Diphenylphosphinoyl chloride as a chlorinating agent – the selective double activation of 1,2-diols

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Supplementary Information

Experimental

For reactions conducted under anhydrous conditions glassware was dried overnight in an oven at 130 °C and was allowed to cool in a dessicator over anhydrous KOH. Anhydrous reactions were carried out under argon. Solvents were BOC standard reagent grade and distilled before use. Reagents/solvents for anhydrous reactions were dried as follows: THF was distilled from sodium wire with benzophenone as indicator. Dichloromethane, carbontetrachloride, hexane, acetonitrile, toluene, pyridine, N,N-dimethylformamide and triethylamine were dried and stored over 4 Å molecular sieves. Methanol was dried and stored over 3 Å molecular sieves. Sulfate buffer was prepared by dissolving 1.5 mol of Na₂SO₄ in 0.5 mol H₂SO₄ and adding water to give a final volume of 2000 cm³. Thin layer chromatography (TLC) was carried out on commercially available pre-coated glass plates (Merck 60 F₂₅₄). The quoted Rf values are rounded to the nearest 0.05. Dry Column Vacuum Chromatography (DCVC) was performed according to the published procedure.¹ ¹H, ¹³C, APT, DEPT, HMBC and COSY NMR spectra were recorded on Bruker Avance 400 (5 mm QNP probe) and Bruker Avance 500 (5 mm dual ¹³C-¹H cryo probe) Fourier transform spectrometers using an internal deuterium lock. ³¹P NMR Spectra were recorded on a Bruker Avance 400 (5 mm QNP probe) Fourier transform spectrometer using 85% H₃PO₄ as external standard. Solvents were used as internal standards when assigning NMR spectra (δH: CDCl₃ 7.26 ppm, DMSO-d₆ 2.50; δC: CDCl₃ 77.0 ppm, DMSO-d₆ 39.4 ppm). Spectra were processed using Mestre-C software.² J values are given in Hz and rounded to the nearest 0.5 Hz. LC-MS Was run on a Waters Alliance LC/MS system consisting of a Waters 2795 Separations Module, a Waters 2996 Photodiode Array Detector and a Waters Micromass ZQ on a C18 analytical Reverse Phase Supercosil™ ABZ+PLUS column (3.3 cm × 4.6mm, 3µm) using the following gradient: 0.00-0.70 min 100% solvent A, 0.70-4.20 min 100% solvent A to 100% solvent B, 4.20-7.70 min 100% solvent B, 7.70-8.00 min 100% solvent B to 100% solvent A (solvent A: 10 mM ammonium acetate in water containing 0.1% formic acid; solvent B: 95% acetonitrile in water) with a flow rate of 1 cm³/min. EI and LSIMS mass spectra were recorded on a Kratos concept 1H double focusing magnetic sector instrument using a MACH 3 data system. +ESI mass spectra were recorded using a Bruker Bio-Apex II FT-ICR instrument or a Micromass Q-Tof 1 machine. Microanalyses were carried out on a CE440 Elemental Analyser from Exeter Analytical, INC. The calculated values were adjusted for residual solvents. Melting points were measured on a microscope hot stage melting point apparatus (C. Reichert Optische Werke AG) and are uncorrected. Infra-red spectra were recorded using a Perkin Elmer Spectrum One (FT-IR) spectrometer with a universal ATR sampling accessory. Optical rotations were recorded on a Perkin Elmer 241 polarimeter using the sodium D line (589 nm) at 22 °C
and are given in units of 10⁻¹ deg dm² g⁻¹. X-ray Crystallographic Data was measured on a Nonius Kappa CCD diffractometer at 180(2) K.

