aromatic), 102.2 (d, J_{CP}=137.9 Hz), 79.3, 62.1 (d, J_{CP}=7.3 Hz), 58.4 (d, J_{CP}=5.0 Hz), 57.9 (d, J_{CP}=6.8 Hz), 48.4 (d, J_{CP}=94.8 Hz), 35.6, 28.1, 19.9 (d, J_{CP}=12.7 Hz), 16.5 (d, J_{CP}=5.3 Hz), 15.4, 15.2; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 42.73; IR (KBr) 3277, 1698, 1049 cm^{-1}; MS *m/z* 430 (MH^+); HRMS calcd for $C_{21}H_{37}NO_6P$: 430.2359 (MH^+). Found: 430.2355. Anal. Calcd for $C_{21}H_{36}NO_6P$: C, 58.73; H, 8.45; N, 3.26. Found: C, 58.74; H, 8.31; N, 3.19.

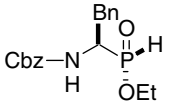
(1*R,*R*$_P$*)-Ethyl 1,1-diethoxyethyl(2-phenyl-1-{[(2,4,6-triisopropylphenyl) sulfonyl]amino}ethyl)phosphinate (37)**



To a solution of **32a** (3.1 g, 12.8 mmol), TrsCl (10.2 g, 19.3mmol) and DMAP (1.6 g, 7.7 mmol) in CH_2Cl_2 (40 mL) was added Et_3N (7.8 mL, 32.1 mmol) and stirred for 25 h at room temperature. To the mixture was added H_2O and extracted with Et_2O. The combined extracts

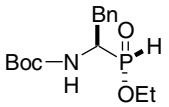
were washed with brine and dried over $MgSO_4$. Removal of the solvent gave a residue which was purified by column chromatography (hexane/EtOAc=5:1 to 2:1) to give **37** (3.0 g, 40 %). White crystals; mp 118-120 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.16-7.00 (7H, m), 6.01-5.97 (1H, m), 4.30 (1H, ddd, *J*=7.0, 7.0, 20.6 Hz), 4.13-3.61 (8H, m), 3.19 (1H, ddd, *J*=7.9, 11.6, 13.9 Hz), 2.92-2.82 (2H, m), 1.54 (3H, d, *J*=11.8 Hz), 1.29-1.20 (21H, m), 1.17 (3H, t, *J*=7.1 Hz), 1.11 (3H, t, *J*=7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.3-123.6 (aromatic), 102.8 (d, J_{CP}=141.4 Hz), 62.1 (d, J_{CP}=7.3 Hz), 58.9 (d, J_{CP}=4.2 Hz), 58.1 (d, J_{CP}=7.6 Hz), 52.5 (d, J_{CP}=85.5 Hz), 37.3, 34.1, 29.8, 24.9, 24.6, 23.6, 23.5, 16.1 (d, J_{CP}=5.6 Hz), 15.3, 15.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 40.73; IR (KBr) 3089, 1328, 1163, 1034 cm^{-1}; MS *m/z* 596 (MH^+); HRMS calcd for $C_{31}H_{51}NO_6PS$: 596.3175 (MH^+). Found: 596.3154. Anal. Calcd for $C_{31}H_{50}NO_6PS$: C, 62.5; H, 8.46; N, 2.35. Found: C, 62.36; H, 8.53; N, 2.10.

(1*R,*S*$_P$*)-Ethyl 1-{[1-(benzyloxy)carbonyl]amino}-2-phenylethylphosphinate (4)**



To a solution of **33** (500 mg, 1.08 mmol) in EtOH (0.23 mL) and CH_2Cl_2 (2.1 mL) was added TMSCl (0.21 mL, 1.62 mmol) at 0 ˚C and stirred for 2 h at room temperature. Concentration of the mixture gave a residue which was purified by column chromatography (hexane/EtOAc=10:1 to 1:1) to give **4** (134 mg, 36 %). A colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35-7.04 (10H, m), 7.10 (1H, *J*=556.3 Hz), 5.22 (1H, br.d, *J*=6.4 Hz), 5.03 (2H, s), 4.31-4.04 (3H, m), 3.25-2.88 (2H, m), 1.32 (3H, t, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 156.0 (d, J_{CP}=2.0 Hz), 136.0-127.0 (aromatic), 67.2, 63.1 (d, J_{CP}=6.6 Hz), 55.8 (d, J_{CP}=109.14 Hz), 33.2, 16.2 (d, J_{CP}=5.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 41.64; IR (neat) 3032, 1715, 1043 cm^{-1}; MS *m/z* 370 (MNa^+); HRMS calcd for $C_{18}H_{22}NO_4NaP$: 370.1184 (MH^+). Found: 370.1184.

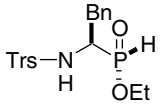
(1*R,*S*$_P$*)-Ethyl 1-[(*tert*-butoxycarbonyl)amino]-2-phenylethylphosphinate (6)**



This compound was prepared from **35** (500 mg, 1.16 mmol) in an analogous manner to that for **4**. Purification of the residue by column chromatography (hexane/EtOAc=10:1 to 1:1.5) gave **6** (243 mg, 67 %). A colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35-7.21 (5H, m), 5.06 (1H, d, *J*=554.8 Hz), 4.80 (1H, br.d, *J*=9.0 Hz), 4.29-4.07 (3H, m), 3.17 (1H, ddd, *J*=5.4, 8.4,

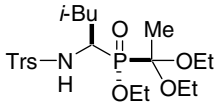
13.9 Hz), 3.00-2.91 (1H, m), 1.34 (9H, s), 1.34-1.26 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.2, 136.1-126.9 (aromatic), 80.4, 63.0 (d, J_{CP}=7.3 Hz), 50.1 (d, J_{CP}=108.5 Hz), 33.3, 28.1, 16.2 (d, J_{CP}=5.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 41.71; IR (neat) 3257, 1709, 1049 cm^{-1}; MS *m/z* 336 (MNa^+); HRMS calcd for $C_{15}H_{24}NO_4NaP$: 336.1341 (MNa^+). Found: 336.1309.

(1*R,S_P*)-Ethyl 2-phenyl-1-{[(2,4,6-triisopropylphenyl)sulfonyl]amino}ethyl phosphinate (8)**



This compound was prepared from **37** (723 mg, 1.21 mmol) in an analogous manner to that for **4**. Purification of the residue by column chromatography (hexane/EtOAc=10:1 to 1.5:1) gave **8** (240 mg, 45 %). White crystals; mp 150-155 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.21-7.04 (7H, m), 7.03 (1H, d, *J*=567.4 Hz), 6.21-6.18 (1H, m), 4.08 (2H, dq, *J*=6.7 Hz), 3.98-3.85 (3H, m), 3.20 (1H, ddd, *J*=7.2, 13.5, 13.5 Hz), 3.00 (1H, ddd, *J*=7.1, 14.5, 14.7 Hz), 2.94-2.84 (1H, m), 1.26-1.21 (18H, m), 1.16 (3H, t, *J*=7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.0-123.7 (aromatic), 62.7 (d, J_{CP}=7.4 Hz), 52.5 (d, J_{CP}=108.5 Hz), 34.1, 29.9, 29.8, 24.9, 24.8. 23.6, 16.0 (d, J_{CP}=5.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 34.85; IR (KBr) 3116, 1330, 1166, 1038 cm^{-1}; MS *m/z* 480 (MH^+); HRMS calcd for $C_{25}H_{39}NO_4PS$: 480.2337 (MH^+). Found: 480.2337. Anal. Calcd for $C_{25}H_{38}NO_4PS$: C, 62.61; H, 7.99; N, 2.92. Found: C, 62.51; H, 7.89; N, 2.82.

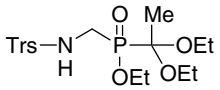
(1*R,R_P*)-Ethyl 1,1-diethoxyethyl(3-methyl-1-{[(2,4,6-triisopropylphenyl) sulfonyl]amino}butyl)phosphinate (38)**



This compound was prepared from **32b** (483 mg, 1.63 mmol) in an analogous manner to that for **37**. Purification of the residue by column chromatography (hexane/EtOAc=5:1 to 2:1) gave **38** (360 mg, 75 %). White crystals; mp 117-118 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.09 (2H, s), 5.70-5.67 (1H, m), 4.25-4.03 (4H, m), 3.99-3.88 (1H, m), 3.79-3.65 (4H, m), 2.94-2.84 (1H, m), 1.74-1.58 (2H, m), 1.59 (3H, d, *J*=11.5 Hz), 1.46-1.36 (1H, m), 1.29-1.17 (27H, m), 0.69 (3H, d, *J*=6.5 Hz), 0.68 (3H, d, *J*=6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.4−123.4 (aromatic) , 103.2 (d, J_{CP}=142.2 Hz), 62.0 (d, J_{CP}=7.2 Hz), 59.0 (d, J_{CP}=4.6 Hz), 58.2 (d, J_{CP}=7.3 Hz), 49.7 (d, J_{CP}=86.5 Hz), 40.6 (d, J_{CP}=2.4 Hz), 34.2, 29.9, 24.9, 24.7, 24.5 (d, J_{CP}=8.0 Hz), 23.7, 22.7,

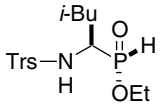
21.7, 16.5 (d, J_{CP}=5.3 Hz), 15.4, 15.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 41.60; IR (KBr) 3096, 1017 cm^{-1}; MS *m/z* 584 (MNa^+); HRMS calcd for $C_{28}H_{52}NO_6NaPS$: 584.3151 (MNa^+). Found: 584.3145.

