Thiourea-Catalyzed Enantioselective Hydrophosphonylation of Imines: Practical Access to Enantiomerically Enriched α -Amino Phosphonic Acids

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Supporting Information

General Procedures. All hydrophosphonylation reactions were performed in oven dried 4-mL to 15-mL vials using unpurified commercial diethyl ether. The vials were sealed with plastic screw caps, and the reactions were run under an ambient atmosphere. All other reactions were performed under an atmosphere of nitrogen in oven-dried or flame-dried round bottomed flasks fitted with rubber septa and/or glass stoppers. Stainless steel syringes or cannulae were used to transfer moisture sensitive liquids.

Materials. Commercial reagents were used as received with the following exceptions: dichloromethane was distilled from calcium hydride at 760 Torr, and toluene was distilled from sodium at 760 Torr. Flash chromatography was performed using silica gel 60 (230-400 mesh), purchased from EM Science. Catalysts **1a**¹ and **1b**² were prepared as previously described.

Instrumentation. Proton nuclear magnetic resonance (¹H NMR) spectra, carbon nuclear magnetic resonance (¹³C NMR) spectra, and phosphorus nuclear magnetic resonance (³¹P NMR) spectra were recorded on Varian-Mercury-400 (400 MHz) or an Inova-500 (500 MHz). Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent (CHCl₃: δ 7.26; H₂O: δ 4.79). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent (CDCl₃: δ 77.16) or to dioxane as an internal standard in D₂O (dioxane: δ 77.16). Chemical shifts for phosphorus are reported in parts per million downfield from phosphoric acid (H₃PO₄) and are referenced to 85% H₃PO₄ as an external standard. All phosphorus nuclear magnetic resonance spectra are proton-decoupled unless indicated otherwise. Data are presented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz), and assignment. Infrared (IR) spectra were obtained on a Mattson Galaxy Series FTIR 3000 spectrophotometer referenced to a polystyrene standard. Data are presented as follows: frequency of absorption (cm⁻¹) and intensity of absorption (s = strong, m = medium, w = weak). Optical rotations were measured using a 2 mL cell with a 1 dm path length on a Jasco DIP 370 digital polarimeter. Melting points were measured on a Mel-Temp apparatus and are uncorrected. The mass spectroscopic data were obtained at the Harvard University mass spectrometry facility. Chiral HPLC analysis was performed on a Shimadzu VP-series instrument.

Reaction scheme showing the synthesis of various chiral amide products (1a-1k) from starting materials 3h and 2c, catalyzed by catalyst 1 (10 mol%) in Et₂O (0.4 M) at 4° C.

Starting materials:

- 3h: 2,4-dinitrobenzoic acid derivative
- 2c: Chiral amine derivative

Reaction conditions:

- Catalyst 1 (10 mol%)
- Et₂O (0.4 M)
- 4° C

Products and their yields/ee values:

- 1a: 85% conversion, 85% ee
- 1b: 98% conversion, 90% ee
- 1c: 96% conversion, 89% ee
- 1d: 95% conversion, 89% ee
- 1e: 83% conversion, 67% ee
- 1f: 87% conversion, 86% ee
- 1g: 87% conversion, 76% ee
- 1h: 66% conversion, 64% ee
- 1i: 92% conversion, 84% ee
- 1j: 92% conversion, 93% ee
- 1k: 87% conversion, 90% ee

Product 4c is also shown as a byproduct of the reaction.

Catalysts **1b** and **1j** were selected for further comparison.

II. Comparison of Catalysts **1b** and **1j**.

substrate	catalyst	time (h)	% conv ^a	% ee
2a	thiourea 1b	48	87	98
	urea 1j	77	81	96
2g	thiourea 1b	48	86	98
	urea 1j	77	74	97
2b	thiourea 1b	24	95	96
	urea 1j	30	69	92
2c	thiourea 1b	24	98	90
	urea 1j	24	92	93
2e	thiourea 1b	30	79	93
	urea 1j	30	46	93

^a Determined by $^1\text{H-NMR}$.

Thiourea catalyst **1b** is generally superior to urea catalyst **1j** in terms of both reaction rate and enantioselectivity. Hydrophosphonylation of imine **2c** provides the lone exception. Thiourea **1b** was selected as the optimal catalyst and was employed in the exploration of additional imine substrates **2** (see Table 2).

III. Imine Preparation.³

2a (representative experimental procedure for imine preparation): A 250-mL round bottomed flask was charged with 30 g of 3Å molecular sieves. The molecular sieves were flame-dried and the flask was placed under nitrogen. The flask was charged with dichloromethane (50 mL) and benzaldehyde (4.24 g, 40.0 mmol, 1.02 equiv).

Benzylamine (4.20 g, 39.2 mmol, 1.0 equiv) was added slowly over two minutes. The reaction was monitored by ¹H NMR. After 3 h, the reaction was vacuum filtered to remove the molecular sieves and was concentrated *in vacuo*. The crude oil was purified by vacuum distillation (118°C, 0.05 mm Hg) to provide **2a** (5.82 g, 29.8 mmol, 76%) as a colorless liquid. IR (thin film, cm⁻¹) 3084 (w), 3063 (m), 3028 (m), 2870 (m), 2837 (m), 1643 (s), 1495 (m), 1452 (s), 1312 (m), 1026 (m); ¹H NMR (500 MHz, CDCl₃) δ 8.41 (1H, s, CH=N), 7.81-7.78 (2H, m, ArH), 7.44-7.40 (3H, m, ArH), 7.37-7.33 (4H, m, ArH), 7.29-7.25 (1H, m, ArH), 4.84 (2H, d, *J* = 1.5 Hz, CH₂-N); ¹³C NMR (101 MHz, CDCl₃) δ 161.8, 139.3, 136.1, 130.7, 128.5, 128.5, 128.2, 127.9, 126.9, 65.0; HRMS (EI) *m/z* for C₁₄H₁₃N [M]⁺ calcd. 195.1048, found 195.1048.

2b: Reaction was performed on a 40 mmol scale using 2-ethylbutyraldehyde (4.84 g, 48.3 mmol) and benzylamine (4.32 g, 40.3 mmol). The product was purified by vacuum distillation (80°C, 0.05 mm Hg) to provide **2b** (5.72 g, 30.2 mmol, 75%) as a colorless liquid. IR (thin film, cm⁻¹) 3063 (w), 3030 (m), 2963 (s), 2930 (s), 2876 (s), 1667 (s), 1495 (m), 1454 (s), 1377 (m), 1028 (m); ¹H NMR (500 MHz, CDCl₃) δ 7.55 (1H, d, *J* = 6.8 Hz, CH=N), 7.35-7.30 (2H, m, ArH), 7.27-7.22 (3H, m, ArH), 4.59 (2H, s, CH₂-N), 2.17-2.09 (1H, m, CH(CH₂CH₃)₂), 1.57-1.44 (4H, m, CH₂CH₃), 0.91 (6H, t, *J* = 7.3 Hz, CH₃); ¹³C NMR (101 MHz, CDCl₃) δ 170.2, 139.3, 128.3, 127.7, 126.7, 64.8, 48.1, 25.0, 11.6; HRMS (ES) *m/z* for C₁₃H₂₀N [M+H]⁺ calcd. 190.1595, found 190.1600.

2c: Reaction was performed on a 40 mmol scale using isobutyraldehyde (5.77 g, 80 mmol) and benzylamine (4.32 g, 40.3 mmol). The product was purified by vacuum distillation (123°C, 30 mm Hg) to provide **2c** (4.42 g, 27.4 mmol, 68%) as a colorless liquid. IR (thin film, cm⁻¹) 3030 (m), 2965 (s), 2874 (s), 1670 (s), 1495 (m), 1454 (s), 1368 (m), 1030 (w); ¹H NMR (500 MHz, CDCl₃) δ 7.68-7.65 (1H, m, CH=N), 7.35-7.30 (2H, m, ArH), 7.27-7.22 (3H, m, ArH), 4.56 (2H, s, CH₂-N), 2.56-2.46 (1H, m, CH(CH₃)₂), 1.12 (6H, d, *J* = 6.8 Hz, CH₃); ¹³C NMR (101 MHz, CDCl₃) δ 171.0, 139.5, 128.4, 127.8, 126.9, 64.9, 34.2, 19.4; LRMS (CI) *m/z*: 161.8 (100%) [M+H]⁺.

2d: Reaction was performed on a 38 mmol scale using cyclohexancarboxaldehyde (4.44 g, 39.6 mmol) and benzylamine (4.04 g, 37.7 mmol). The product was purified by vacuum distillation (111°C, 0.05 mm Hg) to provide **2d** (5.86 g, 29.1 mmol, 77%) as a colorless liquid. IR (thin film, cm⁻¹) 3044 (w), 2990 (m), 2926 (m), 1667 (s), 1495 (s), 1451 (s), 1343 (m), 1028 (m), 966 (m); ¹H NMR (500 MHz, CDCl₃) δ 7.64 (1H, d, *J* = 4.9 Hz, CH=N), 7.34-7.30 (2H, m, ArH), 7.26-7.22 (3H, m, ArH), 4.55 (2H, s, CH₂-N), 2.29-2.20 (1H, m, *c*-hexH), 1.88-1.64 (5H, *c*-hexH), 1.36-1.16 (5H, m, *c*-hexH); ¹³C NMR (101 MHz, CDCl₃) δ 170.2, 139.6, 128.4, 127.8, 126.8, 65.0, 43.6, 29.7, 26.0, 25.5; LRMS (CI) *m/z*: 201.8 (100%) [M+H]⁺.

2e: Reaction was performed on a 40 mmol scale using trimethylacetaldehyde (3.81 g, 44.2 mmol) and benzylamine (4.32 g, 40.3 mmol). The product was purified by vacuum distillation (129°C, 30 mm Hg) to provide **2e** (4.87 g, 27.8 mmol, 69%) as a colorless liquid. IR (thin film, cm⁻¹) 2959 (s), 2812 (s), 1667 (s), 1497 (m), 1476 (m), 1454 (s), 1366 (s), 1208 (w), 1051 (w), 1030 (w); ¹H NMR (500 MHz, CDCl₃) δ 7.66 (1H, s, CH=N), 7.34-7.30 (2H, m, ArH), 7.27-7.22 (3H, m, ArH), 4.58 (2H, s, CH₂-N), 1.12 (9H, s, (CH₃)₃); ¹³C NMR (101 MHz, CDCl₃)

δ 173.5, 139.8, 128.4, 127.6, 126.8, 64.6, 36.4, 27.0; HRMS (CI) m/z for $C_{12}H_{18}N$ $[M+H]^+$ calcd. 176.1439, found 176.1440.