(4R,5S)-5-Chloro-4-diphenylphosphinoyloxy-1,5-diphenyl-pentan-1-one 5 and (4R,5R)-4,5-bisdiphenylphosphinoyloxy-1,5-diphenyl-pentan-1-one 9: diol 1 (0.50 g, 1.85 mmol) was dissolved in anhydrous pyridine (10 cm³) and diphenylphosphinoyl chloride (1.75 g, 7.40 mmol) was added. The reaction mixture was stirred under argon for 14 hours and transferred to a separatory funnel with water (20 cm³) and extracted with ethyl acetate (50 + 2 cm³). The combined organic phases were extracted with aqueous sulfate buffer (50 cm³), saturated aqueous NaHCO₃ (50 cm³), dried (Na₂SO₄), filtered and concentrated in vacuo to give a brown gum. The product was purified by DCVC [id 4 cm; 20 cm³ fractions; 0-100% EtOAc in hexanes (v/v) – 10% increments; 2.5-12.5% MeOH in EtOAc (v/v) – 2.5% increments; two fractions of each solvent mixture] to give 0.60 g (66%) of ketone 5 as a yellow amorphous solid and 46 mg (3%) of bis-phosphinate 9 as a yellow gum; 5: [α]²²⁰D +19.0 (c. 1.0, CHCl₃; Rf 0.65 (EtOAc); m/z (+ESI) found: MH⁺, 489.1377. (C₂₉H₂₇ClO₃P requires M, 489.1386); IR νmax(CHCl₃)/cm⁻¹ 1684 (C=O), 1439 (P-Ph) and 1223 (P=O); ¹H NMR (500 MHz; CDCl₃) δ 7.87-7.75 (2H, m, ortho-PhP and/or ortho-PhC=O), 7.75-7.71 (4H, m, ortho-PhP and/or ortho-Ph=O), 7.55-7.47 (3H, m, meta-PhP and para-PhC=O), 7.45-7.27 (13H, m, meta-PhP, meta-PhC=O and ortho-, meta- and para-PhC), 5.20 (1H, d, J 4.5, CHPh), 4.87 (1H, ddt, J 9.0, 4.5 and 2.5, CHCHPh), 3.05 (1H, ddd, J 18.0, 9.5 and 5.0, CH₂H₃C=O), 2.94 (1H, ddt, J 18.0, 9.5 and 6.0, CH₂H₅C=O), 2.30 (1H, ddt, J 14.5, 9.0 and 5.0, CH₂H₃CH₂C=O) and 2.17-2.10 (1H, m, CH₂H₅CH₂C=O); ³¹P NMR (162 MHz; CDCl₃) δ 32.7; ¹³C NMR (126 MHz; CDCl₃) δ 198.8 (C₁), 137.0, 136.6 (ips-o-PhC=O and ipso-PhCH), 132.9 (para-PhC=O), 132.3 (×2) (2 × d, J 2.5 and 3.0, para-PhP), 131.7 (×2) (d, J 138.5, ipso-PhP and d, J 10.5, ortho-PhP), 131.6 (d, J 10.5, ortho-PhP), 131.3 (d, J 134.8, ipso-PhP), 128.6 (d, J 13.5, meta-PhP), 128.6 (d, J 13.5, meta-PhP), 128.5 (×2), 128.4, 128.0, 127.9 (ortho-, meta- and para-PhCH and meta- and para-PhC=O), 78.5 (d, J 6.5, C₄), 65.8 (d, J 4.0, C₅), 34.4 (C₂) and 24.3 (d, J 3.5, C₃); (Found: C, 68.51; H, 5.31. C₂₉H₂₇ClO₃P·1 H₂O requires C, 68.71; H, 5.57). 9: [α]²²⁰D +8.1 (c. 1.0, CHCl₃; Rf 0.35 (EtOAc); m/z (+ESI) found: MH⁺, 671.2124. (C₄₁H₃₇O₅P₂ requires M, 671.2116); IR νmax(CHCl₃)/cm⁻¹ 1684 (C=O), 1439 (P-Ph) and 1222 (P=O); ¹H NMR (500 MHz; CDCl₃) δ 7.84-7.76 (4H, m, Ph), 7.73-7.71 (2H, m, Ph), 7.67-7.63 (2H, m, Ph), 7.54-7.44 (6H, m, Ph), 7.41-7.31 (8H, m, Ph), 7.24-7.15 (8H, m, Ph), 5.56 (1H, dd, J 9.5 and 6.0, CHPh), 4.95 (1H, ddt, J 8.5, 6.5 and 3.5, CHCHPh), 2.99 (1H, ddd, J 18.0, 9.5 and 6.0, CH₂H₅C=O), 2.92 (1H, ddd, J 18.0, 9.5 and 5.0, CH₂H₅C=O), 2.21-2.14 (1H, m, CH₂H₃CH₂C=O) and 1.80 (1H, ddd, J 13.0, 9.0, 8.0 and 5.5, CH₂H₅CH₂C=O); ³¹P NMR (162 MHz; CDCl₃) δ 32.4 and 32.3; ¹³C NMR (126 MHz; CDCl₃) δ 198.9 (C₁), 136.6 (ips-o-PhC=O), 136.2 (d, J 2.5, ipso-PhC), 132.8 (para-PhC=O), 132.0 (×3) (d, J 2.5, para-PhP, d, J 2.5, para-PhP and d, J 138.0, ipso-PhP), 131.9 (×2), 131.8 (×2), 131.7 (×3), 131.6 (×2), 131.5 (Ph), 131.3 (d, J 141.0, ipso-PhP), 130.8 (d, J 137.0, ipso-PhP), 130.9 (d, J 133.0, ipso-PhP), 128.5, 128.4 (×2), 128.3, 128.2 (×2), 128.1, 128.0, 127.9, 127.7 (Ph), 77.9 (t, J 5.5, C₅), 77.2 (t, J 6.0, C₄), 34.2 (C₂) and 25.2 (d, J 2.0, C₃).
tert-Butyl (4R,5S)-5-chloro-4-diphenylphosphinoyloxy-5-phenyl-pentanoate 6: diol\(^2\) 2 (0.21 g, 0.79 mmol) was dissolved in anhydrous pyridine (5 cm\(^3\)) and diphenylphosphinoyl chloride (0.61 cm\(^3\), 3.2 mmol) was added under argon. After 29 hours aqueous half-saturated NaHCO\(_3\) (20 cm\(^3\)) was added and the mixture extracted with ethyl acetate (3 × 20 cm\(^3\)). The combined organic phases were concentrated \textit{in vacuo} and the residue dissolved in dichloromethane (20 cm\(^3\)) and extracted with saturated aqueous NaHCO\(_3\) (50 cm\(^3\)). The organic phase was dried (Na\(_2\)SO\(_4\)), filtered and concentrated \textit{in vacuo} to give a yellow gum that was purified by DCVC [id 4 cm; 20 cm\(^3\) fractions; 4 × hexanes; 10-100% EtOAc in hexanes (v/v) – 10% increments; 3 × EtOAc] to give 0.32 g (83%) of phosphinate 6 as white needles.