Ethyl 1,1-diethoxyethyl({[(2,4,6-triisopropylphenyl)sulfonyl]amino}methyl) phosphinate (39)



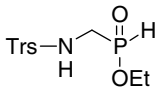
This compound was prepared from **32c** (539 mg, 2.25 mmol) in an analogous manner to that for **37**. Purification of the residue by column chromatography (hexane/EtOAc=5:1 to 2:1) gave **39** (520 mg, 46 %). A colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (2H, s), 5.12-5.08 (1H, m), 4.24-4.06 (4H, m), 3.73-3.58 (4H, m), 3.35 (2H, ddd, *J*=5.8, 9.4 Hz), 2.95-2.85 (1H, m), 1.28 (3H, d, *J*=11.8 Hz), 1.31-1.24 (3H, m), 1.28 (12H, d, *J*=6.7 Hz), 1.25 (6H, t, *J*=6.9 Hz), 1.17 (3H, t, *J*=7.3 Hz), 1.16 (3H, t, *J*=7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.5-123.9 (aromatic), 100.9 (d, J_{CP}=137.3 Hz), 61.9 (d, J_{CP}=7.1 Hz), 58.3 (d, J_{CP}=4.6 Hz), 57.6 (d, J_{CP}=7.4 Hz), 39.3 (d, J_{CP}=92.7 Hz), 34.1, 31.5, 29.6, 24.8, 24.7, 23.55, 23.52, 16.2 (d, J_{CP}=5.4 Hz), 15.3, 15.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 40.68; IR (neat) 2961, 1600, 1037 cm^{-1}.

(1*R,*S*$_P$*)-Ethyl 3-methyl-1-{[(2,4,6-triisopropylphenyl)sulfonyl]amino}butyl phosphinate (9)**



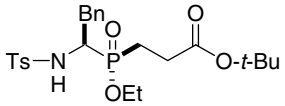
This compound was prepared from **38** (310 mg, 1.05 mmol) in an analogous manner to that for **4**. Purification of the residue by column chromatography (hexane/EtOAc=5:1 to 1:2) gave **9** (139 mg, 30 %). White crystals; mp 167-169 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (2H, s), 6.97 (1H, d, *J*=560.7 Hz), 5.62-5.59 (1H, m), 4.18-4.00 (4H, m), 3.65-3.57 (1H, m), 2.98-2.82 (1H, m), 1.53-1.23 (24H, m), 0.81 (3H, d, *J*=6.0 Hz), 0.68 (3H, t, *J*=6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.0-123.4 (aromatic), 63.0 (d, J_{CP}=7.4 Hz), 50.1 (d, J_{CP}=109.3 Hz), 36.4, 34.2, 29.8, 25.0, 24.8, 23.8 (d, J_{CP}=9.6 Hz), 23.59, 23.55, 22.8, 21.1, 16.7 (d, J_{CP}=5.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 35.69; IR (KBr) 3127, 1329, 1162, 1060 cm^{-1}; MS *m/z* 446 (MH^+); HRMS calcd for $C_{22}H_{41}NO_4PS$: 446.2494 (MH^+). Found: 446.2506. Anal. Calcd for $C_{22}H_{40}NO_4PS$: C, 59.30; H, 9.05; N, 3.14. Found: C, 59.03; H, 8.85; N, 2.96.

Ethyl {[(2,4,6-triisopropylphenyl)sulfonyl]amino}methylphosphinate (10)



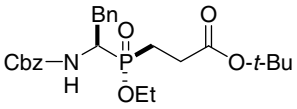
This compound was prepared from **39** (463 mg, 0.92 mmol) in an analogous manner to that for **4**. Purification of the residue by column chromatography (hexane/EtOAc=5:1 to 1:2) gave **10** (308 mg, 86 %). White crystals; mp 108-114 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (2H, s), 7.16 (1H, d, *J*=569.2 Hz), 5.44 (1H, br.s), 4.25-4.06 (4H, m), 3.40 (2H, m), 2.96-2.85 (1H, m), 1.35 (3H, t, *J*=7.1 Hz), 1.30-1.19 (18H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3-123.8 (aromatic), 63.5 (d, J_{CP}=6.6 Hz), 40.4 (d, J_{CP}=104.7 Hz), 34.1, 29.1, 24.8, 23.5, 16.7 (d, J_{CP}=5.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 30.75; IR (KBr) 3131, 1325, 1157, 1040 cm^{-1}; MS *m/z* 390 (MH^+); HRMS calcd for $C_{18}H_{33}NO_4PS$: 390.1868 (MH^+). Found: 390.1874.

(1*R,*R*$_P$*)-*tert*-Butyl 3-[ethoxy(1-{[(4-methylphenyl)sulfonyl]amino}-2-phenylethyl)phosphoryl]propanoate (14)**



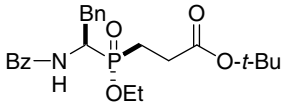
To a stirred solution of **7** (673 mg, 1.83 mmol) and *t*-butyl acrylate (0.3 mL, 2.0 mmol) in THF (3.6 mL) was added a solution of *t*-BuOMgBr in THF (1.8 mL) at -20 ˚C, prepared from *t*-BuOH (136 mg, 1.83 mmol) and 0.98 M hexane solution of MeMgBr (1.87 mL, 1.83 mmol) *in situ*. After stirring for 17 h at 0 ˚C, the mixture was concentrated to give a residue, which was purified by column chromatography (hexane/EtOAc=10:1 to 1:1) to give **14** (800 mg, 83%). White crystals; mp 120-124 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50-7.02 (9H, m), 6.07-5.91 (1H, br.m), 4.09-3.85 (3H, m), 3.09 (1H, ddd, *J*=6.1, 10.0, 14.4 Hz), 2.78 (1H, ddd, *J*=8.2, 12.4, 14.1 Hz), 2.61-2.45 (2H, m), 2.37 (3H, s), 2.11-2.03 (2H, m), 1.44 (9H, s), 1.21 (3H, t, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.1 (d, J_{CP}=15.9 Hz), 143.2-128.7 (aromatic), 81.0, 61.9 (d, J_{CP}=6.9 Hz), 53.7 (d, J_{CP}=99.7 Hz), 35.1 (d, J_{CP}=2.7 Hz), 28.0, 27.6 (d, J_{CP}=2.6 Hz), 21.8 (d, J_{CP}=90.4 Hz), 21.4, 16,5 (d, J_{CP}=5.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 53.88; IR (KBr) 3137, 1333, 1160, 1033 cm^{-1}; MS *m/z* 469 (MH^+); HRMS calcd for $C_{24}H_{35}NO_6PS$: 496.1923 (MH^+). Found: 496.1926. Anal. Calcd for $C_{24}H_{34}NO_6PS$: C, 58.17; H, 6,92; N, 2.83. Found: C, 58.22; H, 7.13; N, 2.76.

(1*R,*R*$_P$*)-*tert*-Butyl 3-[(1-{[(benzyloxy)carbonyl]amino}-2-phenylethyl)(ethoxy) phosphoryl]propanoate (11)**



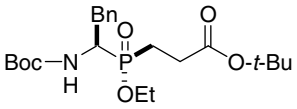
This compound was prepared from **4** (134 mg, 0.39 mmol) in an analogous manner to that for **14**. Purification of the residue by column chromatography (hexane/EtOAc=10:1 to 1:1.5) gave **11** (124 mg, 93 %). White crystals; mp 138-139 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.32-7.06 (10H, m), 5.38 (1H, br.d, *J*=10.2 Hz), 5.00 (1H, d, *J*=12.4 Hz), 4.94 (1H, d, *J*=12.4 Hz), 4.32 (1H, ddd, *J*=4.0, 10.6, 21.4 Hz), 4.11 (2H, dq, *J*=7.1, 7.1 Hz), 3.22 (1H, ddd, *J*=4.4, 4.4, 14.4 Hz), 2.85 (1H, ddd, *J*=8.8, 11.4, 14.1 Hz), 2.61-2.45 (2H, m), 2.07 (2H, dt, *J*=7.9, 13.2 Hz), 1.44 (9H, s), 1.29 (3H, t, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.5 (d, J_{CP}=14.29 Hz), 155.9, 136.61-126.8 (aromatic), 81.1, 66.9, 61.4 (d, J_{CP}=6.7 Hz), 50.31 (d, J_{CP}=105.5 Hz), 34.3, 28.0, 27.7 (d, J_{CP}=2.9 Hz), 21.2 (d, J_{CP}=90.5 Hz), 16.6 (d, J_{CP}=5.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 52.91; IR (KBr) 3204, 1721, 1044 cm^{-1}; MS *m/z* 476 (MH^+); HRMS calcd for $C_{25}H_{35}NO_6P$: 476.2202 (MH^+). Found: 476.2216.