2f: Reaction was performed on a 40 mmol scale using 3-methyl-2-butenal (4.01 g, 47.7 mmol) and benzylamine (4.32 g, 40.3 mmol). The product was purified by vacuum distillation (112°C, 0.05 mm Hg) to provide **2f** (4.33 g, 25.0 mmol, 62%) as a red-orange liquid. IR (thin film, cm^{-1}) 3028 (m), 2864 (s), 1651 (s), 1451 (s), 1377 (s), 1204 (m), 855 (m), 733 (s); 1H NMR (500 MHz, $CDCl_3$) δ 8.28 (1H, d, $J = 9.3$ Hz, $CH=N$), 7.35-7.22 (5H, m, ArH), 6.09-6.06 (1H, m, $CH=C$), 4.65 (2H, s, CH_2-N), 1.95 (3H, s, CH_3), 1.89 (3H, s, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0, 146.7, 139.4, 128.2, 127.7, 126.6, 125.3, 65.1, 26.3, 18.4; HRMS (EI) m/z for $C_{12}H_{15}N$ $[M]^+$ calcd. 173.1204, found 173.1204.

2g: Reaction was performed on a 39 mmol scale using 4-fluorobenzaldehyde (4.98 g, 40.1 mmol) and benzylamine (4.22 g, 39.4 mmol). The product was purified by vacuum distillation (120°C, 0.05 mm Hg) to provide **2g** (5.97 g, 28.0 mmol, 71%) as a pale yellow liquid. IR (thin film, cm^{-1}) 3063 (m), 3030 (m), 2841 (m), 1643 (s), 1601 (s), 1508 (s), 1231 (s), 1152 (m), 1028 (m), 837 (s); 1H NMR (500 MHz, $CDCl_3$) δ 8.36 (1H, s, $CH=N$), 7.81-7.76 (2H, m, ArH), 7.38-7.26 (5H, m, ArH), 7.14-7.08 (2H, m, ArH), 4.82 (2H, s, CH_2-N); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2 (d, $J = 251$ Hz), 160.2 (s), 139.2 (s), 132.4 (d, $J = 2.8$ Hz), 130.1 (d, $J = 8.7$ Hz), 128.4 (s), 127.9 (s), 126.9 (s), 115.5 (d, $J = 22.0$ Hz), 64.8 (s); HRMS (EI) m/z for $C_{14}H_{12}FN$ $[M]^+$ calcd. 213.0954, found 213.0956.

2h: Reaction was performed on a 39 mmol scale using 4-methoxybenzaldehyde (5.60 g, 41.1 mmol) and benzylamine (4.19 g, 39.1 mmol). The product was purified by vacuum distillation (145°C, 0.05 mm Hg) to provide **2h** (6.93 g, 30.8 mmol, 75%) as a colorless liquid which slowly solidified to a white crystalline solid. mp = 39-40°C; IR (thin film, cm^{-1}) 3028 (w), 2837 (m), 1647 (s), 1606 (s), 1512 (s), 1452 (m), 1305 (m), 1250 (s), 1029 (m), 832 (m); 1H NMR (500 MHz, $CDCl_3$) δ 8.33 (1H, s, $CH=N$), 7.73 (2H, d, $J = 8.8$ Hz, ArH), 7.37-7.33 (3H, m, ArH), 7.29-7.24 (2H, m, ArH), 6.93 (2H, d, $J = 8.8$ Hz, ArH), 4.79 (2H, s, CH_2-N), 3.85 (3H, s, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.6, 161.1, 139.6, 129.7, 129.1, 128.4, 127.9, 126.8, 113.9, 64.8, 55.1; HRMS (ES) m/z for $C_{15}H_{16}NO$ $[M+H]^+$ calcd. 226.1232, found 226.1225.

2i: Reaction was performed on a 36 mmol scale using methyl 4-formylbenzoate (6.00 g, 36.5 mmol) and benzylamine (3.92 g, 36.6 mmol). The product was purified by recrystallization from hexanes to provide **2i** (5.06 g, 20.0 mmol, 55%) as a white crystalline solid. mp = 91-94°C; IR (thin film, cm^{-1}) 3082 (w), 2953 (w), 2859 (w), 1711 (s), 1643 (s), 1433 (m), 1373 (m), 1279 (s), 1113 (s), 1045 (m), 735 (s); 1H NMR (500 MHz, $CDCl_3$) δ 8.44 (1H, s, $CH=N$), 8.08 (2H, d, $J = 8.1$ Hz, ArH), 7.85 (2H, d, $J = 8.4$ Hz, ArH), 7.39-7.26 (5H, m, ArH), 4.86 (2H, d, $J = 1.5$ Hz, CH_2-N), 3.93 (3H, s, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 160.9, 140.1, 138.9, 131.9, 129.9, 128.6, 128.2, 128.1, 127.2, 65.2, 52.3; LRMS (CI) m/z : 253.7 (100%) $[M+H]^+$.

2j: Reaction was performed on a 40 mmol scale using 2-methylbenzaldehyde (5.07 g, 42.2 mmol) and benzylamine (4.32 g, 40.3 mmol). The product was purified by vacuum distillation (130°C, 0.05 mm Hg) to provide **2j** (6.45 g, 30.8 mmol, 76%) as a colorless liquid. IR (thin film, cm^{-1}) 3063 (s), 3028 (s), 2882 (s), 1638 (s), 1603 (s), 1495 (s), 1452 (s), 1289 (s), 1028 (s), 698 (s); 1H NMR (500 MHz, $CDCl_3$) δ 8.72 (1H, s, $CH=N$), 7.94 (1H, dd, $J = 7.8, 1.5$ Hz, ArH), 7.39-7.18 (8H, m, ArH), 4.86 (2H, d, $J = 1.5$ Hz, CH_2-N), 2.54 (3H, s, ArCH₃); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.6, 139.6, 137.7, 134.2, 130.8, 130.3, 128.5, 127.9, 127.8, 126.9, 126.2, 65.6, 19.4; LRMS (CI) m/z : 209.7 (100%) $[M+H]^+$.

2k: Reaction was performed on a 41 mmol scale using 2-chlorobenzaldehyde (5.99 g, 42.6 mmol) and benzylamine (4.35 g, 40.6 mmol). The product was purified by vacuum distillation (136°C, 0.05 mm Hg) to provide **2k** (6.27 g, 27.3 mmol, 67%) as a colorless

liquid. IR (thin film, cm^{-1}) 3029 (s), 2890 (s), 1634 (s), 1593 (s), 1444 (s), 1373 (s), 1272 (s), 1052 (s), 1028 (s); ^1H NMR (500 MHz, CDCl_3) δ 8.86 (1H, s, $\text{CH}=\text{N}$), 8.10 (1H, dd, $J = 7.3, 1.5$ Hz, ArH), 7.40-7.26 (8H, m, ArH), 4.87 (2H, d, $J = 1.0$ Hz, $\text{CH}_2\text{-N}$); ^{13}C NMR (101 MHz, CDCl_3) δ 158.4, 139.0, 135.1, 133.1, 131.5, 129.6, 128.4, 128.4, 127.9, 127.0, 126.9, 65.2; HRMS (ES) m/z for $\text{C}_{14}\text{H}_{13}\text{ClN}$ $[\text{M}+\text{H}]^+$ calcd. 230.0736, found 230.0731.

2l: Reaction was performed on a 40 mmol scale using 3-chlorobenzaldehyde (5.96 g, 42.4 mmol) and benzylamine (4.32 g, 40.3 mmol). The product was purified by vacuum distillation (143°C, 0.05 mm Hg) to provide **2l** (7.02 g, 30.6 mmol, 76%) as a colorless liquid. IR (thin film, cm^{-1}) 3063 (s), 3028 (s), 2872 (s), 1645 (s), 1570 (s), 1452 (s), 1431 (s), 1373 (s), 1281 (m), 1215 (s), 1074 (s), 1028 (s); ^1H NMR (500 MHz, CDCl_3) δ 8.34 (1H, d, $J = 1.5$ Hz, $\text{CH}=\text{N}$), 7.83-7.81 (1H, m, ArH), 7.64-7.61 (1H, m, ArH), 7.41-7.33 (6H, m, ArH), 7.30-7.28 (1H, m, ArH), 4.83 (2H, s, $\text{CH}_2\text{-N}$); ^{13}C NMR (101 MHz, CDCl_3) δ 160.4, 139.0, 138.0, 134.8, 130.7, 129.9, 128.6, 128.1, 127.9, 127.2, 126.7, 65.0; LRMS (CI) m/z : 229.7 (100%) $[\text{M}+\text{H}]^+$.

2m: Reaction was performed on a 41 mmol scale using 4-chlorobenzaldehyde (5.90 g, 42.0 mmol) and benzylamine (4.44 g, 41.1 mmol). The product was purified by vacuum distillation (142°C, 0.05 mm Hg) to provide **2m** (7.24 g, 31.5 mmol, 77%) as a colorless liquid which slowly solidified to a white crystalline solid. mp = 31-33°C; IR (thin film, cm^{-1}) 3028 (m), 2875 (m), 1643 (s), 1595 (s), 1489 (s), 1452 (s), 1375 (s), 1295 (s), 1087 (s), 1014 (s), 860 (m); ^1H NMR (500 MHz, CDCl_3) δ 8.36 (1H, s, $\text{CH}=\text{N}$), 7.72 (2H, d, $J = 8.3$ Hz, ArH), 7.41-7.32 (5H, m, ArH), 7.29-7.25 (2H, m, ArH), 4.82 (2H, s, $\text{CH}_2\text{-N}$); ^{13}C NMR (101 MHz, CDCl_3) δ 160.5, 139.1, 136.7, 134.7, 129.5, 128.9, 128.6, 128.0, 127.1, 65.0; HRMS (ES) m/z for $\text{C}_{14}\text{H}_{13}\text{ClN}$ $[\text{M}+\text{H}]^+$ calcd. 230.0736, found 230.0726.