\[\alpha\]\(^{22}\)D +18 (c. 1.0, CHCl\(_3\)); mp 68-69 °C (EtOAc, hexanes); \(R_f\) 0.30 (40% EtOAc in hexanes, v/v); m/z (+ESI) found: MNa\(^+\), 507.1454. (C\(_{27}\)H\(_{30}\)ClO\(_4\)PNa requires M, 507.1468); IR \(\nu_{\max} (CHCl\(_3\))/cm\(^{-1}\) 1726 (C=O), 1439 (P-Ph) and 1228 (P=O); 1H NMR (500 MHz; CDCl\(_3\)) \(\delta\) 7.82-7.78 (2H, m, \textit{ortho}-PhP), 7.71-7.67 (2H, m, \textit{ortho}-PhP), 7.55-7.50 (2H, m, \textit{para}-PhP), 7.47-7.40 (4H, m, \textit{meta}-PhP), 7.30-7.27 (5H, m, Ph), 5.14 (1H, d, \(J_{5.0}\), PhC\(_{2}\)H\(_3\)), 4.79-4.74 (1H, m, PhCHC\(_{2}\)H\(_3\)), 2.37-2.27 (1H, m, C\(_{a}\)H\(_{b}\)C=O), 2.25-2.16 (2H, m, CH\(_{a}\)H\(_{b}\)C=O and C\(_{a}\)H\(_{b}\)CH\(_2\)C=O), 1.97-1.89 (1H, m, CH\(_{a}\)H\(_{b}\)CH\(_2\)C=O) and 1.34 \[9\]H, \(s\), C(CH\(_3\))\(_3\); 31P NMR (162 MHz; CDCl\(_3\)) \(\delta\) 32.6; 13C NMR (126 MHz; CDCl\(_3\)) \(\delta\) 171.9 (C\(_1\)), 137.1 (ipso-Ph), 132.3 (d, \(J_{2.5}\)), 132.2 (d, 3.0) (2 × para-PhP), 131.7 (d, J 10.5), 131.6 (d, J 10.0) (2 × \textit{ortho}-PhP), 131.4 (×2) (d, J 139.0 and d, J 131.5), 128.6-128.4 (m, 2 × meta-PhP and 2 × Ph), 127.8 (para-Ph), 80.3 [C(CH\(_3\))\(_3\)], 78.2 (d, J 6.5, C4), 65.2 (d, J 4.0, C5), 30.8 (C2), 28.0 [C(CH\(_3\))\(_3\)] and 25.3 (d, J 3.5, C3); (Found: C, 66.86%; H, 6.25. C\(_{27}\)H\(_{30}\)ClO\(_4\)P requires C, 66.87%; H, 6.24%).

(1S,2R)-1-Chloro-1-phenyl-2-diphenylphosphinoyloxy-propane 7: to a stirred solution of diol\(^3\) 3 (1.23 g, 8.08 mmol) in pyridine (50 cm\(^3\)) under argon was added diphenylphosphinoyl chloride (4.38 cm\(^3\), 22.3 mmol) and the solution was stirred for 48 hours before it was quenched with half-saturated aqueous NaHCO\(_3\) (50 cm\(^3\)) and brine (50 cm\(^3\)). The mixture was extracted with EtOAc (80 cm\(^3\) + 50 cm\(^3\) + 20 cm\(^3\)) and the combined organic phases were evaporated \textit{in vacuo}. Purification by DCVC [id 4 cm; 20 cm\(^3\) fractions; 0-100% EtOAc in petrol ether (60-80 °C) (v/v) – 10% increments] gave chloride 7 (1.79 g, 60%) as a clear colourless oil; [\(\alpha\)]\(^{22}\)D +18.4 (c. 0.7, CHCl\(_3\)); \(R_f\) 0.40 [30% petrol ether (60-80 °C) in EtOAc, v/v]; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.76-7.70 (2H, m, \textit{ortho}-PhP), 7.59-7.53 (2H, m, \textit{ortho}-PhP), 7.48-7.24 (11H, m, Ph), 5.05 (1H, d, J 5.5, C\(_{2}\)H\(_3\)), 4.81 (1H, dq, J 9.0 and 6.0, CHO), 1.42 (d, 3H, J 6.0, CH\(_3\)); \(^31\)P NMR (162 MHz, CDCl\(_3\)) \(\delta\) 32.1; \(^13\)C NMR (126 MHz; CDCl\(_3\)) \(\delta\) 171.9 (C1), 137.1 (ipso-Ph), 132.3 (d, J 2.5), 132.2 (d, 3.0) (2 × para-PhP), 131.7 (d, J 10.5), 131.6 (d, J 10.0) (2 × \textit{ortho}-PhP), 131.4 (×2) (d, J 139.0 and d, J 131.5), 128.6-128.4 (m, 2 × meta-PhP and 2 × Ph), 127.8 (para-Ph), 80.3 [C(CH\(_3\))\(_3\)], 78.2 (d, J 6.5, C4), 65.2 (d, J 4.0, C5), 30.8 (C2), 28.0 [C(CH\(_3\))\(_3\)] and 25.3 (d, J 3.5, C3); (Found: C, 66.86; H, 6.25. C\(_{21}\)H\(_{20}\)O\(_2\)ClP requires C, 66.87%; H, 6.24%).

(1S,2R)-1-Chloro-1-phenyl-2-diphenylphosphinoyloxy-propane 7: to a stirred solution of diol\(^5\) 4 (1.23 g, 8.08 mmol) in pyridine (50 cm\(^3\)) under argon was added diphenylphosphinoyl chloride (4.38 cm\(^3\), 22.3 mmol) and the solution was stirred for 48 hours before it was quenched with half-saturated aqueous NaHCO\(_3\) (40 cm\(^3\)) and the combined organic phases were evaporated \textit{in vacuo}. The residue was dissolved in dichloromethane (50 cm\(^3\)) and
saturated aqueous NaHCO₃ (50 cm³), the organic phase dried with Na₂SO₄, filtered, and evaporated in vacuo. Purification by DCVC [id 4 cm; 20 cm³ fractions; 0-100% EtOAc in petrol ether (60-80 °C) (v/v) – 10% increments; 2 × EtOAc] gave chloride 8 (0.617 g, 71%). A sample was recrystallised from CHCl₃ : petrol ether (60-80 °C) to give a colourless crystalline solid; [α]D₂² +22.8 (c. 0.75, CHCl₃); mp 172–174 °C; Rf 0.40 [40% petrol ether (60-80 °C) in EtOAc, v/v]; ¹H NMR (400 MHz, CDCl₃) δ 7.48-7.44 (5H, m, Ph), 7.35-6.93 (15H, m, Ph), 5.73 (1H, dd, J 9.0, 6.5, CHO), 5.28 (1H, d, J 6.5, CHCl); ³¹P NMR (162 MHz, CDCl₃) δ 33.5; ¹³C NMR (101 MHz, CDCl₃) δ 137.3, 136.3 (d, J 2.0), 132.1 (d, J 3.0), 131.9 (d, J 3.0), 131.7 (d, J 10.5), 131.4 (d, J 138.5), 131.4 (d, J 10.5), 131.1 (d, J 135.5), 128.7, 128.5, 128.3, 128.3 (d, J 13.5), 128.1, 128.1 (d, J 13.5), 127.8, 80.0 (d, J 5.5), 65.5 (d, J 6.5); m/z (+ESI) found: MH⁺ 433.1124 (C₂₆H₂₃ClO₂P⁺ requires 433.1119); (found: C, 71.80%; H, 5.15%; C₂₆H₂₂ClO₂P 1.5 H₂O requires C, 71.54%; H, 5.17%).