(1*R,*R*$_P$*)-*tert*-Butyl 3-[[1-(benzoylamino)-2-phenylethyl](ethoxy)phosphoryl] propanoate (12)**



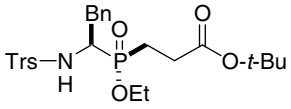
This compound was prepared from **5** (0.28mg, 0.76 mmol) in an analogous manner to that for **14**. Purification of the residue by column chromatography (hexane/EtOAc=10:1 to 1:1) gave **12** (256 mg, 78%). White crystals; mp 159-163 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.72-7.14 (10H, m), 4.93 (1H, m), 4.14 (2H, dq, *J*=7.1, 7.1 Hz), 3.30 (1H, ddd, *J*=4.8, 4.8, 14.4 Hz), 3.11 (1H, ddd, *J*=9.3, 11.1, 14.3Hz), 2.86-2.45 (2H, m), 2.17-2.16 (2H, m), 1.41 (9H, s), 1.33 (3H, t, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.6 (d, J_{CP}=14,3 Hz), 167.4 (d, J_{CP}=3.9 Hz), 136.4-126.7 (aromatic), 81.0, 61.4 (d, J_{CP}=6.9 Hz), 48.5 (d, J_{CP}=74.0 Hz), 33.7, 28.0, 27.8, 21.6 (d, J_{CP}=89.9 Hz), 16,6 (d, J_{CP}=5.3 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 53.77; IR (KBr) 3261, 1722, 1657, 1034 cm^{-1}; MS *m/z* 446 (MH^+); HRMS calcd for $C_{24}H_{33}NO_5P$: 446.2096 (MH^+). Found: 446.2068.

(1*R,*R*$_P$*)-*tert*-Butyl 3-[{1-[(*tert*-butoxycarbonyl)amino]-2-phenylethyl}(ethoxy) phosphoryl]propanoate (13)**



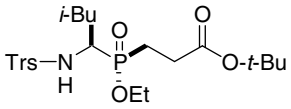
This compound was prepared from **6** (243 mg, 0.78 mmol) in an analogous manner to that for **14**. Purification of the residue by column chromatography (hexane/EtOAc=10:1 to 1:1) gave **13** (309 mg, 90%). White crystals; mp 118-120 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.30-7.29 (5H, m), 5.05 (1H, br.d, *J*=10.3 Hz), 4.29-4.27 (1H, m), 4.12 (2H, dq, *J*=6.8, 6.8 Hz), 3.21-3.16 (1H, m), 2.86-2.83 (1H, m), 2.58-2.52 (2H, m), 2.11-2.04 (2H, m), 1.44 (9H, s), 1.33-1.32 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.5 (d, J_{CP}=15.6 Hz), 155.2 (d, J_{CP}=2.6 Hz), 136.8-126.5 (aromatic), 80.9, 80.0, 61.2 (d, J_{CP}=6.6 Hz), 49.3 (d, J_{CP}=107.0 Hz), 34.1, 30.8, 28.0, 27.7, 21.3 (d, J_{CP}=90.2 Hz), 16.5 (d, J_{CP}=5.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 53.75; IR (KBr) 3271, 3215, 1732, 1708, 1032 cm^{-1}; MS *m/z* 442 (MH^+); HRMS calcd for $C_{22}H_{37}NO_6P$: 442.2359 (MH^+). Found: 442.2362. Anal. Calcd for $C_{22}H_{36}NO_6P$: C, 59.85; H, 8.22; N, 3.17. Found: C, 59.55; H, 8.27; N, 2.83.

(1*R,*R*$_P$*)-*tert*-Butyl 3-[ethoxy(2-phenyl-1-{[(2,4,6-triisopropylphenyl)sulfonyl] amino}ethyl)phosphoryl]propanoate (15)**



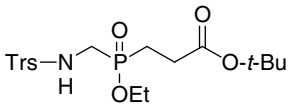
This compound was prepared from **8** (200 mg, 0.42 mmol) in an analogous manner to that for **14**. Purification of the residue by column chromatography (hexane/EtOAc=10:1 to 1:1) gave **15** (235 mg, 92 %). White crystals; mp 145-147 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14-7.04 (7H, m), 6.13 (1H, br.d, *J*=8.8 Hz), 4.08 (2H, dq, *J*=6.8, 13.4 Hz), 4.02-3.89 (2H, m), 3.81-3.71 (1H, m), 3.17 (1H, ddd, *J*=7.7, 13.6, 13.6 Hz), 2.94 (2H, m), 2.50 (2H, ddd, *J*=7.7, 7.7, 12.5 Hz), 2.13-1.97 (2H, m), 1.42 (9H, s), 1.28-1.23 (18H, m), 1.10 (3H, t, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4 (d, J_{CP}=14.1 Hz), 152.7-123.7 (aromatic), 80.9, 61.0 (d, J_{CP}=6.8 Hz), 52.6 (d, J_{CP}=103.5 Hz), 35.8 (d, J_{CP}=1.9 Hz), 34.1, 29.8, 27.9, 27.7 (d, J_{CP}=3.5 Hz), 24.9, 24.8, 23.54, 23.46, 21.5 (d, J_{CP}=92.1 Hz), 16.2 (d, J_{CP}=5.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 52.93; IR (KBr) 3136, 1729, 1363, 1195, 1037 cm^{-1}; MS *m/z* 630 (MNa^+); HRMS calcd for $C_{32}H_{50}NO_6NaPS$: 630.2994 (MNa^+). Found: 630.2983.; Anal. Calcd for $C_{32}H_{50}NO_6PS$: C, 63.24; H, 8.29; N, 2.30. Found: C, 63.10; H, 8.20; N, 2.00.

(1*R,*R*$_P$*)-*tert*-Butyl 3-[ethoxy(3-methyl-1-{[(2,4,6-triisopropylphenyl)sulfonyl] amino}butyl)phosphoryl]propanoate (16)**



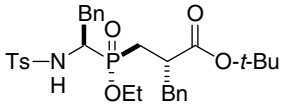
This compound was prepared from **9** (100 mg, 0.22 mmol) in an analogous manner to that for **14**. Purification of the residue by column chromatography (hexane/EtOAc=5:1 to 2:1) gave **16** (86 mg, 67 %). White crystals; mp 174-176 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (2H, s), 5.40 (1H, br.d, *J*=8.5 Hz), 4.16-3.98 (4H, m), 3.76-3.62 (1H, m), 1.61-1.23 (24H, m), 1.46 (9H, s), 0.69 (3H, d, *J*=6.6 Hz), 0.66 (3H, d, *J*=6.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8 (d, J_{CP}=7.4 Hz), 152.8-123.6 (aromatic), 81.1, 61.3 (d, J_{CP}=6.9 Hz), 50.1 (d, J_{CP}=104.7 Hz), 38.8 (d, J_{CP}=2.0 Hz), 34.2, 29.9, 28.0, 27.9 (d, J_{CP}=3.5 Hz), 24.9, 24.8, 24.5 (d, J_{CP}=8.9 Hz), 23.61, 23.59, 22.8, 21.5, 20.9 (d, J_{CP}=91.0 Hz), 16.5 (d, J_{CP}=5.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 53.69; IR (KBr) 3137, 1726, 1326, 1153, 1039 cm^{-1}; MS *m/z* 574 (MH^+); HRMS calcd for $C_{29}H_{53}NO_6PS$: 574.3331 (MH^+). Found: 574.3325.