2n: Reaction was performed on a 40 mmol scale using 2-naphthaldehyde (6.25 g, 40.0 mmol) and benzylamine (4.32 g, 40.3 mmol). The product was purified by recrystallization from hexanes to provide **2n** (7.31 g, 29.8 mmol, 74%) as a white crystalline solid. mp = 84-86°C; IR (thin film, cm^{-1}) 3057 (m), 3026 (m), 2866 (s), 1638 (s), 1495 (m), 1451 (m), 1350 (m), 1045 (m), 955 (m); ^1H NMR (500 MHz, CDCl_3) δ 8.56 (1H, s, $\text{CH}=\text{N}$), 8.10-8.04 (2H, m, ArH), 7.92-7.84 (3H, m, ArH), 7.56-7.50 (2H, m, ArH), 7.41-7.35 (4H, m, ArH), 7.30-7.26 (1H, m, ArH), 4.90 (2H, s, $\text{CH}_2\text{-N}$); ^{13}C NMR (101 MHz, CDCl_3) δ 162.1, 139.4, 134.8, 133.9, 133.1, 130.2, 128.7, 128.6, 128.5, 128.1, 127.9, 127.2, 127.1, 126.5, 124.0, 65.2; LRMS (CI) m/z : 245.7 (100%) $[\text{M}+\text{H}]^+$.

2o: Reaction was performed on a 41 mmol scale using 3-pyridinecarboxaldehyde (4.56 g, 42.6 mmol) and benzylamine (4.35 g, 40.6 mmol). The product was purified by vacuum distillation (140°C, 0.05 mm Hg) to provide **2o** (4.61 g, 23.5 mmol, 58%) as a colorless liquid. IR (thin film, cm^{-1}) 3029 (m), 2843 (m), 1643 (s), 1589 (m), 1572 (m), 1452 (m), 1420 (s), 1376 (m), 1325 (m), 1187 (m), 1027 (s); ^1H NMR (500 MHz, CDCl_3) δ 8.90 (1H, d, $J = 1.5$ Hz, ArH), 8.66 (1H, dd, $J = 4.9, 1.5$ Hz, ArH), 8.43 (1H, s, $\text{CH}=\text{N}$), 8.19-8.15 (1H, m, ArH), 7.39-7.33 (5H, m, ArH), 7.30-7.26 (1H, m, ArH), 4.86 (2H, s, $\text{CH}_2\text{-N}$); ^{13}C NMR (101 MHz, CDCl_3) δ 158.5, 151.1, 149.9, 138.5, 134.1, 131.2, 128.1, 127.6, 126.7, 123.2, 64.7; HRMS (ES) m/z for $\text{C}_{13}\text{H}_{13}\text{N}_2$ $[\text{M}+\text{H}]^+$ calcd. 197.1078, found 197.1078.

2p: Reaction was performed on a 41 mmol scale using 2-furaldehyde (4.18 g, 43.5 mmol) and benzylamine (4.41 g, 41.2 mmol). The product was purified by vacuum distillation (110°C, 0.05 mm Hg) to provide **2p** (5.74 g, 31.0 mmol, 75%) as a yellow liquid. IR (thin film, cm^{-1}) 3094 (m), 2996 (m), 2836 (m), 1643 (s), 1580 (m), 1483 (s), 1452 (s), 1360 (s), 1273 (s), 1153 (s), 1017 (s); ^1H NMR (500 MHz, CDCl_3) δ 8.17 (1H, s, $\text{CH}=\text{N}$), 7.53-7.51 (1H, m, ArH), 7.36-7.31 (4H, m, ArH), 7.29-7.25 (1H, m, ArH), 6.78 (1H, d, $J = 3.4$ Hz, ArH), 6.48 (1H, dd, $J = 3.4, 1.5$ Hz, ArH), 4.78 (2H, d, $J = 1.0$ Hz, $\text{CH}_2\text{-N}$); ^{13}C NMR (101 MHz, CDCl_3) δ 151.4, 150.2, 144.6, 138.7, 128.4, 128.1, 127.0, 114.0, 111.5, 65.0; LRMS (CI) m/z : 185.7 (100%) $[\text{M}+\text{H}]^+$.

2q: Reaction was performed on a 41 mmol scale using 2-thiophenecarboxaldehyde (4.80 g, 42.8 mmol) and benzylamine (4.37 g, 40.8 mmol). The product was purified by vacuum distillation (129°C, 0.05 mm Hg) to provide **2q** (5.30 g, 26.3 mmol, 65%) as a yellow liquid which slowly solidifies to a yellow solid. mp = 28-31°C; IR (thin film, cm⁻¹) 3027 (m), 2869 (m), 1632 (s), 1496 (m), 1452 (m), 1431 (s), 1346 (m), 1218 (m), 1045 (m), 859 (m); ¹H NMR (500 MHz, CDCl₃) δ 8.46 (1H, s, CH=N), 7.42-7.40 (1H, m, ArH), 7.37-7.30 (5H, m, ArH), 7.29-7.25 (1H, m, ArH), 7.08 (1H, dd, *J* = 4.9, 3.9 Hz, ArH), 4.80 (2H, s, CH₂-N); ¹³C NMR (101 MHz, CDCl₃) δ 155.1, 142.4, 139.0, 130.6, 129.0, 128.4, 128.0, 127.3, 127.0, 64.4; HRMS (ES) *m/z* for C₁₂H₁₂NS [M+H]⁺ calcd. 202.0690, found 202.0681.

2r: Reaction was performed on a 40 mmol scale using pyrrole-2-carboxaldehyde (3.80 g, 40.0 mmol) and benzylamine (4.32 g, 40.3 mmol). The product was purified by recrystallization from hexanes to provide **2r** (6.12 g, 33.2 mmol, 83%) as white needles. IR (thin film, cm⁻¹) 3208 (s), 3167 (s), 3088 (m), 2830 (m), 1634 (s), 1422 (s), 1132 (m), 1028 (s); ¹H NMR (500 MHz, CDCl₃) δ 9.33 (1H, brs, NH), 8.18 (1H, s, CH=N), 7.36-7.24 (5H, m, ArH), 6.84 (1H, s, ArH), 6.52 (1H, dd, *J* = 3.4, 1.5 Hz, ArH), 6.24 (1H, dd, *J* = 3.4, 2.9 Hz, ArH), 4.72 (2H, s, CH₂-N); ¹³C NMR (101 MHz, CDCl₃) δ 153.4, 139.6, 130.1, 128.6, 128.0, 127.1, 122.5, 115.1, 109.6, 64.3; LRMS (CI) *m/z*: 184.7 (100%) [M+H]⁺.

IV. Phosphite Preparation.⁴

3h: A flame-dried 500-mL 3-neck round bottomed flask equipped with a glass stopper, gas inlet adapter, rubber septum, and magnetic stir bar was charged with toluene (120 mL). The glass stopper was replaced with an oven-dried 50 mL pressure-equalizing addition funnel equipped with a rubber septum. The addition funnel was charged with 2-nitrobenzyl alcohol (6.126 g, 40 mmol), toluene (40 mL), and *N,N*-dimethylaniline (4.85 g, 40 mmol). Phosphorus trichloride (2.75 g, 20 mmol) was added to the 500 mL rbf. The mixture in the addition funnel was heated via a heat gun until homogeneous. This solution was added to the pot in small portions over 30 min, re-heating as necessary. After 1 h, 2-nitrobenzyl alcohol (3.06 g, 20 mmol) in warm toluene (40 mL) was added to the reaction over 15 min via the addition funnel. The reaction vessel was wrapped with aluminum foil to exclude light. After 12 h, the reaction mixture was washed with deionized water (3 X 50 mL), an aqueous solution of ammonia (5M, 2 X 50 mL), deionized water (2 X 50 mL), and brine (50 mL). The organic solution was dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The resulting orange oil was dissolved in toluene (80 mL) and hexane (30 mL) was added to this solution slowly and with efficient mixing. The recrystallization was wrapped in aluminum foil to exclude light and allowed to stand at 23°C until the white solid product precipitated out of solution. It was then cooled to 4°C and kept at this temperature for 12 h. The white solid was collected by vacuum filtration and was washed with hexanes (120 mL). This material was then dissolved in toluene (100 mL) by gently heating (temperature should not exceed 50°C) until homogeneous. Hexane (35 mL) was added slowly and with efficient mixing to this warm solution and the recrystallization was carried out as before. The white solid was collected by vacuum filtration and washed with 40:60 hexanes:toluene (120 mL) followed by a hexanes wash (20 mL). Residual solvent was removed by high vacuum to provide **3h** (3.67 g, 10.4 mmol, 52%) as a white powder. mp = 88-92°C; IR (thin film, cm⁻¹) 1613 (w), 1526 (s), 1451 (w), 1344 (s), 1256 (s), 1092 (m), 1053 (m), 1042 (m), 995 (m); ¹H NMR (500 MHz, CDCl₃) δ 8.16 (2H, dd, *J* = 8.3, 1.0 Hz, ArH), 7.77 (2H, d, *J* = 7.8 Hz, ArH), 7.71 (2H, dt, *J* = 1.0, 7.8 Hz, ArH), 7.56-7.51 (2H, m, ArH), 7.17 (1H, d, *J* = 716 Hz, PH), 5.62 (2H, dd, *J* = 14.6, 8.8 Hz, OCH₂), 5.55 (2H, dd, *J* = 14.6, 8.3 Hz, OCH₂); ¹³C NMR (101 MHz, CDCl₃) δ 146.9 (s), 134.4 (s), 132.1 (d, *J* = 7.3 Hz), 129.3 (s), 128.8 (s), 125.3 (s), 64.3

(d, $J = 4.1$ Hz); ^{31}P NMR (162 MHz, CDCl_3 , proton-coupled) δ 8.72 (ddd, $J = 716, 8.4, 8.4$ Hz); HRMS (ES) m/z for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_7\text{P}$ $[\text{M}+\text{H}]^+$ calcd. 353.0538, found 353.0551.