(2R,3S)-Methyl 3-chloro-2-bis(diphenylphosphinoyloxy)-3-phenylpropanoate 11, (2R,3R)-methyl 2-chloro-3-bis(diphenylphosphinoyloxy)-3-phenylpropanoate 12 and (2S,3R)-methyl 2,3-bis(diphenylphosphinoyloxy)-3-phenylpropanoate 13: to a stirred solution of diol 10 (0.098 g, 0.5 mmol) in pyridine (5 cm³) under argon was added diphenylphosphinoyl chloride (0.38 cm³, 2.0 mmol) and the solution was stirred for 48 hours before it was quenched with half-saturated aqueous NaHCO₃ (10 cm³). The mixture was extracted with EtOAc (3 × 20 cm³) and the combined organic phases were evaporated in vacuo. The residue was dissolved in dichloromethane (25 cm³) and saturated aqueous NaHCO₃ (40 cm³), the organic phase dried with Na₂SO₄, filtered, and evaporated in vacuo. Purification by DCVC [id 4 cm; 20 cm³ fractions; 0-100% EtOAc in petrol ether (60-80 °C) (v/v) – 10% increments; then 5-20% MeOH in EtOAc (v/v) – 5% increments] gave bis-phosphinate 13 as a light yellow oil (0.073 g, 24%) and a mixture of chloro-phosphinates 11 and 12 (11:12 1:2.5 by ¹H NMR) (0.115 g, 56%). 11 and 12 ¹H NMR (400 MHz, CDCl₃) 7.80-7.22 (m, Ph, both isomers), 5.76 (1H, dd, J 9.5, 8.0, PhCHOP, minor isomer), 5.25 (1H, d, J 8.0, PhCHCl, major isomer), 5.17 (1H, dd, J 9.5, 8.0, POCHCO₂, major isomer), 4.75 (1H, dd, J 8.5 and 5.5, PhCO), 3.33 (3H, s, OCH₃ minor isomer) and 3.60 (3H, s, OCH₃ major isomer); m/z (+ESI) found: MH⁺ 435.1474 (C₂₃H₂₉O₄ClP⁺ requires 435.1492). A sample of bis-phosphinate 13 was recrystallised from CHCl₃ : petrol ether (60-80°C); [α]D₂² −12.0 (c. 0.43, CHCl₃); mp 145.5-147.7 °C; Rf 0.05 [40% petrol ether (60-80 °C) in EtOAc, v/v]; ¹H NMR (400 MHz, CDCl₃) δ 7.85-7.75 (4H, m, Ph), 7.52-7.32 (12H, m, Ph), 7.25-7.09 (9H, m, Ph), 5.81 (1H, dd, J 9.5 and 5.5, CHPh), 5.10 (1H, dd, J 8.5 and 5.5, CHCO), 3.33 (3H, s, CH₃); ³¹P NMR (162 MHz, CDCl₃) δ 35.2 and 33.3; ¹³C NMR (101 MHz, CDCl₃) δ 167.7, 135.3 (d, J 1.5), 132.3, 132.2 (×2), 132.1 (×2), 132.0 (×3), 131.9 (×2), 131.8 (×2), 131.7 (×2), 131.3, 130.5, 130.4 (×2), 129.9, 128.7, 128.4 (×2), 128.3 (×2), 128.2 (×3), 128.0, 127.2, 77.0 (t, J 26.0), 76.2 (t, J 25.0); m/z (+ESI) found: MH⁺ 597.1602 (C₃₄H₃₉O₃P₂⁺ requires 597.1590); (found: C, 67.89%; H, 5.10%; C₃₄H₃₉O₃P₂ 0.25 H₂O requires C, 67.94%; H, 5.11%).

(2R,3R)-Ethyl 2-chloro-3-(diphenylphosphinoyloxy)-4-methylpentanoate 15: to a stirred solution of diol 14 (0.600 g, 3.4 mmol) in pyridine (15 cm³) under argon was added diphenylphosphinoyl chloride...
(2.6 cm³, 14 mmol) and the solution was stirred for 48 hours before it was quenched with half-saturated aqueous NaHCO₃ (30 cm³). The mixture was extracted with EtOAc (3 × 40 cm³) and the combined organic phases were evaporated in vacuo. The residue was dissolved in CH₂Cl₂ (40 cm³) and saturated aqueous NaHCO₃ (60 cm³), the organic phase dried with Na₂SO₄, filtered, and evaporated in vacuo. Purification by DCVC [id 4 cm; 20 cm³ fractions; 0-100% EtOAc in petrol ether (60-80 °C) (v/v) – 10% increments; then 5-20% MeOH in EtOAc (v/v) – 5% increments] gave chloride 15 as colourless crystals (0.610 g, 45%); [α]ᵢ²²D −6.6 (c. 0.80, CHCl₃); mp 66-68 °C; Rᵣ 0.40 [40% petrol ether (60-80 °C) in EtOAc, v/v]; ¹H NMR (400 MHz, CDCl₃) δ 7.84-7.74 (4H, m, Ph), 7.51-7.37 (6H, m, Ph), 4.90-4.82 (1H, m, CHOP), 4.58 (1H, d, J 6.5, CHCl), 3.96-3.78 (2H, m, CH₂), 2.27 (1H, dq, J 13.5 and 6.5, CHCH₃), 1.19-1.11 (3H, m, CH₃CH₂), 0.94 (3H, d, J 7.0, CH₂CH), 0.83 (3H, d, J 7.0, CH₂CH); ³¹P NMR (162 MHz, CDCl₃) δ 32.0; ¹³C NMR (101 MHz, CDCl₃) δ 167.3, 132.2 (d, J 137.0 Hz), 132.1 (d, J 137.0), 132.1 (d, J 2.5), 131.5 (d, J 10.5), 128.4 (d, J 13.5), 80.4 (d, J 7.0), 62.2, 58.5 (d, J 3.5), 29.8 (d, J 3.5), 19.0, 17.0, 13.7; m/z (+ESI) found MH⁺ 395.1163 (C₂₀H₂₅ClO₄P⁺ requires 395.1174); (found: C, 60.71%; H, 6.08%; C₂₀H₂₄ClO₄P requires C, 60.84%; H, 6.13%).