***tert*-Butyl 3-[ethoxy({[(2,4,6-triisopropylphenyl)sulfonyl]amino}methyl) phosphoryl]propanoate (17)**

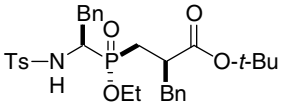


This compound was prepared from **10** (100 mg, 0.26 mmol) in an analogous manner to that for **14**. Purification of the residue by column chromatography (hexane/EtOAc=5:1 to 2:1) gave **17** (132 mg, 99 %). White crystals; mp 114-116 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (2H, s), 5.10-5.06 (1H, m), 4.16-3.96 (4H, m), 3.24 (2H, dd, *J*=6.3, 10.3 Hz), 2.96-2.85 (1H, m), 2.64-2.47 (2H, m), 2.18-1.98 (2H, m), 1.43 (9H, s), 1.32-1.25 (21H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3 (d, J_{CP}=104.7 Hz), 153.3-123.9 (aromatic), 81.5, 61.5 (d, J_{CP}=6.6 Hz), 39.7 (d, J_{CP}=98.7 Hz), 34.4, 29.7, 28.0, 27.5 (d, J_{CP}=2.8 Hz), 24.9, 23.5, 22.0 (d, J_{CP}=96.5 Hz), 16.7 (d, J_{CP}=5.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 49.41; IR (KBr) 3221, 1720, 1322, 1158, 1038 cm^{-1}; MS *m/z* 518 (MH^+); HRMS calcd for $C_{25}H_{45}NO_6PS$: 518.2705 (MH^+). Found: 518.2733. Anal. Calcd for $C_{25}H_{44}NO_6PS$: C, 58.00; H, 8.57; N, 2.71. Found: C, 57.90; H, 8.39; N, 2.50.

(1*R,*R*$_P$*,2*S**) and (1*R**,*R*$_P$*,2*R**)-*tert*-Butyl 2-benzyl-3-[ethoxy(1-{[(4-methylphenyl)sulfonyl]amino}-2-phenylethyl)phosphoryl]propanoate (21a and 21b)**



21a



21b

To a stirred solution of **14** (100 mg, 0.20 mmol) in THF (3.0 mL) was added 1.0 M THF solution of LHMDS (0.61 mL, 0.61 mmol) at -78 ˚C and stirred for 30 minutes at the same temperature. To the mixture was added benzyl bromide (0.08 mL, 0.61 mmol) and stirred for 2 h at the same temperature. The mixture was diluted with saturated NH_4Cl solution at 0 ˚C and extracted with Et_2O. The combined extracts were washed with brine and dried over $MgSO_4$. Removal of the solvent gave a residue which was purified by column chromatography (hexane/EtOAc=5:1 to 1:1) to give a 4:1 mixture of **21a** and **21b** (107 mg, 90%). Analytical samples of individual isomers were obtained upon re-purification by preparative TLC (hexane/EtOAc=1:1).

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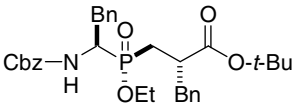
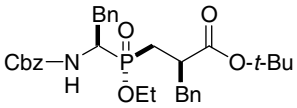
21a; white crystals; mp 155-158 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.54-7.03 (14H, m), 6.42 (1H, br.s), 4.07-4.01 (1H, m), 3.92-3.82 (2H, m), 3.13-3.01 (2H, m), 2.89-2.74 (3H, m), 2.33 (3H, s), 2.18-1.97 (2H, m), 1.31 (9H, s), 1.18 (3H, t, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.6 (d, J_{CP}=5.0 Hz), 142.9-126.5 (aromatic), 81.0, 61.6 (d, J_{CP}=6.9 Hz), 54.5 (d, J_{CP}=103.1 Hz), 42.0 (d, J_{CP}=4.3Hz), 40.1 (d, J_{CP}=12.0 Hz), 34.9, 28.4 (d, J_{CP}=90.0 Hz), 27.8, 21.4, 16.4 (d, J_{CP}=5.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 51.50; IR (KBr) 3139, 1725, 1329, 1031 cm^{-1}; MS *m/z* 586 (MH^+); HRMS calcd for $C_{31}H_{41}NO_6PS$: 586.2392 (MH^+). Found: 586.2404.

21b; white crystals; mp 110-115 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52-7.02 (14H, m), 6.18 (1H, br.d, *J*=8.8 Hz), 4.01-3.39 (3H, m), 3.12-3.02 (2H, m), 2.89 (1H, dd, *J*=6.3, 13.6 Hz), 2.84 (1H, dd, *J*=8.9, 13.6 Hz), 2.76 (1H, ddd, *J*=8.0, 12.4, 14.0 Hz), 2.37 (1H, ddd, *J*=10.0, 15.0, 15.0 Hz), 1.96 (1H, ddd, *J*=3.8, 13.1, 15.7 Hz), 1.28 (9H, s), 1.17 (3H, t, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.4 (d, J_{CP}=4.4 Hz), 142.3-126.5 (aromatic), 81.0, 61.4 (d, J_{CP}=6.8 Hz), 53.2 (d, J_{CP}=103.4 Hz), 41.6, 40.4 (d, J_{CP}=13.5 Hz), 34.9, 27.840, 27.839 (d, J_{CP}=90.2 Hz), 21.5, 16.4 (d, J_{CP}=5.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 52.52; IR (KBr) 3088, 1723, 1333, 1161, 1039 cm^{-1}; MS *m/z* 608 (MH^+); HRMS calcd for $C_{31}H_{40}NO_6NaPS$: 608.2212 (MNa^+). Found: 608.2177.

(1*R,*R*$_P$*,2*S**) and (1*R**,*R*$_P$*,2*R**)-*tert*-Butyl 2-benzyl-3-[(1-{[(benzyloxy) carbonyl]amino}-2-phenylethyl)(ethoxy)phosphoryl]propanoate (18a and 18b)**



18a



18b

These compounds were prepared from **11** (100 mg, 0.29 mmol) in an analogous manner to that for **21a**. Purification of the residue by column chromatography (hexane/EtOAc=5:1 to 1:1) gave a 1.1:1 mixture of **18a** and **18b** (104 mg, 64 %). Analytical samples of individual isomers were obtained upon re-purification by preparative TLC (hexane/EtOAc=1:1).

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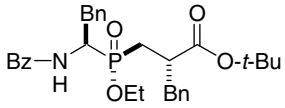
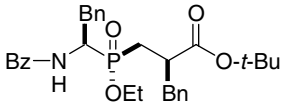
18a; a colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.30-7.12 (15H, m), 5.13 (1H, br.d, *J*=9.2 Hz), 4.97 (1H, d, *J*=12.4 Hz), 4.91 (1H, d, *J*=12.4 Hz), 4.33-4.25 (1H, m), 4.16-4.05 (2H, m), 3.21-3.19 (1H, m), 3.03-2.97 (1H, m), 2.89-2.78 (3H, m), 2.20-2.14 (1H, m), 1.83-1.78 (1H, m), 1.33 (9H, s), 1.25 (3H, t, *J*=6.5 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 173.7 (d, J_{CP}=3.6 Hz), 155.9 (d, J_{CP}=3.3 Hz), 137.9-126.6 (aromatic), 81.1, 66.9, 61.6 (d, J_{CP}=4.7 Hz), 51.4 (d, J_{CP}=105.4 Hz), 42.1, 40.1 (d, J_{CP}=11.0 Hz), 34.5, 29.2 (d, J_{CP}=85.9 Hz), 27.9, 16.6 (d, J_{CP}=4.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 50.92; IR (neat) 3223, 1723, 1035 cm^{-1}; MS *m/z* 566 (MH^+); HRMS calcd for $C_{32}H_{41}NO_6P$: 566.2672 (MH^+). Found: 566.2657.

18b; white crystals; mp 136-137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.32-7.14 (15H, m), 5.08 (1H, br.d, *J*=8.8 Hz), 5.00 (1H, d, *J*=12.4 Hz), 4.94 (1H, d, *J*=12.4 Hz), 4.37-4.36 (1H, m), 4.20-4.02 (2H, m), 3.20-3.17 (1H, m), 3.02-2.94 (1H, m), 2.91-2.70 (3H, m), 2.34-2.17 (1H, m), 1.84-1.73 (1H, m), 1.32 (9H, s), 1.26 (3H, t, *J*=6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.3 (d, J_{CP}=2.4 Hz), 155.8 (d, J_{CP}=3.2 Hz), 137.9-126.6 (aromatic), 81.1, 66.9, 61.4 (d, J_{CP}=4.1 Hz), 51.1 (d, J_{CP}=108.3 Hz), 41.6 (d, J_{CP}=3.4 Hz), 40.4 (d, J_{CP}=4.6 Hz), 34.2, 29.3 (d, J_{CP}=76.3 Hz), 27.9, 16.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ:52.23; IR (KBr) 3234, 1716, 1047 cm^{-1}; MS *m/z* 566 (MH^+); HRMS calcd for $C_{32}H_{41}NO_6P$: 566.2672 (MH^+). Found: 566.2664.