V. Enantioselective Hydrophosphonylation.

4a (representative experimental procedure for enantioselective hydrophosphonylation): An oven dried 4-mL vial equipped with a magnetic stir bar was charged with **1b** (0.0288 g, 0.0501 mmol, 0.10 equiv), **3h** (0.177 g, 0.501 mmol, 1.0 equiv), and diethyl ether (1.2 mL). The vial was sealed with a plastic cap and cooled to 0°C in an ice-water bath with stirring. To this suspension was added **2a** (0.0979 g, 0.501 mmol, 1.0 equiv). The heterogeneous reaction was warmed to 4°C (note: **3h** is only sparingly soluble in the reaction mixture). After 72 h, an aqueous solution of hydrochloric acid (1N, 0.5 mL) and tetrahydrofuran (0.5 mL) were added, and this mixture was stirred at 4°C for 1 h. The reaction was then partitioned between an aqueous solution of hydrochloric acid (1N) and dichloromethane (1:1, 40 mL). The layers were mixed well and separated. The aqueous layer was extracted with dichloromethane (5 mL). The combined organic solution was washed with a saturated aqueous sodium carbonate solution (20 mL). The sodium carbonate solution was back-extracted with dichloromethane (2 X 5 mL), and the combined organic extracts were dried over sodium sulfate, filtered, and concentrated *in vacuo*. The resulting residue was purified via flash chromatography on silica gel (60:40 hexanes:ethyl acetate) to provide the product **4a** as a very pale yellow solid (0.239 g, 0.436 mmol, 87%) in 98% *ee*. Chiral HPLC (Pirkle L-Leucine, 95:05 hexane:IPA, 1.0 mL/min, $\lambda = 208$ nm) $t_R(\text{major}) = 87.9$ min, $t_R(\text{minor}) = 100.1$ min; $[\alpha]_D^{25} = +24.4^\circ$ ($c = 1.2$, CHCl_3); mp = $78-80^\circ\text{C}$; IR (thin film, cm^{-1}) 3304 (m), 1526 (s), 1343 (s), 1248 (s), 1055 (s), 1024 (s), 999 (s); ^1H -NMR (500 MHz, CDCl_3) δ 8.13 (1H, dd, $J = 8.3, 1.5$ Hz, ArH), 8.04 (1H, dd, $J = 8.1, 1.2$ Hz, ArH), 7.71-7.62 (2H, m, ArH), 7.51-7.34 (8H, m, ArH), 7.30-7.21 (6H, m, ArH), 5.63 (1H, dd, $J = 15, 7.8$ Hz, O-CH₂), 5.55 (1H, dd, $J = 15, 6.8$ Hz, O-CH₂), 5.34 (1H, dd, $J = 15, 7.3$ Hz, O-CH₂), 5.22 (1H, dd, $J = 15, 8.3$ Hz, O-CH₂), 4.21 (1H, d, $J = 21$ Hz, P-CH), 3.85 (1H, d, $J = 13$ Hz, N-CH₂), 3.57 (1H, d, $J = 13$ Hz, N-CH₂), 2.41 (1H, s, N-H); ^{13}C -NMR (101 MHz, CDCl_3) δ 146.8 (s), 146.6 (s), 139.0 (s), 135.2 (d, $J = 2.3$ Hz), 134.1 (s), 134.0 (s), 133.2 (d, $J = 6.9$ Hz), 132.9 (d, $J = 6.9$ Hz), 129.0 (d, $J = 2.3$ Hz), 128.8 (s), 128.8 (s), 128.7 (s), 128.7 (s), 128.6 (s), 128.6 (s), 128.5 (s), 128.3 (s), 127.4 (s), 125.0 (s), 124.9 (s), 65.7 (d, $J = 6.1$ Hz), 64.9 (d, $J = 6.1$ Hz), 59.7 (d, $J = 156$ Hz), 51.2 (d, $J = 18.3$ Hz); ^{31}P -NMR (162 MHz, CDCl_3) δ 25.1; HRMS (ES) m/z for $\text{C}_{28}\text{H}_{27}\text{N}_3\text{O}_7\text{P}$ $[\text{M}+\text{H}]^+$ calcd. 548.1586, found 548.1596.

4b: Reaction was performed on a 0.48 mmol scale at 4°C for 24 h using 10 mol% **1b** (0.0273 g, 0.0475 mmol), **3h** (0.167 g, 0.475 mmol), **2b** (0.0899 g, 0.475 mmol), and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (70:30 to 60:40 hexanes:ethyl acetate gradient) to provide **4b** as a very viscous pale yellow oil (0.231 g, 0.426 mmol, 90%) in 96% *ee*. Chiral HPLC (Chiralcel OD, 97:03 hexane:EtOH, 1.0 mL/min, $\lambda = 208$ nm)

$t_R(\text{minor}) = 28.6$ min, $t_R(\text{major}) = 34.8$ min; $[\alpha]_D^{25} = -19.7^\circ$ ($c = 1.1$, CHCl_3); IR (thin film, cm^{-1}) 3351 (m), 3086 (m), 2963 (s), 2874 (s), 1530 (s), 1454 (m), 1344 (s), 1242 (s), 1042 (s), 1018 (s); ^1H -NMR (500 MHz, CDCl_3) δ 8.08 (2H, dd, $J = 8.3, 1.0$ Hz, ArH), 8.10-8.07 (2H, m, ArH), 7.65-7.61 (2H, m, ArH), 7.50-7.46 (2H, m, ArH), 7.33-7.21 (5H, m, ArH), 5.58-5.47 (4H, m, O-CH₂), 4.00 (1H, d, $J = 13$ Hz, N-CH₂), 3.88 (1H, dd, $J = 13, 1.2$ Hz, N-CH₂), 3.24 (1H, dd, $J = 16, 2.9$ Hz, P-CH), 1.76-1.60 (m, 2H, CH₂CH₃), 1.57 (1H, s, N-H), 1.54-1.48 (2H, m, CH₂CH₃), 1.38-1.27 (1H, m, CH(CH₂CH₃)₂), 0.92 (3H, t, $J = 7.6$ Hz, CH₃), 0.82 (3H, t, $J = 7.3$ Hz, CH₃); ^{13}C -NMR (101 MHz, CDCl_3) δ 147.1 (s), 147.1 (s), 139.8 (s), 134.1 (s), 134.1 (s), 133.0 (d, $J = 6.0$ Hz), 132.9 (d, $J = 6.4$ Hz), 129.0 (s), 129.0 (s), 129.0 (s), 128.9 (s), 128.5 (s), 128.5 (s), 127.3 (s), 125.1 (s), 125.1 (s), 64.5 (d, $J = 6.9$ Hz), 64.4 (d, $J = 6.4$ Hz), 56.5 (d, $J = 143$ Hz), 53.4 (d, $J = 5.5$ Hz), 43.2 (d, $J = 5.5$ Hz), 23.1 (d, $J = 12.8$ Hz), 22.8 (d, $J = 2.3$ Hz), 12.3 (s), 12.3

(s); ^{31}P -NMR (162 MHz, CDCl_3) δ 31.2; HRMS (ES) m/z for $\text{C}_{27}\text{H}_{33}\text{N}_3\text{O}_7\text{P}$ $[\text{M}+\text{H}]^+$ calcd. 542.2056, found 542.2062.

4c: Reaction was performed on a 0.50 mmol scale at 4 °C for 24 h using 10 mol% **1b** (0.0289 g, 0.0503 mmol), **3h** (0.177 g, 0.503 mmol), **2c** (0.0812 g, 0.503 mmol), and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (60:40 hexanes:ethyl acetate) to provide **4c** as a very viscous pale yellow oil (0.240 g, 0.467 mmol, 93%) in 90% *ee*. Chiral HPLC (Chiralcel OD, 97:03 hexane:EtOH, 1.0 mL/min, λ = 208 nm) t_R (minor) = 41.7 min, t_R (major) = 49.5 min; $[\alpha]_D^{25} = -15.1^\circ$ (c = 1.1, CHCl_3); IR (thin film, cm^{-1}) 3351 (m), 3065 (w), 2965 (s), 2874 (m), 1530 (s), 1344 (s), 1246 (s), 1042 (s), 1020 (s); ^1H -NMR (500 MHz, CDCl_3) δ 8.08 (2H, d, J = 8.3 Hz, ArH), 7.73-7.70 (2H, m, ArH), 7.64-7.61 (2H, m, ArH), 7.49-7.45 (2H, m, ArH), 7.33-7.22 (5H, m, ArH), 5.58-5.47 (4H, m, O-CH₂), 4.00 (1H, d, J = 13 Hz, N-CH₂), 3.90 (1H, d, J = 13, N-CH₂), 3.01 (1H, dd, J = 14, 3.9 Hz, P-CH), 2.33-2.21 (m, 1H, CH(CH₃)₂), 1.56 (1H, s, N-H), 1.10 (3H, d, J = 6.8 Hz, CH₃), 1.08 (3H, d, J = 7.3 Hz, CH₃); ^{13}C -NMR (101 MHz, CDCl_3) δ 147.1 (s), 147.1 (s), 139.8 (s), 134.1 (s), 134.1 (s), 133.0 (d, J = 6.1 Hz), 132.9 (d, J = 6.9 Hz), 129.0 (s), 129.0 (s), 128.9 (s), 128.9 (s), 128.5 (s), 128.5 (s), 127.3 (s), 125.1 (s), 125.1 (s), 64.6 (d, J = 6.9 Hz), 64.4 (d, J = 6.1 Hz), 60.5 (d, J = 143 Hz), 53.6 (d, J = 5.3 Hz), 29.3 (d, J = 5.3 Hz), 20.8 (d, J = 13 Hz), 18.2 (d, J = 3.8 Hz); ^{31}P -NMR (162 MHz, CDCl_3) δ 30.1; HRMS (ES) m/z for $\text{C}_{25}\text{H}_{29}\text{N}_3\text{O}_7\text{P}$ $[\text{M}+\text{H}]^+$ calcd. 514.1743, found 514.1741.