(1'R,2'R)-1-Diphenylphosphinoyloxy-2-hydroxy-1,2-diphenylethane 16: to a stirred solution of diol 4 (0.214 g, 1.0 mmol) in pyridine (5 cm³) under argon was added diphenylphosphinoyl chloride (0.19 cm³, 1.0 mmol) and the solution was stirred for 48 hours before it was quenched with half-saturated aqueous NaHCO₃ (20 cm³). The mixture was extracted with EtOAc (2 × 30 + 20 cm³) and the combined organic phases were evaporated in vacuo. The residue was dissolved in dichloromethane (25 cm³) and saturated aqueous NaHCO₃ (40 cm³), the organic phase dried with Na₂SO₄, filtered, and evaporated in vacuo. Purification by DCVC [id 4 cm; 20 cm³ fractions; 0-100% EtOAc in petrol ether (60-80 °C) (v/v) – 10% increments] gave phosphinate 16 as a clear colourless oil (0.100 g, 24%). A sample of 16 was recrystallised from CHCl₃ : petrol ether (60-80 °C) (v/v) – 10% increments] gave phosphinate 16 as a clear colourless oil (0.100 g, 24%). A sample of 16 was recrystallised from CHCl₃ : petrol ether (60-80 °C) (v/v) – 10% increments] gave phosphinate 16 as a clear colourless oil (0.100 g, 24%).
extracted with sulfate buffer (20 cm³) and saturated aqueous NaHCO₃ (20 cm³). The organic phase was dried with Na₂SO₄, filtered, and evaporated in vacuo. Purification by DCVC [id 4 cm; 20 cm³ fractions; 0-100% EtOAc in petrol ether (60-80 °C) (v/v) – 10% increments; then 5-20% MeOH in EtOAc (v/v) – 10% increments] gave bis-phosphinate 17 as clear colourless oil (0.220 g, 36%); [α]²²D +53.2 (c. 0.95, CHCl₃); Rf 0.35 (EtOAc); 1H NMR (400 MHz, CDCl₃) δ 7.81-7.76 (4H, m, Ph), 7.55-7.49 (4H, m, Ph), 7.40-7.35 (2H, m, Ph), 7.28-7.23 (6H, m, Ph), 7.14-7.10 (4H, m, Ph), 7.02-6.88 (10H, m, Ph), 5.75-5.67 (2H, m, CΗOP); 31P NMR (162 MHz, CDCl₃) δ 32.5; 13C NMR (101 MHz, CDCl₃) δ 135.9 (d, J 1.5), 132.2, 132.0, 131.9 (×2), 131.8, 131.7 (×3), 131.6, 131.5 (d, J 140.0), 131.3 (d, J 133.5), 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 79.4 (t, J 6.0); m/z (ESI+) found: MH⁺ 615.1848 (C₃₈H₃₃O₄P₂⁺ requires 615.1849); (found: C, 73.46%; H, 5.27%; C₃₈H₃₂O₄P₂ 0.33 H₂O requires C, 73.54%; H, 5.31%).

(1R,2S)-2-Chloro-1,2-diphenyl-1-diphenylphosphinoyloxyethane 8: to a stirred solution of hydroxy-phosphinate 16 (60 mg, 0.145 mmol) in pyridine (5 cm³) under argon was added diphenylphosphinoyl chloride (0.58 mmol) and the solution was stirred for 48 hours before it was quenched with half-saturated aqueous NaHCO₃ (20 cm³). The mixture was extracted with EtOAc (3 × 20 cm³) and the combined organic phases were evaporated in vacuo. The residue was dissolved in dichloromethane (50 cm³) and saturated aqueous NaHCO₃ (50 cm³), the organic phase dried with Na₂SO₄, filtered, and evaporated in vacuo to give crude chloro-phosphinate 8 (>95% conversion by 1H NMR).

Reaction of diol 4 with Ph₂PCl₃ in pyridine: to a solution of Ph₂PCl (0.72 cm³, 4.0 mmol) in CCl₄ (20 cm³) under argon at −15 °C was added SO₂Cl₂ (0.32 cm³, 4.0 mmol) (dropwise), and the mixture was stirred for 2 hours at −15 to −10 °C. The solvent was removed in vacuo to give Ph₂PCl₃ as a white crystalline solid. The solid was dissolved in pyridine under argon and diol 4 (0.86 g, 4.0 mmol) was added. The reaction was stirred at ambient temperature for 48 hours. Evaporation of the pyridine gave a crude product containing diol 4, chloro-phosphinate 8 and hydroxy-phosphinate 16 in a 43:31:26 ratio (by 1H NMR).