(1*R,*R*$_P$*,2*S**) and (1*R**,*R*$_P$*,2*R**)-*tert*-Butyl 3-[[1-(benzoylamino)-2-phenylethyl](ethoxy)phosphoryl]-2-benzylpropanoate (19a and 19b)**



19a



19b

These compounds were prepared from **12** (91 mg, 0.21 mmol) in an analogous manner to that for **21a**. Purification of the residue by column chromatography (hexane/EtOAc=5:1 to 1:1) gave a 3.4:1 mixtture of **19a** and **19b** (87 mg, 79 %). Analytical samples of individual isomers were obtained upon re-purification by preparative TLC (hexane/EtOAc=1:1).

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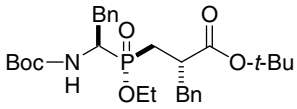
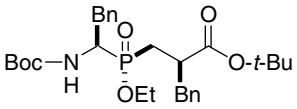
19a; white crystals; mp 135-140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.68-6.98 (15H, m), 4.89 (1H, ddd, *J*=4.5, 10.1, 20.3 Hz), 4.12 (2H, m), 3.25 (1H, ddd, *J*=5.1, 6.6, 14.8 Hz), 3.08-2.93 (2H, m), 2.80 (2H, ddd, *J*=7.4, 13.5, 27.3 Hz), 2.23 (1H, *J*=9.6, 11.9, 15.7 Hz), 1.91 (1H, ddd, *J*=4.0, 11.9, 15.8 Hz), 1.30 (3H, t, *J*=7.3 Hz), 1.28 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.5 (d, J_{CP}=4.9 Hz), 167.2 (d, J_{CP}=4.2 Hz), 137.8-126.5 (aromatic), 81.0, 61.6 (d, J_{CP}=7.0 Hz), 49.6 (d, J_{CP}=104.5 Hz), 42.0 (d, J_{CP}=4.5 Hz), 40.1 (d, J_{CP}=11.9 Hz), 34.0, 28.4 (d, J_{CP}=87.8 Hz), 27.8, 16.5 (d, J_{CP}=5.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 51.30; IR (KBr) 3283, 1724, 1657, 1045 cm^{-1}; MS *m/z* 536 (MH^+); HRMS calcd for $C_{31}H_{39}NO_5P$: 536.2566 (MH^+). Found: 536.2540.; Anal. Calcd for $C_{31}H_{38}NO_5P$: C, 69.52; H, 7.15; N, 2.62. Found: C, 69.27; H, 7.45; N, 2.43.

19b; white crystals; mp 158-160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.65-7.07 (15H, m), 7.01 (1H, br.d, *J*=10.0 Hz), 4.98 (1H, ddd, *J*=4.4, 10.0, 20.1 Hz), 4.18-3.99 (2H, m), 3.27 (1H, ddd, *J*=4.9, 4.9, 14.4 Hz), 3.21-2.76 (4H, m), 2.28 (1H, ddd, *J*=10.4, 15.1, 15.1 Hz), 1.82 (1H, *J*=3.1, 13.0, 15.8 Hz), 1.31 (9H, s), 1.28 (3H, t, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.5 (d, J_{CP}=3.3 Hz), 159.5, 132.7-122.4 (aromatic), 80.7, 62.7 (d, J_{CP}=6.3 Hz), 50.5 (d, J_{CP}=96.3 Hz), 44.4, 43.6 (d, J_{CP}=12.4 Hz), 37.5, 32.0, 31.6 (d, J_{CP}=80.9 Hz), 21.7 (d, J_{CP}=4.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 52.67; IR (KBr) 3270, 1723, 1655, 1028 cm^{-1}; MS *m/z* 558 (MNa^+); HRMS calcd for $C_{31}H_{38}NO_5NaP$: 558.2385 (MNa^+). Found: 558.2332.; Anal. Calcd for $C_{31}H_{38}NO_5P$: C, 69.52; H, 7.15; N, 2.62. Found: C, 69.62; H, 7.32; N, 2.49.

(1*R,*R*$_P$*,2*S**) and (1*R**,*R*$_P$*,2*R**)-*tert*-Butyl 2-benzyl-3-[{1-[(*tert*-butoxycarbonyl) amino]-2-phenylethyl}(ethoxy)phosphoryl]propanoate (20a and 20b)**



20a



20b

These compounds were prepared from **13** (150 mg, 0.35 mmol) in an analogous manner to that for **21a**. Purification of the residue by column chromatography (hexane/EtOAc=10:1 to 1:1) gave a 4.5:1 mixture of **20a** and **20b** (170 mg, 91 %). Analytical samples of individual isomers were obtained upon re-purification by preparative TLC (hexane/EtOAc=1:1).

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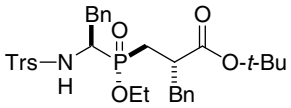
20a; white crystals; mp 118-123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.36-7.15 (10H, m), 4.84 (1H, br.d, *J*=10.4 Hz), 4.26-4.24 (1H, m), 4.14-4.07 (2H, m), 3.20-3.17 (1H, m), 3.05-3.04 (1H, m), 2.90-2.79 (3H, m), 2.23-2.16 (1H, m), 1.88-1.80 (1H, m), 1.33 (9H, s), 1.33 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.6 (d, J_{CP}=5.7 Hz), 155.2 (d, J_{CP}=1.8 Hz), 137.0-126.6 (aromatic), 81.0, 79.9, 61.4 (d, J_{CP}=6.6 Hz), 50.6 (d, J_{CP}=107.4 Hz), 41.8 (d, J_{CP}=3.9 Hz), 40.1

(d, J_{CP}=11.0 Hz), 34.7, 28.4 (d, J_{CP}=56.1 Hz), 28.1, 27.9, 16.6 (d, J_{CP}=5.3 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 51.37; IR (KBr) 3256, 1710, 1038 cm^{-1}; MS *m/z* 532 (MH^+); HRMS calcd for $C_{29}H_{43}NO_6P$: 532.2828 (MH^+). Found: 532.2806.

20b; white crystals; mp 121-124 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.30-7.17 (10H, m), 4.77 (1H, br.d, *J*=10.3 Hz), 4.18-3.99 (2H, m), 3.17 (1H, ddd, *J*=4.3, 4.3, 14.3 Hz), 3.07-3.00 (1H, m), 2.90-2.74 (3H, m), 2.25 (1H, ddd, *J*=9.8, 15.0, 15.0 Hz), 1.87 (1H, ddd, *J*=3.1, 12.5, 15.6 Hz), 1.30 (18H, s), 1.30-1.26 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.3 (d, J_{CP}=4.6 Hz), 155.1 (d, J_{CP}=1.8 Hz), 137.0-126.6 (aromatic), 80.9, 80.0, 61.3, 49.0 (d, J_{CP}=105.4 Hz), 41.5, 40.6 (d, J_{CP}=12.3 Hz), 34.3, 28.1, 27.889, 27.884 (d, J_{CP}=90.2 Hz), 16.6 (d, J_{CP}=5.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ:52.23; IR (KBr) 3226, 1723, 1791, 1033 cm^{-1}; MS *m/z* 532 (MH^+); HRMS calcd for $C_{29}H_{43}NO_6P$: 532.2828 (MH^+). Found: 532.2807.

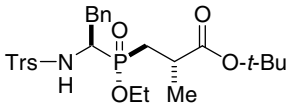
(1*R,*R*$_P$*,2*S**)-*tert*-Butyl 2-benzyl-3-[ethoxy(2-phenyl-1-{[(2,4,6-triisopropyl phenyl)sulfonyl]amino}ethyl)phosphoryl]propanoate (22a)**



22a

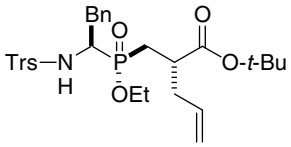
This compound was prepared from **15** (100 mg, 0.16 mmol) in an analogous manner to that for **21a**. Purification of the residue by column chromatography (hexane/EtOAc=5:1 to 1:1) gave **22a** (89 mg, 78%). The diastereomeric ratio (21:1) was determined by ^{31}P NMR (121 MHz, $CDCl_3$) based on two peaks (δ 51.03 (major isomer), 49.99 (minor isomer)) corresponding to the phosphorus atoms). White crystals; mp 157-159 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-6.99 (12H, m), 5.36 (1H, m), 4.12-3.96 (4H, m), 3.91-3.82 (1H, m), 3.14-2.72 (6H, m), 2.02-1.92 (1H, m), 1.70 (1H, ddd, *J*=3.8, 12.1, 15.8 Hz), 1.31 (9H, s), 1.28-1.23 (18H, m), 1.15 (3H, t, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6 (d, J_{CP}=4.5 Hz), 152.7-123.8 (aromatic), 81.0, 61.3 (d, J_{CP}=6.9 Hz), 53.6 (d, J_{CP}=100.5 Hz), 41.9 (d, J_{CP}=4.5 Hz), 40.1 (d, J_{CP}=12.5 Hz), 35.9, 34.1, 29.9, 28.7 (d, J_{CP}=94.6 Hz), 27.8, 24.9 (d, J_{CP}=12.7 Hz), 23.6 (d, J_{CP}=3.2 Hz), 16.3 (d, J_{CP}=5.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 50.85; IR (KBr) 3114, 1729, 1328, 1146, 1038 cm^{-1}; MS *m/z* 698 (MH^+); HRMS calcd for $C_{39}H_{56}NO_6PS$: 698.3644 (MH^+). Found: 698.3671.; Anal. Calcd for $C_{39}H_{56}NO_6PS$: C, 67.12; H, 8.09; N, 2.01. Found: C, 67.09; H, 7.99; N, 1.76.