4d: Reaction was performed on a 0.48 mmol scale at 4 °C at 24 h using 10 mol% **1b** (0.0273 g, 0.0475 mmol), **3h** (0.167 g, 0.475 mmol), **2d** (0.0957 g, 0.475 mmol), and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (60:40 hexanes:ethyl acetate) to provide **4d** as a very viscous pale yellow oil (0.238 g, 0.430 mmol, 91%) in 90% *ee*. Chiral HPLC (Chiralcel OD, 95:05 hexane:EtOH, 1.0 mL/min, λ = 208 nm) t_R (minor) = 20.8 min, t_R (major) = 26.4 min; $[\alpha]_D^{25} = -11.0^\circ$ (c = 1.2, CHCl_3); IR (thin film, cm^{-1}) 3345 (w), 3086 (w), 2929 (s), 2854 (s), 1530 (s), 1450 (s), 1343 (s), 1242 (s), 1042 (s), 1019 (s); ^1H -NMR (500 MHz, CDCl_3) δ 8.09-8.07 (2H, m, ArH), 7.73-7.69 (2H, m, ArH), 7.64-7.60 (2H, m, ArH), 7.49-7.45 (2H, m, ArH), 7.32-7.21 (5H, m, ArH), 5.58-5.46 (4H, m, O-CH₂), 4.00 (1H, d, J = 13 Hz, N-CH₂), 3.90 (1H, dd, J = 13, 1.2 Hz, N-CH₂), 3.00 (1H, dd, J = 15, 3.9 Hz, P-CH), 1.93-1.84 (2H, m, *c*-C₆H₁₁), 1.79-1.74 (2H, m, *c*-C₆H₁₁), 1.71-1.64 (2H, m, *c*-C₆H₁₁), 1.58 (1H, s, N-H), 1.50-1.41 (1H, m, *c*-C₆H₁₁), 1.31-1.10 (4H, m, *c*-C₆H₁₁); ^{13}C -NMR (101 MHz, CDCl_3) δ 147.0 (s), 147.0 (s), 139.7 (s), 134.0 (s), 134.0 (s), 133.0 (d, J = 6.0 Hz), 132.9 (d, J = 6.4 Hz), 128.9 (s), 128.9 (s), 128.9 (s), 128.8 (s), 128.4 (s), 128.4 (s), 127.3 (s), 125.0 (s), 125.1 (s), 64.7 (d, J = 6.4 Hz), 64.4 (d, J = 6.9 Hz), 60.5 (d, J = 144 Hz), 53.7 (d, J = 6.0 Hz), 39.5 (d, J = 5.0 Hz), 31.0 (d, J = 11.5 Hz), 28.5 (d, J = 4.1 Hz), 26.6 (s), 26.4 (s), 26.1 (s); ^{31}P -NMR (162 MHz, CDCl_3) δ 30.0; HRMS (ES) m/z for $\text{C}_{28}\text{H}_{33}\text{N}_3\text{O}_7\text{P}$ $[\text{M}+\text{H}]^+$ calcd. 554.2056, found 554.2062.

4e: Reaction was performed on a 0.50 mmol scale at 4 °C for 72 h using 10 mol% **1b** (0.0287 g, 0.0500 mmol), **3h** (0.176 g, 0.500 mmol), **2e** (0.0876 g, 0.500 mmol), and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (60:40 hexanes:ethyl acetate) to provide **4e** as a very viscous pale yellow oil (0.219 g, 0.415 mmol, 83%) in 93% *ee*. Chiral HPLC (Chiralcel OD, 95:05 hexane:EtOH, 1.0 mL/min, λ = 208 nm) t_R (minor) = 19.6 min, t_R (major) = 26.0 min; $[\alpha]_D^{25} = -8.3^\circ$ (c = 1.2, CHCl_3); IR (thin film, cm^{-1}) 3362 (w), 3086 (w), 2957 (s), 2870 (s), 1530 (s), 1342 (s), 1242 (s), 1042 (s), 1015 (s); ^1H -NMR (500 MHz, CDCl_3) δ 8.09-8.04 (2H, m, ArH), 7.73-7.68 (2H, m, ArH), 7.64-7.57 (2H, m, ArH), 7.49-7.43 (2H, m, ArH), 7.33-7.22 (5H, m, ArH), 5.53 (2H, d, J = 7.8 Hz, O-CH₂), 5.47 (2H, d, J = 8.3 Hz, O-CH₂), 4.04 (1H, dd, J = 13, 1.5 Hz, N-CH₂), 3.84 (1H, d, J = 13 Hz, N-CH₂), 2.83 (1H, d, J = 15 Hz, P-CH), 1.49 (1H, s, N-H), 1.14 (9H, s, (CH₃)₃); ^{13}C -NMR (101 MHz, CDCl_3) δ 146.9 (s), 146.8 (s), 139.7 (s), 133.9 (s), 133.9 (s), 132.8 (d, J = 6.1 Hz), 132.6 (d, J = 6.1 Hz), 128.8 (s), 128.8 (s), 128.8 (s), 128.8 (s), 128.3 (s), 128.2 (s), 127.1 (s), 124.9 (s), 124.8 (s), 65.4 (d, J = 132 Hz), 64.7 (d, J = 3.1 Hz), 64.0 (d, J = 6.9 Hz), 55.3 (d, J = 3.8 Hz), 35.5 (d, J = 6.9 Hz), 27.6 (d, J = 6.9 Hz); ^{31}P -NMR (162 MHz, CDCl_3) δ 29.8; HRMS (CI) m/z for $\text{C}_{26}\text{H}_{31}\text{N}_3\text{O}_7\text{P}$ $[\text{M}+\text{H}]^+$ calcd. 528.1899, found 528.1895.

4f: Reaction was performed on a 2.19 mmol scale at 4 °C using 10 mol% **1b** (0.126 g, 0.219 mmol), **3h** (0.770 g, 2.19 mmol), **2f** (0.379 g, 2.19 mmol), and diethyl ether (5.3 mL). After 72 h, an aqueous solution of hydrochloric acid (1N, 2.2 mL) and tetrahydrofuran (2.2 mL) were added, and this mixture was stirred at 4°C for 1 h. The reaction was then partitioned between an aqueous solution of hydrochloric acid (1N) and dichloromethane (1:1, 160 mL). The layers were mixed well and separated. The aqueous layer was extracted with dichloromethane (20 mL). The combined organic solution was washed with a saturated aqueous sodium carbonate solution (80 mL). The sodium carbonate solution was back-extracted with dichloromethane (2 X 20 mL), and the combined organic extracts were dried over sodium sulfate, filtered, and concentrated *in vacuo*. The resulting residue was purified via flash chromatography on silica gel (60:40 to 50:50 hexanes:ethyl acetate gradient) to provide **4f** as a very pale yellow crystalline solid (1.04 g, 1.98 mmol, 91%) in 82% *ee*. Chiral HPLC (Chiralcel OD, 97:03 hexane:EtOH, 1.0 mL/min, λ = 208 nm) t_R (minor) = 48.4 min, t_R (major) = 55.1 min; $[\alpha]_D^{25}$ = +30.7° (c = 1.0, CHCl₃); mp = 98-101°C. The product (1.00 g, 1.90 mmol) was dissolved in hot ethyl acetate (15 mL) and hexane (23 mL) was added. The resulting solution was heated to reflux and then allowed to slowly cool to rt and then to 4°C. The fine white needles were collected by vacuum filtration and washed with 60:40 hexanes:ethyl acetate (40 mL). The recrystallization was repeated to provide **4f** (0.701 g, 1.33 mmol, 70% recovery, 64% overall from **2f**) in 99% *ee*. Chiral HPLC (Chiralcel OD, 97:03 hexane:EtOH, 1.0 mL/min, λ = 208 nm) t_R (minor) = 48.5 min, t_R (major) = 54.8 min; $[\alpha]_D^{25}$ = +38.0° (c = 1.1, CHCl₃); mp = 107-110°C; IR (thin film, cm⁻¹) 3314 (m), 3084 (w), 3028 (m), 2972 (m), 2855 (m), 1528 (s), 1343 (s), 1242 (s), 1024 (s), 1001 (s); ¹H-NMR (500 MHz, CDCl₃) δ 8.14-8.09 (2H, m, ArH), 7.80-7.71 (2H, m, ArH), 7.67-7.61 (2H, m, ArH), 7.51-7.45 (2H, m, ArH), 7.30-7.22 (5H, m, ArH), 5.63 (1H, dd, *J* = 15, 7.8 Hz, O-CH₂), 5.56 (1H, dd, *J* = 15, 6.8 Hz, O-CH₂), 5.58-5.48 (2H, m, O-CH₂), 5.21-5.16 (1H, m, CHC(CH₃)₂), 3.93 (1H, d, *J* = 13 Hz, N-CH₂), 3.89 (1H, dd, *J* = 18, 10 Hz, P-CH), 3.69 (1H, d, *J* = 13 Hz, N-CH₂), 1.82 (3H, d, *J* = 3.9 Hz, CH₃), 1.80 (1H, s, N-H), 1.58 (3H, dd, *J* = 3.4, 1.0 Hz, CH₃); ¹³C-NMR (101 MHz, CDCl₃) δ 146.7 (s), 146.7 (s), 139.9 (d, *J* = 15 Hz), 139.4 (s), 134.0 (s), 134.0 (s), 133.2 (d, *J* = 6.4 Hz), 133.1 (d, *J* = 6.4 Hz), 128.7 (s), 128.7 (s), 128.5 (s), 128.5 (s), 128.4 (s), 128.4 (s), 127.2 (s), 125.0 (s), 125.0 (s), 119.2 (d, *J* = 5.0 Hz), 65.2 (d, *J* = 6.0 Hz), 64.9 (d, *J* = 6.0 Hz), 53.5 (d, *J* = 160 Hz), 51.1 (d, *J* = 17.9 Hz), 26.0 (d, *J* = 2.7 Hz), 18.7 (d, *J* = 1.8 Hz); ³¹P-NMR (162 MHz, CDCl₃) δ 26.8; HRMS (ES) *m/z* for C₂₆H₂₉N₃O₇P [M+H]⁺ calcd. 526.1743, found 526.1725.