(4R,5R)-5-Azido-1,5-diphenyl-4-diphenylphosphinoyloxy-pentan-1-one 21: chloride 5 (0.25 g, 0.51 mmol) was dissolved in anhydrous DMF (5 cm³). To the stirred solution, at room temperature under argon, sodium azide (40 mg, 0.62 mmol) was added and the reaction mixture heated to 120 °C. After 28 hours the reaction was transferred to a separatory funnel with water (25 cm³) and brine (10 cm³) and extracted with ethyl acetate (50 + 2 × 25 cm³). The combined organic phases were extracted with aqueous sulfate buffer (25 cm³), saturated aqueous NaHCO₃ (25 cm³), dried (Na₂SO₄), filtered and concentrated in vacuo to give a yellow gum. The product was purified by DCVC [id 4 cm; 20 cm³ fractions; 2 × hexanes, 10-100% EtOAc in hexanes (v/v) – 10% increments; 5 × EtOAc] to give 0.17 g (67%) of azide 21 as yellow needles. [α]²²D +62 (c. 1.2, CHCl₃); mp 91-92 °C (EtOAc, hexanes); Rf 0.35 (50% EtOAc in hexanes, v/v); m/z (+ESI) found: MNa⁺, 518.1619. (C₃₈H₃₂N₃O₃PNa requires M, 518.1609); IR νmax(CHCl₃)/cm⁻¹ 2103 (N₃), 1684 (C=O) 1439 (P-Ph) and 1224 (P=O); ¹H NMR (500
(1R,2R)-1-Azido-2-diphenylphosphinoyloxy-1-phenylpropane 22: to a stirred solution of chlorophosphinate 7 (0.370 g, 1.0 mmol) in DMF (20 cm³) under argon was added sodium azide (0.260 g, 4.0 mmol) and the mixture was stirred at 120 °C. After 48 hours heating was stopped, water (20 cm³) and brine (20 cm³) were added and the aqueous phase was extracted with EtOAc (3 × 25 cm³), the combined organic phases were extracted with sulfate buffer (25 cm³) followed by saturated aqueous NaHCO₃ (25 cm³), dried with Na₂SO₄, filtered, and evaporated in vacuo. Purification by DCVC [id 4 cm; 20 cm³ fractions; 0-100% EtOAc in petrol ether (60-80 °C) (v/v) – 10% increments] gave azido-phosphinate 22 as a clear light yellow oil (0.280 g, 74%); [α]D⁻⁹⁴.⁵ (c. 1.7, CHCl₃); Rf 0.30 [40% petrol ether (60-80 °C) in EtOAc, v/v]; ¹H NMR (400 MHz, CDCl₃) δ 7.87-7.72 (4H, m, Ph), 7.45-7.31 (6H, m, Ph), 7.30-7.19 (5H, m, Ph), 4.71-4.59 (2H, m, CH₂), 1.18 (3H, d, J 6.0, CH₃); ³¹P NMR (162 MHz, CDCl₃) δ 32.1; ¹³C NMR (101 MHz, CDCl₃) δ 135.7, 132.2 (d, J 139.5), 132.1 (d, J 3.0), 131.7 (d, J 10.5), 131.5 (d, J 10.0), 131.4 (d, J 136.0), 128.7 (s), 128.5 (d, J 13.0), 128.4 (d, J 13.5), 127.8, 74.9 (d, J 6.5), 70.5 (d, J 6.5), 19.0 (d, J 1.5); m/z (ESI+) found: MH⁺ 378.1374 (C₂₁H₂₁N₃O₂P⁺ requires 378.1366); (found: C, 65.43%; H, 5.36%; N, 10.79%; C₂₁H₂₀N₃O₂P 0.5 H₂O requires C, 65.28%; H, 5.48%; N, 10.88%).

(1R,2R)-2-Azido-1,2-diphenyl-1-(diphenylphosphinoyloxy)ethane 23: to a stirred solution of chlorophosphinate 8 (0.110 g, 0.25 mmol) in DMF (10 cm³) under argon was added sodium azide (0.066 g, 1.0 mmol) and the mixture was stirred at 120 °C. After 48 hours heating was stopped, water (10 cm³) and brine (10 cm³) were added and the aqueous phase was extracted with EtOAc (2 × 30 + 10 cm³), the combined organic phases were extracted with sulfate buffer (30 cm³), saturated aqueous NaHCO₃ (30 cm³), dried with Na₂SO₄, filtered, and evaporated in vacuo. Purification by DCVC [id 4 cm; 20 cm³ fractions; 0-100% EtOAc in petrol ether (60-80 °C) (v/v) – 10% increments] gave azido-phosphinate 23 as a clear light yellow oil (0.060 g, 55%); [α]D⁻⁴⁴.⁴ (c. 0.23, CHCl₃); Rf 0.35 [40% petrol ether (60-80 °C) in EtOAc, v/v]; ¹H NMR (400 MHz, CDCl₃) δ 7.88-7.72 (2H, m, Ph), 7.61-7.41 (5H, m, Ph), 7.39-7.31 (1H, m, Ph), 5.48 (1H, dd, J 9.5 and 7.5, CH₃O), 4.97 (1H, d, J 7.5, CH₂N₃); ³¹P NMR (162 MHz, CDCl₃) δ 33.4; ¹³C NMR (101 MHz, CDCl₃) δ 136.3 (d, J 2.5), 135.0, 132.2 (d, J 3.0), 131.9 (d, J 3.0), 131.8 (d, J 10.5 Hz), 131.6 (d, J 139.5), 131.6 (d, J 10.5), 131.1 (d, J 134.5), 128.5, 128.4 (s), 128.2 (s), 128.0, 127.9, 127.5, 79.8 (d, J 6.0), 70.7 (d, J 5.5); m/z
(ESI+) found: MH+ 440.1541 (C26H23N3O2P+ requires 440.1522); (found: C, 69.72%; H, 5.07%; N, 8.87; C26H22N3O2P·2/3H2O requires C, 69.17%; H, 5.21%; N, 9.31%).