(1*R,*R*$_P$*,2*S**)-*tert*-Butyl 3-[ethoxy(2-phenyl-1-{[(2,4,6-triisopropylphenyl) sulfonyl]amino}ethyl)phosphoryl]-2-methylpropanoate (23)**



This compound was prepared from **15** (20 mg, 0.03 mmol) and methyl iodide (7 μL, 0.11 mmol) in an analogous manner to that for **21a**. Purification of the residue by column chromatography (hexane/EtOAc=5:1 to 2:1) gave **23** (16.7 mg, 82%). The diastereomeric ratio (24:1) was determined by ^{31}P NMR (121 MHz, $CDCl_3$) based on two peaks (δ 51.06 (major isomer), 50.31 (minor isomer)) corresponding to the phosphorus atoms). White crystals; mp 146-147 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15-7.05 (7H, m), 5.56-6.63 (1H, m), 4.08-3.97 (4H, m), 3.89-3.73 (1H, m), 3.13 (1H, ddd, *J*=7.1, 13.9, 13.9 Hz), 2.95-2.85 (2H, m), 2.79-2.71 (1H, m), 2.11 (1H, ddd, *J*=8.4, 12.3, 15.7 Hz), 1.65 (1H, ddd, *J*=5.2, 11.7, 15.7 Hz), 1.43 (9H, s), 1.30-1.23 (18H, m), 1.16 (3H, t, *J*=6.9 Hz), 1.14 (3H, t, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9 (d, J_{CP}=6.9 Hz), 153.4-123.7 (aromatic), 80.6, 61.2 (d, J_{CP}=7.0 Hz), 53.6 (d, J_{CP}=101.6 Hz), 35.8 (d, J_{CP}=1.6 Hz), 35.0 (d, J_{CP}=4.7 Hz), 34.1, 29.90 (d, J_{CP}=70.5 Hz), 29.86, 27.9, 25.1, 24.8, 23.6, 23.5, 19.4 (d, J_{CP}=11.0 Hz), 16.2 (d, J_{CP}=5.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 51.13; IR (KBr) 3120, 1733, 1326, 1153, 1038 cm^{-1}; MS *m/z* 622 (MH^+); HRMS calcd for $C_{33}H_{53}NO_6PS$: 622.3331 (MH^+). Found: 622.3320.; Anal. Calcd for $C_{33}H_{52}NO_6PS$: C, 63.78; H, 8.43; N, 2.25. Found: C, 63.69; H, 8.38; N, 1.92.

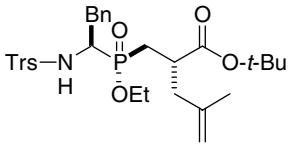
(1*R,R_P*,2*S**)-*tert*-Butyl 2-{[ethoxy(2-phenyl-1-{[(2,4,6-triisopropylphenyl) sulfonyl]amino}ethyl)phosphoryl]methyl}pent-4-enoate (24)**



This compound was prepared from **15** (20 mg, 0.03 mmol) and allyl bromide (9 μL, 0.11 mmol) in an analogous manner to that for **21a**. Purification of the residue by column chromatography (hexane/EtOAc=5:1 to 3:2) gave **24** (18 mg, 83%). The diastereomeric ratio (21:1) was determined by ^{31}P NMR (121 MHz, $CDCl_3$) based on two peaks (δ 51.32 (major isomer), 50.29 (minor isomer)) corresponding to the phosphorus atoms). White crystals; mp 115-118 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14-7.03 (7H, m), 5.62 (1H, dddd, *J*=7.0, 7.0, 10.1, 16.9 Hz), 5.46-5.43 (1H, m), 5.04-4.99 (2H, m), 4.11-3.98 (4H, m), 3.86 (1H, ddd, *J*=2.9, 7.1, 14.2 Hz), 3.11 (1H, ddd, *J*=7.1, 14.3, 14.3 Hz), 2.94-2.85 (2H, m), 2.83-2.74 (1H, m), 2.28-2.25 (2H, m), 2.01 (1H, ddd, *J*=9.8, 12.0, 15.7 Hz), 1.69 (1H, ddd, *J*=3.9, 12.1, 15.8 Hz), 1.43 (9H, s), 1.28-1.23 (18H, m), 1.15 (3H, t, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6 (d, J_{CP}=4.7

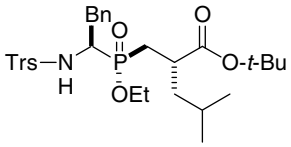
Hz), 152.7-123.7 (aromatic),134.0, 117.8, 81.0, 61.3 (d, J_{CP}=7.0 Hz), 53.6 (d, J_{CP}=101.0 Hz), 39.8 (d, J_{CP}=4.5 Hz), 38.1 (d, J_{CP}=12.0 Hz), 35.9 (d, J_{CP}=2.0 Hz), 34.1, 29.9, 28.0, 27.9 (d, J_{CP}=90.5 Hz), 24.9, 24.8, 23.6, 23.5, 16.2 (d, J_{CP}=5.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 51.14; IR (KBr) 3137, 1728, 1330, 1156, 1044 cm^{-1}; MS *m/z* 648 (MH^+); HRMS calcd for $C_{35}H_{55}NO_6PS$: 648.3488 (MH^+). Found: 648.3504.

(1*R,*R*$_P$*,2*S**)-*tert*-Butyl 2-{[ethoxy(2-phenyl-1-{[(2,4,6-triisopropylphenyl)sulfonyl] amino}ethyl)phosphoryl]methyl}-4-methylpent-4-enoate (25)**



This compound was prepared from **15** (100 mg, 0.16 mmol) and methallyl bromide (0.05 mL, 0.53 mmol) in an analogous manner to that for **21a**. Purification of the residue by column chromatography (hexane/EtOAc=5:1 to 1:1) gave **25** (73 mg, 69%). The diastereomeric ratio (29:1) was determined by ^{31}P NMR (121 MHz, $CDCl_3$) based on two peaks (δ 51.30 (major isomer), 50.34 (minor isomer)) corresponding to the phosphorus atoms). A colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13-7.03 (7H, m), 5.48-5.45 (1H, m), 4.76 (1H, s), 4.65 (1H, s), 4.11-3.98 (4H, m), 3.86 (1H, ddd, *J*=2.9, 7.1, 14.2 Hz), 3.11 (1H, ddd, *J*=7.2, 14.2, 14.2 Hz), 2.94-2.83 (3H, m), 2.26 (1H, dd, *J*=8.1, 13.7 Hz), 2.11 (1H, dd, *J*=7.1, 13.7 Hz), 1.97 (1H, dd, *J*=10.1, 11.6, 15.6 Hz), 1.74-1.66 (1H, m), 1.71 (3H, s), 1.43 (9H, s), 1.28-1.23 (18H, m), 1.15 (3H, t, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0 (d, J_{CP}=4.4 Hz), 152.6-123.7 (aromatic), 134.3, 113.5, 81.0, 61.3 (d, J_{CP}=6.8 Hz), 53.6 (d, J_{CP}=100.6 Hz), 42.7 (d, J_{CP}=12.5 Hz), 38.4 (d, J_{CP}=4.7 Hz), 35.9 (d, J_{CP}=2.0 Hz), 34.1, 29.9, 28.4 (d, J_{CP}=94.3 Hz), 28.0, 24.9, 24.8, 23.55, 23.50, 21.7, 16.2 (d, J_{CP}=5.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 51.13; IR (KBr) 3143, 1725, 1650, 1332, 1161 cm^{-1}; MS *m/z* 684 (MNa^+); HRMS calcd for $C_{36}H_{56}NO_6NaPS$: 684.3464 (MNa^+). Found: 684.3469.; Anal. Calcd for $C_{36}H_{56}NO_6PS$: C, 65.33; H, 8.53; N, 2.12. Found: C, 65.26; H, 8.44; N, 1.79.