4g: Reaction was performed on a 0.51 mmol scale at 4 °C for 72 h using 10 mol% **1b** (0.0292 g, 0.0507 mmol), **3h** (0.179 g, 0.507 mmol), **2g** (0.108 g, 0.507 mmol), and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (60:40 hexanes:ethyl acetate) to provide **4g** as a very pale yellow crystalline solid (0.254 g, 0.449 mmol, 89%) in 98% *ee*. Chiral HPLC (Chiralpak AD, 70:30 hexane:IPA, 1.0 mL/min, λ = 208 nm) t_R (major) = 35.2 min, t_R (minor) = 55.2 min; $[\alpha]_D^{25}$ = +19.9° (c = 1.4, CHCl₃); mp = 80-82°C; IR (thin film, cm⁻¹) 3314 (w), 3067 (w), 2923 (w), 1527 (s), 1508 (s), 1449 (m), 1342 (s), 1246 (s), 1024 (s), 999 (s); ¹H-NMR (500 MHz, CDCl₃) δ 8.13 (1H, dd, *J* = 8.3, 1.0 Hz, ArH), 8.05 (1H, dd, *J* = 8.3, 1.0 Hz, ArH), 7.68-7.62 (2H, m, ArH), 7.53-7.48 (2H, m, ArH), 7.45-7.39 (3H, m, ArH), 7.31-7.19 (6H, m, ArH), 7.09-7.05 (2H, m, ArH), 5.62 (1H, dd, *J* = 15, 7.8 Hz, O-CH₂), 5.54 (1H, dd, *J* = 15, 7.3 Hz, O-CH₂), 5.36 (1H, dd, *J* = 15, 7.3 Hz, O-CH₂), 5.28 (1H, dd, *J* = 15, 8.3 Hz, O-CH₂), 4.18 (1H, d, *J* = 21 Hz, P-CH), 3.83 (1H, d, *J* = 13 Hz, N-CH₂), 3.54 (1H, d, *J* = 13 Hz, N-CH₂), 2.38 (1H, s, N-H); ¹³C-NMR (101 MHz, CDCl₃) δ 162.8 (dd, *J* = 247, 3.7 Hz), 146.9 (s), 146.8 (s), 138.8 (s), 134.1 (s), 134.0 (s), 133.0 (d, *J* = 6.9 Hz), 132.6 (d, *J* = 6.4 Hz), 131.0 (dd, *J* = 3.2, 3.2 Hz), 130.4 (dd, *J* = 8.0, 6.6 Hz), 128.9 (s), 128.9 (s), 128.7 (s), 128.6 (s), 128.5 (s), 128.5 (s), 127.5 (s), 125.1 (s), 125.0 (s), 115.9 (dd, *J* = 22, 1.8 Hz), 65.7 (d, *J* = 6.0 Hz), 65.0 (d, *J* = 6.0 Hz), 58.9 (d, *J* = 157 Hz), 51.1 (d, *J* = 18 Hz); ³¹P-NMR (162 MHz, CDCl₃) δ 24.9; HRMS (ES) *m/z* for C₂₈H₂₆FN₃O₇P [M+H]⁺ calcd. 566.1492, found 566.1490.

4h: Reaction was performed on a 0.50 mmol scale at 4 °C for 48 h using 10 mol% **1b** (0.0287 g, 0.0500 mmol), **3h** (0.176 g, 0.500 mmol), **2h** (0.113 g, 0.500 mmol), and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (55:45 hexanes:ethyl acetate) to provide **4h** as a

very pale yellow crystalline solid (0.261 g, 0.452 mmol, 90%) in 96% *ee*. Chiral HPLC (Chiralpak AD, 70:30 hexane:IPA, 1.0 mL/min, λ = 208 nm) t_R (major) = 58.4 min, t_R (minor) = 66.3 min; $[\alpha]_D^{25} = +33.4^\circ$ (c = 1.0, CHCl_3); mp = 100-102°C; IR (thin film, cm^{-1}) 3320 (w), 3065 (w), 2937 (w), 1527 (s), 1453(m), 1341 (s), 1250 (s), 1086 (m), 1025 (s), 999 (s); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 8.13 (1H, dd, J = 8.1, 1.2 Hz, ArH), 8.04 (1H, dd, J = 8.1, 1.2 Hz, ArH), 7.73-7.71 (1H, m, ArH), 7.62-7.66 (1H, m, ArH), 7.52-7.47 (2H, m, ArH), 7.43-7.39 (1H, m, ArH), 7.36-7.21 (8H, m, ArH), 6.92-6.88 (2H, m, ArH), 5.62 (1H, dd, J = 15, 7.8 Hz, O-CH₂), 5.54 (1H, dd, J = 15, 6.8 Hz, O-CH₂), 5.33 (1H, dd, J = 15, 6.8 Hz, O-CH₂), 5.23 (1H, dd, J = 15, 7.8 Hz, O-CH₂), 4.14 (1H, d, J = 21 Hz, P-CH), 3.84 (1H, d, J = 13 Hz, N-CH₂), 3.84 (3H, s, O-CH₃), 3.56 (1H, d, J = 13 Hz, N-CH₂), 2.34 (1H, s, N-H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 159.7 (d, J = 2.8 Hz), 146.6 (s), 146.5 (s), 139.0 (s), 134.0 (s), 133.9 (s), 133.2 (d, J = 6.9 Hz), 132.8 (d, J = 6.4 Hz), 129.8 (d, J = 6.4 Hz), 128.7 (s), 128.5 (s), 128.5 (s), 128.4 (s), 128.4 (s), 128.3 (s), 128.2 (s), 126.8 (d, J = 2.7 Hz), 124.9 (s), 124.8 (s), 114.2 (d, J = 2.3 Hz), 65.5 (d, J = 6.0 Hz), 64.8 (d, J = 6.0 Hz), 58.8 (d, J = 157 Hz), 55.3 (s), 50.9 (d, J = 18 Hz); $^{31}\text{P-NMR}$ (162 MHz, CDCl_3) δ 25.5; HRMS (ES) m/z for $\text{C}_{29}\text{H}_{29}\text{N}_3\text{O}_8\text{P}$ $[\text{M}+\text{H}]^+$ calcd. 578.1692, found 578.1687.

4i: Reaction was performed on a 0.50 mmol scale at 23 °C for 48 h using 10 mol% **1b** (0.0287 g, 0.0500 mmol), **3h** (0.176 g, 0.500 mmol), **2i** (0.127 g, 0.500 mmol), and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (55:45 hexanes:ethyl acetate) to provide **4i** as a very pale yellow crystalline solid (0.237 g, 0.391 mmol, 78%) in 96% *ee*. Chiral HPLC (Chiralpak AD, 70:30 hexane:IPA, 1.0 mL/min, λ = 208 nm) t_R (major) = 46.6 min, t_R (minor) = 54.2 min; $[\alpha]_D^{25} = +33.4^\circ$ (c = 1.2, CHCl_3); mp = 79-82°C; IR (thin film, cm^{-1}) 3318 (m), 3063 (m), 2951 (m), 1715 (s), 1529 (s), 1497(s), 1343 (s), 1248 (s), 1111 (s), 1018 (s); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 8.13 (1H, d, J = 8.8 Hz, ArH), 8.05-8.03 (3H, m, ArH), 7.66-7.61 (2H, m, ArH), 7.53-7.40 (5H, m, ArH), 7.31-7.18 (6H, m, ArH), 5.62 (1H, dd, J = 15, 7.8 Hz, O-CH₂), 5.54 (1H, dd, J = 15, 7.3 Hz, O-CH₂), 5.37 (1H, dd, J = 15, 6.8 Hz, O-CH₂), 5.28 (1H, dd, J = 15, 8.3 Hz, O-CH₂), 4.27 (1H, d, J = 21 Hz, P-CH), 3.95 (3H, s, O-CH₃), 3.83 (1H, d, J = 13 Hz, N-CH₂), 3.54 (1H, d, J = 13 Hz, N-CH₂), 2.45 (1H, s, N-H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 166.7 (s), 146.8 (s), 146.7 (s), 140.5 (d, J = 2.3 Hz), 138.6 (s), 134.1 (s), 134.0 (s), 132.8 (d, J = 6.9 Hz), 132.4 (d, J = 6.1 Hz), 130.3 (d, J = 3.1 Hz), 130.1 (s), 130.1 (s), 128.9 (s), 128.9 (s), 128.8 (s), 128.7 (s), 128.6 (s), 128.4 (s), 127.5 (s), 125.0 (s), 125.0 (s), 65.7 (d, J = 5.3 Hz), 65.0 (d, J = 6.1 Hz), 59.5 (d, J = 155 Hz), 52.3 (s), 51.2 (d, J = 18 Hz); $^{31}\text{P-NMR}$ (162 MHz, CDCl_3) δ 24.3; HRMS (ES) m/z for $\text{C}_{30}\text{H}_{29}\text{N}_3\text{O}_9\text{P}$ $[\text{M}+\text{H}]^+$ calcd. 606.1641, found 606.1633.

4j: Reaction was performed on a 0.49 mmol scale at 4 °C for 72 h using 10 mol% **1b** (0.0282 g, 0.0491 mmol), **3h** (0.173 g, 0.491 mmol), **2j** (0.103 g, 0.491 mmol), and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (65:35 hexanes:ethyl acetate) to provide **4j** as a very viscous pale yellow oil (0.224 g, 0.398 mmol, 81%) in 92% *ee*. Chiral HPLC (Pirkle L-Leucine, 99:01 hexane:EtOH, 1.0 mL/min, λ = 208 nm) t_R (major) = 123.2 min, t_R (minor) = 136.5 min; $[\alpha]_D^{25} = +25.6^\circ$ (c = 0.9, CHCl_3); IR (thin film, cm^{-1}) 3314 (m), 3065 (m), 2944 (m), 1530 (s), 1452 (s), 1344 (s), 1248 (s), 1198 (s), 1086 (m), 1024 (s); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 8.13 (1H, dd, J = 8.3, 1.0 Hz, ArH), 8.03 (1H, dd, J = 8.3, 1.0 Hz, ArH), 7.72-7.62 (3H, m, ArH), 7.51-7.38 (3H, m, ArH), 7.32-7.14 (9H, m, ArH), 5.63 (1H, dd, J = 15, 7.8 Hz, O-CH₂), 5.56 (1H, dd, J = 15, 7.3 Hz, O-CH₂), 5.31 (1H, dd, J = 15, 6.8 Hz, O-CH₂), 5.15 (1H, dd, J = 15, 8.3 Hz, O-CH₂), 4.49 (1H, d, J = 21 Hz, P-CH), 3.85 (1H, d, J = 13 Hz, N-CH₂), 3.55 (1H, d, J = 13 Hz, N-CH₂), 2.48 (1H, s, N-H), 2.18 (3H, s, ArCH₃); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 146.8 (s), 146.6 (s), 139.0 (s), 137.5 (d, J = 7.6 Hz), 134.1 (s), 134.0 (s), 133.4 (d, J = 1.5 Hz), 133.2 (d, J = 6.9 Hz), 132.8 (d, J = 6.1 Hz), 130.8 (d, J = 1.5 Hz), 128.8 (s), 128.6 (s), 128.6 (s), 128.5 (s), 128.5 (s), 128.3 (s), 128.1 (d, J = 3.8 Hz), 127.5 (d, J = 3.8 Hz), 127.4 (s), 126.8 (d, J = 3.1 Hz), 125.0 (s), 124.9 (s), 65.6 (d, J = 5.3 Hz), 64.8 (d, J = 6.1 Hz), 54.6 (d, J = 157 Hz), 51.0 (d, J = 18 Hz), 19.7 (s); $^{31}\text{P-NMR}$ (162 MHz, CDCl_3) δ 26.1; HRMS (ES) m/z for $\text{C}_{29}\text{H}_{29}\text{N}_3\text{O}_7\text{P}$ $[\text{M}+\text{H}]^+$ calcd. 562.1743, found 562.1752.