(4R,5R)-5-Azido-4-hydroxy-1,5-diphenylpentan-1-one 24: to a stirred solution of azido-phosphinate 21 (0.049 g, 0.10 mmol) in methanol (5 cm³) under argon was added potassium carbonate (0.055 g, 0.40 mmol). After stirring overnight the reaction mixture was evaporated to dryness and the residue purified by DCVC [id 4 cm; 20 cm³ fractions; 0-100% EtOAc in petrol ether (60-80 °C) (v/v) – 10% increments] to give azido-alcohol 24 as a clear colourless oil (22 mg, 75%); [α]22D −90.0 (c. 1.2, CHCl3); Rf 0.50 [50% petrol ether (60-80 °C) in EtOAc, v/v]; 1H NMR (500 MHz, CDCl3) δ 7.92-7.88 (2H, m, Ph), 7.54-7.49 (1H, m, Ph), 7.44-7.29 (7H, m, Ph), 4.40 (1H, d, J 7.5, CHN3), 3.85-3.78 (1H, m, CHOH), 3.18-3.01 (2H, m, CH2OH), 2.68 (1H, br s, OH), 1.78-1.68 (2H, m, CH2C=O); 13C NMR (126 MHz, CDCl3) δ 200.0, 136.7, 136.3, 133.1, 129.0, 128.8, 128.5, 128.4, 128.0, 127.8, 73.9, 72.1, 60.4, 34.6, 27.3; m/z (ESI+) found: MNa+ 318.1201 (C17H17N3O2Na+ requires 318.1213).

(1R,2R)-1-Azido-1-phenylpropan-2-ol 25: to a stirred solution of azido-phosphinate 22 (0.034 g, 0.10 mmol) in methanol (2 cm³) under argon was added potassium carbonate (0.028 g, 0.20 mmol). After stirring overnight the reaction mixture was evaporated to dryness and the residue purified by DCVC [id 4 cm; 20 cm³ fractions; 0-100% EtOAc in petrol ether (60-80 °C) (v/v) – 10% increments] to give azido-alcohol 25 as a clear light yellow oil (15 mg, 86%); [α]22D −167.8 (c. 1.0, CHCl3); Rf 0.40 [40% petrol ether (60-80 °C) in EtOAc, v/v]; 1H NMR (500 MHz, CDCl3) δ 7.42-7.27 (5H, m, Ph), 4.30 (1H, d, J 8.0, CHN3), 3.92-3.84 (1H, m, CHOH), 2.43 (1H, br s, OH), 1.03 (3H, d, J 6.5, CH3); 13C NMR (126 MHz, CDCl3) δ 136.6, 128.9, 128.7, 73.3, 70.8, 19.1; m/z (ESI+) found: MNa+ 200.0792 (C9H11N3ONa+ requires 200.7943).

(1R,2R)-2-Azido-1,2-diphenylethanol 26: to a stirred solution of azido-phosphinate 23 (0.060 g, 0.14 mmol) in methanol (3 cm³) under argon was added potassium carbonate (0.028 g, 0.20 mmol). After stirring overnight the reaction mixture was evaporated to dryness and the residue purified by DCVC [id 4 cm; 20 cm³ fractions; 0-100% EtOAc in petrol ether (60-80 °C) (v/v) – 10% increments] to give azido-alcohol 26 as a clear light yellow oil (19 mg, 57%); [α]22D −85.4 (c. 0.85, CHCl3); Rf 0.65 [40% petrol ether (60-80 °C) in EtOAc, v/v]; 1H NMR (500 MHz, CDCl3) δ 7.26-7.17 (6H, m, Ph), 7.11-7.05 (4H, m, Ph), 4.74 (1H, d, J 8.0, CHF), 4.68 (1H, d, J 7.5, CHF), 2.79 (1H, br s, OH); 13C NMR (126 MHz, CDCl3) δ 139.2, 136.0, 128.5, 128.2, 128.1 (×2), 127.8, 126.8, 78.0, 72.9; m/z (ESI+) found: MNa+ 262.0943 (C14H13N3ONa+ requires 262.0951). Data consistent with that previously reported.9

(2R,3R)-2,3-Diphenyloxirane 27: to a stirred solution of chloro-phosphinate 8 (0.200 g, 0.46 mmol) in methanol (10 cm³) under argon was added potassium carbonate (0.256 g, 1.85 mmol). After stirring overnight the reaction mixture was evaporated to dryness and the residue purified by DCVC [id 4 cm; 20 cm³ fractions; 0-100% EtOAc in petrol ether (60-80 °C) (v/v) – 10% increments] to give epoxide 27 as white crystals (0.078 g, 86%); [α]22D +250.8 (c. 0.85, CHCl3), (lit. [α]22D +239.2).10 NMR data
consistent with that previously reported. The $^1$H NMR spectrum of the crude product showed no trace of cis-epoxide product.

(1'R,2'S)-2-Azido-1,2-diphenylethanol 28: to a stirred solution of epoxide 27 (0.020 g, 0.10 mmol) in wet DMF (5 cm$^3$) under argon was added sodium azide (0.054 g, 0.83 mmol) and the mixture was stirred at 100 °C. After 48 hours heating was stopped and half-saturated aqueous NaHCO$_3$ (20 cm$^3$) was added. The mixture was extracted with EtOAc (3 × 20 cm$^3$), the combined organic phases washed with sulfate buffer (20 cm$^3$), saturated aqueous NaHCO$_3$ (20 cm$^3$), dried with Na$_2$SO$_4$, filtered, and evaporated in vacuo. Purification by DCVC [id 4 cm; 20 cm$^3$ fractions; 0-100% EtOAc in petrol ether (60-80 °C) (v/v) – 10% increments] gave azido-alcohol 28 as a clear light yellow oil 0.018 g (75%); $[\alpha]_{D}^{22} +67.8$ (c. 0.90, CHCl$_3$) (lit. $[\alpha]_{D}^{22} +44$); $R_f$ 0.30 [40% petrol ether (60-80 °C) in EtOAc, v/v]; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.38-7.22 (10H, m, Ph), 4.71-4.59 (1H, br d, $J$ 6.5, CH$_2$OH), 4.68 (1H, d, $J$ 7.0, CH$_2$N$_3$), 2.09 (1H, br d, $J$ 2.5, OH); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 139.6, 135.9, 128.7, 128.6, 128.4, 128.3, 128.0, 127.0, 77.0, 71.2; $m/z$ (+ESI) found: MNa$^+$ 262.0939 (C$_{14}$H$_{13}$N$_3$ONa$^+$ requires 262.0951). NMR data consistent with that previously reported.