(1*R,*R*$_P$*,2*S**)-*tert*-Butyl 2-{[ethoxy(2-phenyl-1-{[(2,4,6-triisopropylphenyl) sulfonyl]amino}ethyl)phosphoryl]methyl}-4-methylpentanoate (26)**



This compound was prepared from **15** (100 mg, 0.16 mmol) and *i*-butyl iodide (0.06 mL, 0.53 mmol) in an analogous manner to that for **21a** except for stirring the final reaction mixture at rt in 3 h. Purification of the residue by column chromatography (hexane/EtOAc=5:1 to 3:1) gave **26** (67 mg, 62%). The diastereomeric ratio (14:1) was determined by ^{31}P NMR (121 MHz, $CDCl_3$) based on two peaks (δ 51.88 (major isomer), 53.21 (minor isomer)) corresponding to the phosphorus atoms). White crystals; mp 152-153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12-7.03 (7H, m), 5.31-5.28 (1H, m), 4.11-3.97 (4H, m), 3.86 (1H, ddd, *J*=2.9, 7.1, 14.2 Hz), 3.10 (1H, ddd, *J*=7.3, 14.1, 14.1 Hz), 1.97 (1H, ddd, *J*=9.8, 11.9, 15.5 Hz), 1.66 (1H, ddd, *J*=4.0, 11.8, 15.6 Hz), 1.60-1.48 (1H, m), 1.44 (9H, s), 1.28-1.23 (20H, m), 1.14 (3H, t, *J*=7.0 Hz), 0.90 (3H, d, *J*=6.5 Hz), 0.87 (3H, d, *J*=6.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7 (d, J_{CP}=5.0 Hz), 152.7-123.8 (aromatic), 80.7, 61.3 (d, J_{CP}=6.8 Hz), 53.6 (d, J_{CP}=100.3 Hz), 43.5 (d, J_{CP}=11.5 Hz), 38.5 (d, J_{CP}=4.6 Hz), 35.9, 34.1, 29.9, 29.3 (d, J_{CP}=90.0 Hz), 28.0, 25.7, 24.94, 24.85, 23.6 (d, J_{CP}=11.0 Hz), 22.9, 22.0, 16.2 (d, J_{CP}=5.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 51.10; IR (KBr) 3113, 1726, 1330, 1164, 1036 cm^{-1}; MS *m/z* 686 (MNa^+); HRMS calcd for $C_{36}H_{58}NO_6NaPS$: 686.3620 (MNa^+). Found: 686.3615.

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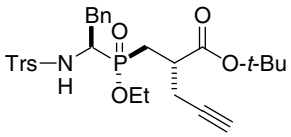
(1*R,*R*$_P$*,2*S**)-*tert*-Butyl 2-{[ethoxy(2-phenyl-1-{[(2,4,6-triisopropylphenyl) sulfonyl]amino}ethyl)phosphoryl]methyl}but-3-ynoate (27)**



This compound was prepared from **15** (20 mg, 0.03 mmol) and propargyl chloride (8 mL, 0.11 mmol) in an analogous manner to that for **21a** except for stirring the final reaction mixture at –20°C in 17 h. Purification of the residue by column chromatography (hexane/EtOAc=5:1 to 1:1) gave **27** (18 mg, 84%). The diastereomeric ratio (17:1) was determined by ^{31}P NMR (121 MHz, $CDCl_3$) based on two peaks (δ 50.83 (major isomer), 49.86 (minor isomer)) corresponding to the phosphorus atoms). A colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19-7.04 (7H, m), 5.37-5.34 (1H, m), 4.15-3.95 (4H, m), 3.86 (1H, ddd, *J*=2.9, 7.0, 14.1 Hz), 3.13 (1H, ddd, *J*=7.1, 14.2, 14.2 Hz), 2.97-2.84 (3H, m), 2.59-2.41 (2H, m), 2.19 (1H, ddd, *J*=8.5, 12.5, 15.7 Hz), 1.98 (1H, t, *J*=2.5 Hz), 1.88 (1H, ddd, *J*=4.7, 11.7, 16.1 Hz), 1.46 (9H, s), 1.27-1.22 (18H, m), 1.14 (3H, t, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2 (d, J_{CP}=6.4 Hz), 152.9-123.8 (aromatic), 81.5, 79.9, 71.1, 61.4 (d, J_{CP}=6.8 Hz), 54.1 (d, J_{CP}=102.1 Hz), 39.2 (d, J_{CP}=4.1 Hz), 35.9 (d, J_{CP}=1.8 Hz), 34.1, 29.9, 27.9, 27.2 (d, J_{CP}=91.1 Hz), 24.9, 24.8, 23.6, 23.5, 22.9 (d, J_{CP}=11.1 Hz), 16.2 (d, J_{CP}=5.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 50.94;

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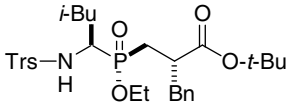
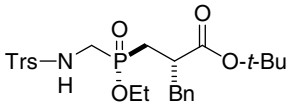
IR (neat) 3311, 3065, 2121, 1733, 1329 cm^{-1}; MS *m/z* 668 (MNa^+); HRMS calcd for $C_{35}H_{52}NO_6NaPS$: 668.3151 (MNa^+). Found: 668.3153.

(1*R,R_P*,2*S**)-*tert*-Butyl 2-benzyl-3-[ethoxy(3-methyl-1-{[(2,4,6-triisopropyl phenyl)sulfonyl]amino}butyl)phosphoryl]propanoate (28)**



This compound was prepared from **16** (49 mg, 0.09 mmol) in an analogous manner to that for **21a**. Purification of the residue by column chromatography (hexane/EtOAc=5:1 to 3:1) gave **28** (30 mg, 54%). The diastereomeric ratio (14:1) was determined by ^{31}P NMR (121 MHz, $CDCl_3$) based on two peaks (δ 51.44 (major isomer), 53.40 (minor isomer)) corresponding to the phosphorus atoms). White crystals; mp 142-143 ˚C; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.28-7.11 (7H, m), 5.20 (1H, br.d, *J*=8.8 Hz), 4.12-4.03 (4H, m), 3.77-3.68 (1H, m), 3.13-3.04 (1H, m), 2.95-2.80 (4H, m), 2.25-2.51 (1H, m), 2.06-1.99 (1H, m), 1.51-1.43 (1H, m), 1.33 (9H, s), 1.30-1.23 (21H, m), 0.66 (3H, d, *J*=7.2 Hz), 0.65 (3H, d, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 174.0 (d, J_{CP}=3.8 Hz), 152,7-123.6 (aromatic), 81.1, 61.5 (d, J_{CP}=6.3 Hz), 50.4 (d, J_{CP}=103.9 Hz), 42.3, 40.4 (d, J_{CP}=12.4 Hz), 39.0, 34.2, 30.0, 29.2 (d, J_{CP}=102.2 Hz), 27.9, 24.9, 24.8, 24.2 (d, J_{CP}=8.7 Hz), 23.64, 23.61, 22.9, 21.5, 16.5 (d, J_{CP}=5.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 51.52; IR (KBr) 3106, 1732, 1040 cm^{-1}; MS *m/z* 664 (MH^+); HRMS calcd for $C_{36}H_{59}NO_6PS$: 664.3801 (MH^+). Found: 664.3802.

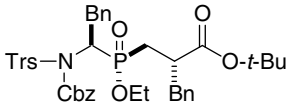
(R_P*,2*S)-*tert*-Butyl 2-benzyl-3-[ethoxy({[(2,4,6-triisopropylphenyl)sulfonyl] amino}methyl)phosphoryl]propanoate (29)**



This compound was prepared from **17** (88 mg, 0.17 mmol) in an analogous manner to that for **21a**. Purification of the residue by column chromatography (hexane/EtOAc=10:1 to 1:1) gave **29** (31 mg, 30%). The diastereomeric ratio (18:1) was determined by ^{31}P NMR (121 MHz, $CDCl_3$) based on two peaks (δ 47.41 (major isomer), 49.43 (minor isomer)) corresponding to the phosphorus atoms). White crystals; mp 116-118 ˚C; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.28-7.14 (7H, m), 4.99-4.95 (1H, m), 4.15-4.00 (4H, m), 3.26 (1H, ddd, *J*=6.9, 10.8, 14.3 Hz), 3.15 (1H, ddd, *J*=5.3, 9.3, 14.4 Hz), 3.06-2.80 (5H, m), 2.19 (1H, ddd, *J*=9.4, 12.8, 15.4 Hz), 1.89 (1H, ddd, *J*=3.7, 15.1, 15.1 Hz), 1.34 (9H, s), 1.28-1.25 (21H, m); ^{13}C NMR (100 MHz,

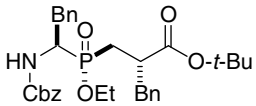
$CDCl_3$) δ: 173.3 (d, J_{CP}=4.3 Hz), 153.2-123.9 (aromatic), 81.4, 61.7 (d, J_{CP}=6.6 Hz), 41.7 (d, J_{CP}=3.6 Hz), 41.4 (d, J_{CP}=97.1 Hz), 34.1, 29.7, 28.8 (d, J_{CP}=94.6 Hz), 27.9, 24.93, 24.91, 23.5, 16.5 (d, J_{CP}=5.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 47.51; IR (KBr) 3136, 1731, 1035 cm^{-1}; MS *m/z* 608 (MH^+); HRMS calcd for $C_{32}H_{51}NO_6PS$: 608.3175 (MH^+). Found: 608.3195.