4k: Reaction was performed on a 0.50 mmol scale at 4 °C for 72 h using 20 mol% **1b** (0.0575 g, 0.100 mmol), **3h** (0.176 g, 0.500 mmol), **2k** (0.115 g, 0.500 mmol),

and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (67:33 hexanes:ethyl acetate) to provide **4k** as a very viscous pale yellow oil (0.153 g, 0.263 mmol, 52%) in 96% *ee*. Chiral HPLC (Chiralpak AD, 70:30 hexane:IPA, 1.0 mL/min, λ = 208 nm) t_R (major) = 35.5 min, t_R (minor) = 44.0 min; $[\alpha]_D^{25} = +4.7^\circ$ (c = 1.1, CHCl_3); IR (thin film, cm^{-1}) 3306 (m), 3065 (m), 2942 (m), 1530 (s), 1447 (s), 1343 (s), 1248 (s), 1198 (m), 1086 (s), 1024 (s), 999 (s); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 8.15 (1H, dd, J = 8.3, 1.0 Hz, ArH), 8.06 (1H, dd, J = 8.3, 1.0 Hz, ArH), 7.78-7.63 (3H, m, ArH), 7.53-7.47 (2H, m, ArH), 7.44-7.34 (4H, m, ArH), 7.31-7.21 (6H, m, ArH), 5.72 (1H, dd, J = 15, 7.3 Hz, O-CH₂), 5.62 (1H, dd, J = 15, 6.8 Hz, O-CH₂), 5.37 (1H, dd, J = 15, 6.8 Hz, O-CH₂), 5.24 (1H, dd, J = 15, 7.8 Hz, O-CH₂), 4.93 (1H, d, J = 22 Hz, P-CH), 3.79 (1H, d, J = 13 Hz, N-CH₂), 3.56 (1H, d, J = 13 Hz, N-CH₂), 2.45 (1H, s, N-H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 146.7 (s), 146.4 (s), 138.8 (s), 134.9 (d, J = 8.7 Hz), 134.1 (s), 134.0 (s), 134.0 (s), 133.5 (s), 133.1 (d, J = 6.9 Hz), 132.8 (d, J = 6.8 Hz), 129.8 (d, J = 2.3), 129.5 (d, J = 3.2 Hz), 129.3 (d, J = 4.1 Hz), 128.7 (s), 128.6 (s), 128.5 (s), 128.5 (s), 128.1 (s), 127.7 (d, J = 3.2 Hz), 127.4 (s), 125.0 (s), 124.9 (s), 65.9 (d, J = 5.5 Hz), 64.8 (d, J = 6.0 Hz), 55.2 (d, J = 159 Hz), 51.4 (d, J = 18 Hz); $^{31}\text{P-NMR}$ (162 MHz, CDCl_3) δ 24.6; HRMS (ES) m/z for $\text{C}_{28}\text{H}_{26}\text{ClN}_3\text{O}_7\text{P}$ $[\text{M}+\text{H}]^+$ calcd. 582.1197, found 582.1202.

4l: Reaction was performed on a 0.50 mmol scale at 23 °C for 48 h using 10 mol% **1b** (0.0287 g, 0.0500 mmol), **3h** (0.176 g, 0.500 mmol), **2l** (0.115 g, 0.500 mmol), and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (60:40 hexanes:ethyl acetate) to provide **4l** as a very viscous pale yellow oil (0.242 g, 0.415 mmol, 83%) in 98% *ee*. Chiral HPLC (Chiralpak AD, 87:13 hexane:EtOH, 1.0 mL/min, λ = 208 nm) t_R (minor) = 71.6 min, t_R (major) = 76.5 min; $[\alpha]_D^{25} = +22.7^\circ$ (c = 1.0, CHCl_3); IR (thin film, cm^{-1}) 3300 (m), 3064 (m), 2944 (w), 1531 (s), 1455 (s), 1344 (s), 1247 (s), 1197 (s), 1085 (s), 1022 (s), 998 (s); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 8.13 (1H, d, J = 8.3 Hz, ArH), 8.07 (1H, dd, J = 8.3, 1.0 Hz, ArH), 7.68-7.63 (2H, m, ArH), 7.56-7.41 (4H, m, ArH), 7.35-7.19 (9H, m, ArH), 5.62 (1H, dd, J = 15, 7.8 Hz, O-CH₂), 5.55 (1H, dd, J = 15, 6.8 Hz, O-CH₂), 5.38 (1H, dd, J = 15, 6.8 Hz, O-CH₂), 5.31 (1H, dd, J = 15, 7.8 Hz, O-CH₂), 4.18 (1H, d, J = 21 Hz, P-CH), 3.85 (1H, d, J = 13 Hz, N-CH₂), 3.56 (1H, d, J = 13 Hz, N-CH₂), 2.41 (1H, s, N-H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 146.8 (s), 146.6 (s), 138.6 (s), 137.5 (d, J = 2.8 Hz), 134.8 (d, J = 2.8 Hz), 134.2 (s), 134.1 (s), 132.8 (d, J = 6.9 Hz), 132.5 (d, J = 6.9), 130.2 (d, J = 2.8), 128.9 (s), 128.8 (s), 128.8 (d, J = 6.9 Hz), 128.7 (d, J = 3.2 Hz), 128.6 (s), 128.6 (s), 128.4 (s), 128.4 (s), 127.5 (s), 126.8 (d, J = 6.0 Hz), 125.1 (s), 125.0 (s), 65.7 (d, J = 6.0 Hz), 65.0 (d, J = 5.5 Hz), 59.2 (d, J = 156 Hz), 51.2 (d, J = 18 Hz); $^{31}\text{P-NMR}$ (162 MHz, CDCl_3) δ 24.3; HRMS (ES) m/z for $\text{C}_{28}\text{H}_{26}\text{ClN}_3\text{O}_7\text{P}$ $[\text{M}+\text{H}]^+$ calcd. 582.1197, found 582.1201.

4m: Reaction was performed on a 0.50 mmol scale at 4 °C for 72 h using 10 mol% **1b** (0.0287 g, 0.0500 mmol), **3h** (0.176 g, 0.500 mmol), **2m** (0.115 g, 0.500 mmol), and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (60:40 hexanes:ethyl acetate) to provide **4m** as a very pale yellow crystalline solid (0.253 g, 0.434 mmol, 87%) in 99% *ee*. Chiral HPLC (Chiralpak AD, 70:30 hexane:IPA, 1.0 mL/min, λ = 208 nm) t_R (major) = 38.6 min, t_R (minor) = 58.4 min; $[\alpha]_D^{25} = +29.7^\circ$ (c = 1.1, CHCl_3); mp = 98-101°C; IR (thin film, cm^{-1}) 3314 (m), 3065 (m), 2943 (m), 1526 (s), 1451 (m), 1343 (s), 1248 (s), 1198 (m), 1088 (m), 1015 (s), 999 (s); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 8.13 (1H, d, J = 7.8 Hz, ArH), 8.05 (1H, dd, J = 8.3, 1.5 Hz, ArH), 7.66-7.62 (2H, m, ArH), 7.53-7.42 (3H, m, ArH), 7.38-7.19 (10H, m, ArH), 5.62 (1H, dd, J = 15, 7.8 Hz, O-CH₂), 5.54 (1H, dd, J = 15, 6.8 Hz, O-CH₂), 5.37 (1H, dd, J = 15, 7.3 Hz, O-CH₂), 5.30 (1H, dd, J = 15, 7.8 Hz, O-CH₂), 4.17 (1H, d, J = 21 Hz, P-CH), 3.83 (1H, d, J = 13 Hz, N-CH₂), 3.53 (1H, d, J = 13 Hz, N-CH₂), 2.38 (1H, s, N-H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 146.7 (s), 146.6 (s), 138.6 (s), 134.2 (d, J = 3.7 Hz), 134.0 (s), 133.9 (s), 133.8 (d, J = 2.7 Hz), 132.9 (d, J = 6.9 Hz), 132.4 (d, J = 6.4 Hz), 130.0 (d, J = 6.4 Hz), 129.0 (s), 129.0 (s), 128.8 (s), 128.8 (s), 128.5 (s), 128.4 (s), 128.3 (s), 127.4 (s), 125.0 (s), 124.9 (s), 65.6 (d, J = 6.0 Hz), 64.9 (d, J = 6.0 Hz), 58.8 (d, J = 156 Hz), 51.0 (d, J = 18 Hz); $^{31}\text{P-NMR}$ (162 MHz, CDCl_3) δ 24.6; HRMS (ES) m/z for $\text{C}_{28}\text{H}_{26}\text{ClN}_3\text{O}_7\text{P}$ $[\text{M}+\text{H}]^+$ calcd. 582.1197, found 582.1194.