(1'R,2'R,1''S)-{2'-(1''-Hydroxy-1''-phenyl)-methyl}-cyclopropyl]-1-phenyl-methanone 30: to a stirred solution of chloro-phosphinate 5 (0.049 g, 0.10 mmol) in methanol (2 cm$^3$) under argon was added potassium carbonate (0.038 g, 0.27 mmol) and after stirring for 48 hours the reaction mixture was evaporated in vacuo. Purification by DCVC [id 4 cm; 20 cm$^3$ fractions; 0-100% EtOAc in petrol ether (60-80 °C) (v/v) – 10% increments] gave cyclopropane 30 as a white amorphous solid (0.020 g, 79%). Data consistent with that previously reported.

(1'R,2'R,1''S)-{2'-(1''-Azido-1''-phenyl)-methyl}-cyclopropyl]-1-phenyl-methanone 31 and (1'S,2'R,1''S)-{2'-(1''-azido-1''-phenyl)-methyl}-cyclopropyl]-1-phenyl-methanone 32: ketone 21 (0.13 g, 0.26 mmol) was dissolved in anhydrous THF (5 cm$^3$) under argon and cooled to -78 °C. Freshly prepared LDA (0.27 mmol) in anhydrous THF (3 cm$^3$) cooled to -78 °C was added by cannula and the reaction mixture stirred at -78 °C for 2 hours and then warmed to 0 °C. The reaction was maintained at 0 °C for 4 hours and then allowed to warm to room temperature overnight (16 hours). Saturated aqueous NH$_4$Cl (10 cm$^3$) was added and the mixture transferred to a separatory funnel with water (10 cm$^3$) and extracted with CH$_2$Cl$_2$ (3 × 25 cm$^3$). The combined organic phases were dried with Na$_2$SO$_4$, filtered and concentrated in vacuo to give a yellow gum. The product was purified by DCVC [id 4 cm; 25 cm$^3$ fractions; 0-50% EtOAc in hexanes – 5% increments; two fractions of each solvent mixture were collected] to give 34 mg (47%) of cyclopropanes 31 and 32 in a 9:1 ratio. An analytically pure sample of cyclopropane 31 was obtained. Analytical data for cyclopropane 31: $[\alpha]_{D}^{22} −100$ (c. 0.6, CHCl$_3$); $R_f$ 0.35 (15% EtOAc in hexanes, v/v); $m/z$ (+ESI) found: MNa$^+$, 300.1106. C$_{17}$H$_{15}$N$_3$ONa$^+$ requires M, 300.1106; IR $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 2097 (N$_3$) and 1669 (C=O); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.87-7.85 (2H, m, ortho-PhC=O), 7.55 (1H, tt, $J$ 7.5 and 1.0, meta-PhC=O), 7.44-7.33 (5H, m, Ph), 4.40 (1H, d, $J$ 6.5, PhCH)$_2$, 2.68 (1H, dt, $J$ 8.5 and 4.5, CHC=O), 2.11 (1H, dt, $J$ 8.5, 6.5 and 4.0,
CHCHN₃), 1.63 (1H, ddd, J 9.0, 5.0 and 4.0, CH₂H₁b), 1.32 (1H, ddd, J 8.5, 6.5 and 4.0, CH₂H₁a); ¹³C NMR (126 MHz; CDCl₃) δ 198.6 (C₁), 138.3, 137.5 (2 × ipso-Ph), 133.0, 128.9, 128.7, 128.5, 128.0, 127.1 (6 × Ph), 66.8 (C₁'''), 29.0 (C₂'''), 21.9 (C₁’) and 16.0 (C₃’). NMR data for cyclopropane 32 (extracted from NMR spectra of a mixture of 31 and 32. Peaks were overlapping in the aromatic region): H NMR (500 MHz; CDCl₃) δ 7.70-7.68 (2H, m, ortho-PhC=O), 7.44-7.33 (6H, m, Ph), 4.54 (1H, d, J 10.0, PhCH), 2.78 (1H, ddd, J 9.0, 7.5 and 5.5, CHC=O), 2.04 (1H, dtd, J 9.0, 8.5 and 7.0, CHCHN₃), 1.84 (1H, ddd, J 7.0, 5.5 and 4.5, CH₂H₁b), 1.44 (1H, td, J 8.0 and 4.5, CH₂H₁a); ¹³C NMR (126 MHz; CDCl₃) δ 198.8 (C₁), 139.2, 138.6 (2 × ipso-Ph), 132.7, 128.3, 127.8, 126.7, (4 × Ph, two phenyl peaks were overlapping with compound 31 peaks and could not be identified), 63.3 (C₁''), 30.2 (C₂''), 22.1 (C₁’) and 14.5 (C₃’).

Crystal data for chloro phosphinate 6: C₂₇H₃₀ClO₄P, M = 484.93, Orthorhombic, P₂₁₂₁₂₁, a = 5.8203(10), b = 11.4038(2), c = 37.8022(9) Å, α = 90°, β = 90°, γ = 90°, V = 2509.1(4) Å³, Z = 4, µ(Mo-Kα) = 0.247 mm⁻¹, 10165 reflections collected at 180(2) K using an Oxford Cryosystems Cryostream cooling apparatus, 4316 unique (Rint = 0.056); R₁ = 0.053, wR² = 0.127 [I > 2σ(I)]. Absolute structure parameter 0.02(10).

The structure was solved with SHELXS-97,¹³ and refined with SHELXL-97.¹³ CCDC reference number 600429. See http://www.rsc.org/suppdata for crystallographic data in .cif or other electronic format.

References