(1*R,*R*$_P$*,2*S**)-*tert*-Butyl 2-benzyl-3-[(1-{[(benzyloxy)carbonyl][(2,4,6-triisopropylphenyl)sulfonyl]amino}-2-phenylethyl)(ethoxy)phosphoryl]propanoate (30)**



To sodium hydride (50%, 21 mg, 0.84 mmol) was added a solution of **22a** (200 mg, 0.29 mmol) in THF (1.2 mL) at 0 ˚C and stirred for 30 minutes at the same temperature. To the mixture was added CbzCl (0.11 mL, 0.84 mmol), DMAP (35 mg, 0.29 mmol) and stirred for 17 h at room temperature. The mixture was diluted with saturated NH_4Cl solution and extracted with Et_2O. The combined extracts were washed with brine and dried over $MgSO_4$. Removal of the solvent gave a residue which was purified by column chromatography (hexane/EtOAc=5:1 to 4:1) to give **30** (199.9 mg, 84 %). White crystals; mp 110-115 ˚C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71-6.97 (17H, m), 5.18 (1H, d, *J*=12.4 Hz), 5.15 (1H, d, *J*=13.1 Hz), 4.90 (1H, ddd, *J*=2.6, 11.1, 11.1 Hz), 4.07-3.96 (3H, m), 3.94-3.84 (1H, m), 3.71 (1H, ddd, *J*=10.7, 12.5, 12.5 Hz), 3.05 (1H, ddd, *J*=2.3, 13.9, 23.6 Hz), 2.95-2.86 (3H, m), 2.79-2.73 (1H, m), 1.28-1.25 (12H, m), 1.27 (9H, m), 1.17 (3H, t, *J*=7.1 Hz), 1.15 (6H, t, *J*=6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0 (d, J_{CP}=8.6 Hz), 154.0-124.1 (aromatic), 80.5, 68.6, 61.5 (d, J_{CP}=6.8 Hz), 57.6 (d, J_{CP}=91.0 Hz), 41.4 (d, J_{CP}=4.2 Hz), 39.6 (d, J_{CP}=9.3 Hz), 36.8, 34.2, 31.8 (d, J_{CP}=92.8 Hz), 29.4, 27.8, 24.8, 24.7, 23.5, 16.3 (d, J_{CP}=6.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 48.01; IR (KBr) 1729, 1338, 1152, 1042 cm^{-1}; MS *m/z* 832 (MH^+); HRMS calcd for $C_{47}H_{63}NO_8PS$: 832.4012 (MH^+). Found: 832.4039.; Anal. Calcd for $C_{47}H_{62}NO_8PS$: C, 67.85; H, 7.51; N, 1.68. Found: C, 67.90; H, 7.40; N, 1.69.

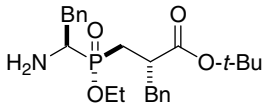
(1*R,*R*$_P$*,2*S**)-*tert*-Butyl 2-benzyl-3-[(1-{[(benzyloxy)carbonyl]amino}-2-phenylethyl)(ethoxy)phosphoryl]propanoate (18a)**



To a stirred solution of **30** (40 mg, 0.05 mmol) in THF (1.4 mL) was added a 0.1 M THF

solution of SmI_2 (2.3 mL, 0.23 mmol) at 0 ˚C and stirred for 30 minutes at the same temperature. The mixture was diluted with saturated K_2CO_3 solution and extracted with EtOAc. The combined extracts were washed with brine and dried over $MgSO_4$. Removal of the solvent gave a residue which was purified by column chromatography (hexane/EtOAc=10:1 to 2:1) to give **18a** (17 mg, 61 %). The ^1H and ^{13}C NMR spectra were identical to those of a sample prepared from **11** with benzyl bromide.

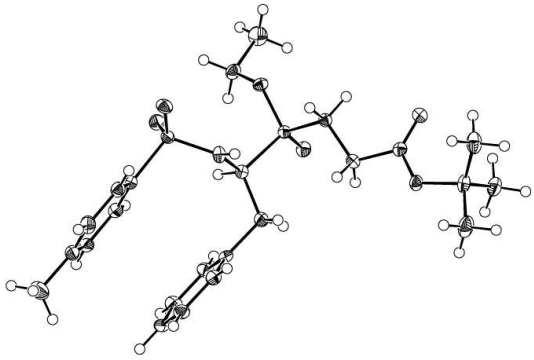
(1*R,*R*P*,2*S**)-*tert*-Butyl 3-[[1-amino-2-phenylethyl](ethoxy)phosphoryl] -2-benzylpropanoate (31)**



To a solution of **18a** (17 mg, 0.03 mmol) in MeOH (0.3 mL) wad added 20% $Pd(OH)_2$-C (4 mg) and stirred for 3 h at room temperature under a hydrogen atmosphere. The catalyst was removed by filtration through a pad of Celite and the filtrate was concentrated to give a residue. To a solution of the residue in CH_2Cl_2 (0.3 mL) was added Et_3N (4.2 μL, 0.03 mmol) and stirred for 30 minutes at room temperature. The mixture was concentrated to give a residue which was purified by preparative TLC (hexane/EtOAc=1:1) to give **31** (9.6 mg, 74 %). A colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32-7.17 (10H, m), 4.16-3.75 (2H, m), 5.15 (4H, m), 2.85 (1H, ddd, *J*=5.8, 5.8, 11.6 Hz), 2.57 (1H, ddd, *J*=7.8, 10.9, 13.8 Hz), 2.34 (1H, ddd, *J*=9.0, 12.1, 15.5 Hz), 1.85 (1H, ddd, *J*=3.7, 13.2, 15.5 Hz), 1.35 (9H, s), 1.30 (3H, t, *J*=7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6 (d, J_{CP}=4.8 Hz), 138.2-126.6 (aromatic), 80.9, 60.8 (d, J_{CP}=7.0 Hz), 52.1 (d, J_{CP}=5.3 Hz), 42.1 (d, J_{CP}=3.5 Hz), 40.2 (d, J_{CP}=11.4 Hz), 36.6, 27.8, 26.3 (d, J_{CP}=86.6 Hz), 16.7 (d, J_{CP}=11.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 54.38; IR (neat) 3381, 3303, 1727, 1369, 1153 cm^{-1}; MS *m/z* 432 (MH^+); HRMS calcd for $C_{24}H_{35}NO_4P$: 432.2304 (MH^+). Found: 432.2311.

Crystallographic data of 15

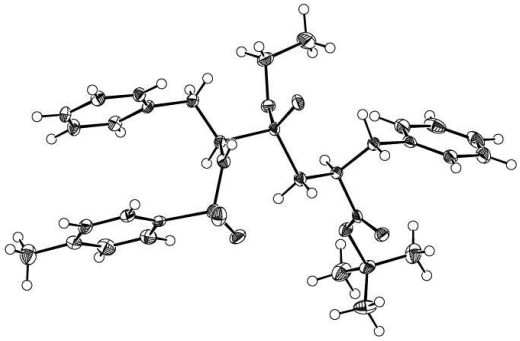
Crystallographic data (excluding structure factor) for the X-ray crystal structure analysis of **15** have been deposited with cambridge Crystallographic Data Center (CCDC) as supplementary publication No. CCDC 690666. This data can be obtained free of charge from the CCDC via www.ccdc.cam.ac.uk/data_request/cif.



Ortep drawing of **15**

Crystallographic data of 21a

Crystallographic data (excluding structure factor) for the X-ray crystal structure analysis of **21a** have been deposited with cambridge Crystallographic Data Center (CCDC) as supplementary publication No. CCDC 690665. This data can be obtained free of charge from the CCDC via www.ccdc.cam.ac.uk/data_request/cif.



Ortep drawing of **21a**

References

1. Yamagishi, T.; Haruki, T.; Yokomatsu, T. *Tetrahedron* **2006**, *62*, 9210.
2. Haruki, T.; Yamagishi, T.; Yokomatsu, T. *Tetrahedron: Asymmetry* **2007**, *18*, 2886.