4n: Reaction was performed on a 0.50 mmol scale at 4 °C for 72 h using 10 mol% **1b** (0.0287 g, 0.0500 mmol), **3h** (0.176 g, 0.500 mmol), **2n** (0.123 g,

0.500 mmol), and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (67:33 hexanes:ethyl acetate) to provide **4n** as a very pale yellow crystalline solid (0.257 g, 0.430 mmol, 86%) in 98% *ee*. Chiral HPLC (Chiralpak AD, 70:30 hexane:IPA, 1.0 mL/min, $\lambda = 208$ nm) t_R (major) = 57.7 min, t_R (minor) = 70.8 min; $[\alpha]_D^{25} = +41.7^\circ$ ($c = 1.0$, CHCl_3); mp = 116–119°C; IR (thin film, cm^{-1}) 3306 (w), 3059 (w), 2942 (w), 1526 (s), 1451 (w), 1343 (s), 1246 (s), 1198 (w), 1086 (m), 1053 (s), 1022 (s); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 8.12 (1H, dd, $J = 6.8, 1.5$ Hz, ArH), 7.94 (1H, dd, $J = 8.3, 1.5$ Hz, ArH), 7.89–7.77 (4H, m, ArH), 7.68–7.65 (1H, m, ArH), 7.61–7.45 (5H, m, ArH), 7.31–7.21 (6H, m, ArH), 7.19–7.16 (1H, m, ArH), 7.12–7.09 (1H, m, ArH), 5.66 (1H, dd, $J = 15, 7.8$ Hz, O-CH₂), 5.57 (1H, dd, $J = 15, 7.3$ Hz, O-CH₂), 5.34 (1H, dd, $J = 15, 6.8$ Hz, O-CH₂), 5.28 (1H, dd, $J = 15, 7.8$ Hz, O-CH₂), 4.37 (1H, d, $J = 21$ Hz, P-CH), 3.88 (1H, d, $J = 13$ Hz, N-CH₂), 3.60 (1H, d, $J = 13$ Hz, N-CH₂), 2.53 (1H, s, N-H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 146.7 (s), 146.4 (s), 138.9 (s), 134.0 (s), 133.7 (s), 133.3 (d, $J = 1.5$ Hz), 133.2 (d, $J = 2.3$), 133.0 (d, $J = 6.1$), 132.6 (d, $J = 3.0$ Hz), 132.5 (d, $J = 6.1$ Hz), 128.8 (s), 128.7 (s), 128.5 (s), 128.5 (s), 128.4 (s), 128.3 (s), 128.2 (s), 128.2 (s), 127.9 (s), 127.8 (s), 127.3 (s), 126.5 (s), 126.4 (s), 125.8 (d, $J = 4.6$), 124.9 (s), 124.7 (s), 65.6 (d, $J = 6.1$ Hz), 64.8 (d, $J = 5.3$ Hz), 59.7 (d, $J = 156$ Hz), 51.1 (d, $J = 18$ Hz); $^{31}\text{P-NMR}$ (162 MHz, CDCl_3) δ 25.1; HRMS (ES) m/z for $\text{C}_{32}\text{H}_{29}\text{N}_3\text{O}_7\text{P}$ $[\text{M}+\text{H}]^+$ calcd. 598.1743, found 598.1757.

4o: Reaction was performed on a 0.50 mmol scale at 23 °C for 48 h using 10 mol% **1b** (0.0286 g, 0.0498 mmol), **3h** (0.175 g, 0.498 mmol), **2o** (0.0977 g, 0.498 mmol), and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (10:90 hexanes:ethyl acetate) to provide **4o** as a very viscous pale yellow oil (0.210 g, 0.383 mmol, 77%) in 96% *ee*. Chiral HPLC (Chiralpak AS, 85:15 hexane:EtOH, 1.5 mL/min, $\lambda = 208$ nm) t_R (minor) = 11.8 min, t_R (major) = 34.4 min; $[\alpha]_D^{25} = +23.7^\circ$ ($c = 1.0$, CHCl_3); IR (thin film, cm^{-1}) 3307 (m), 3063 (m), 2944 (w), 1531 (s), 1452 (m), 1343 (s), 1249 (s), 1198 (m), 1086 (s), 1026 (s); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 8.62–8.57 (2H, m, ArH), 8.13 (1H, d, $J = 8.3$ Hz, ArH), 8.06 (1H, dd, $J = 7.8, 1.0$ Hz, ArH), 7.89–7.85 (1H, m, ArH), 7.67–7.62 (2H, m, ArH), 7.55–7.42 (3H, m, ArH), 7.36–7.19 (7H, m, ArH), 5.63 (1H, dd, $J = 15, 7.8$ Hz, O-CH₂), 5.55 (1H, dd, $J = 15, 6.8$ Hz, O-CH₂), 5.40 (1H, dd, $J = 15, 6.8$ Hz, O-CH₂), 5.32 (1H, dd, $J = 15, 7.8$ Hz, O-CH₂), 4.24 (1H, d, $J = 21$ Hz, P-CH), 3.85 (1H, d, $J = 13$ Hz, N-CH₂), 3.56 (1H, d, $J = 13$ Hz, N-CH₂), 2.41 (1H, s, N-H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 150.3 (d, $J = 7.8$ Hz), 149.8 (d, $J = 2.8$ Hz), 146.8 (s), 146.6 (s), 138.4 (s), 135.9 (d, $J = 5.5$ Hz), 134.1 (s), 134.0 (s), 132.6 (d, $J = 6.9$ Hz), 132.2 (d, $J = 6.4$ Hz), 131.2 (d, $J = 2.8$ Hz), 128.9 (s), 128.9 (s), 128.6 (s), 128.5 (s), 128.4 (s), 128.3 (s), 127.5 (s), 125.1 (s), 125.0 (s), 123.9 (d, $J = 2.3$ Hz), 65.8 (d, $J = 5.5$ Hz), 65.0 (d, $J = 6.0$ Hz), 57.2 (d, $J = 157$ Hz), 51.2 (d, $J = 17$ Hz); $^{31}\text{P-NMR}$ (162 MHz, CDCl_3) δ 24.2; HRMS (ES) m/z for $\text{C}_{27}\text{H}_{26}\text{N}_4\text{O}_7\text{P}$ $[\text{M}+\text{H}]^+$ calcd. 549.1539, found 549.1533.

4p: Reaction was performed on a 0.50 mmol scale at 4 °C for 72 h using 10 mol% **1b** (0.0288 g, 0.0500 mmol), **3h** (0.176 g, 0.500 mmol), **2p** (0.0926 g, 0.500 mmol), and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (60:40 hexanes:ethyl acetate) to provide **4p** as a very viscous pale yellow oil (0.239 g, 0.445 mmol, 89%) in 92% *ee*. Chiral HPLC (Chiralpak AD, 70:30 hexane:IPA, 1.0 mL/min, $\lambda = 208$ nm) t_R (major) = 41.2 min, t_R (minor) = 46.2 min; $[\alpha]_D^{25} = +35.0^\circ$ ($c = 1.0$, CHCl_3); IR (thin film, cm^{-1}) 3326 (w), 3065 (w), 2944 (w), 1530 (s), 1449 (m), 1343 (s), 1252 (s), 1197 (m), 1086 (s), 1025 (s); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 8.14 (1H, dd, $J = 8.3, 1.0$ Hz, ArH), 8.09 (1H, dd, $J = 7.8, 1.0$ Hz, ArH), 7.77–7.73 (1H, m, ArH), 7.67–7.63 (1H, m, ArH), 7.61–7.43 (5H, m, ArH), 7.30–7.22 (5H, m, ArH), 6.44–6.40 (2H, m, ArH), 5.69 (1H, dd, $J = 15, 7.8$ Hz, O-CH₂), 5.58 (1H, dd, $J = 15, 6.8$ Hz, O-CH₂), 5.47 (1H, dd, $J = 15, 6.8$ Hz, O-CH₂), 5.36 (1H, dd, $J = 15, 7.8$ Hz, O-CH₂), 4.29 (1H, d, $J = 23$ Hz, P-CH), 3.90 (1H, d, $J = 13$ Hz, N-CH₂), 3.62 (1H, d, $J = 13$ Hz, N-CH₂), 2.31 (1H, s, N-H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 148.9 (d, $J = 2.3$ Hz), 146.6 (s), 146.5 (s), 143.1 (d, $J = 3.2$ Hz), 138.6 (s), 134.1 (s), 134.1 (s), 133.0 (d, $J = 6.9$ Hz), 132.8 (d, $J = 6.9$ Hz), 128.7 (s), 128.6 (s), 128.4 (s), 128.4 (s), 128.4 (s), 128.2 (s), 127.3 (s), 124.9 (s), 124.9 (s), 110.8 (d, $J = 2.3$ Hz), 110.0 (d, $J = 8.2$ Hz), 65.7 (d, $J = 5.5$ Hz), 65.0 (d, $J = 5.5$ Hz), 53.2 (d, $J = 164$ Hz), 51.3 (d, $J = 17$ Hz); $^{31}\text{P-NMR}$ (162 MHz, CDCl_3) δ 22.3; HRMS (ES) m/z for $\text{C}_{26}\text{H}_{25}\text{N}_3\text{O}_8\text{P}$ $[\text{M}+\text{H}]^+$ calcd. 538.1397, found 538.1390.

4q: Reaction was performed on a 0.50 mmol scale at 23 °C for 48 h using 10 mol% **1b** (0.0290 g, 0.0505 mmol), **3h** (0.178 g, 0.505 mmol), **2q** (0.102 g, 0.505 mmol), and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (60:40 hexanes:ethyl acetate) to provide **4q** as a very viscous pale yellow oil (0.249 g, 0.450 mmol, 89%) in 94% *ee*. Chiral HPLC (Chiralcel OD, 95:05

hexane:EtOH, 1.0 mL/min, λ = 208 nm) t_R (minor) = 44.8 min, t_R (major) = 50.6 min; $[\alpha]_D^{25}$ = +17.4° (c = 1.2, CHCl₃); IR (thin film, cm⁻¹) 3314 (w), 3065 (m), 2853 (m), 1528 (s), 1448 (s), 1342 (s), 1251 (s), 1196 (m), 1086 (s), 1023 (s); ¹H-NMR (500 MHz, CDCl₃) δ 8.13 (1H, dd, J = 8.3, 1.0 Hz, ArH), 8.07 (1H, dd, J = 8.3, 1.2 Hz, ArH), 7.73-7.70 (1H, m, ArH), 7.67-7.63 (1H, m, ArH), 7.57-7.42 (4H, m, ArH), 7.35-7.24 (6H, m, ArH), 7.16-7.13 (1H, m, ArH), 7.06-7.03 (1H, m, ArH), 5.64 (1H, dd, J = 15, 7.8 Hz, O-CH₂), 5.57 (1H, dd, J = 15, 6.8 Hz, O-CH₂), 5.43 (1H, dd, J = 15, 6.8 Hz, O-CH₂), 5.33 (1H, dd, J = 15, 7.8 Hz, O-CH₂), 4.47 (1H, d, J = 21 Hz, P-CH), 3.95 (1H, d, J = 13 Hz, N-CH₂), 3.67 (1H, d, J = 13 Hz, N-CH₂), 2.30 (1H, s, N-H); ¹³C-NMR (101 MHz, CDCl₃) δ 146.6 (s), 146.5 (s), 138.7 (s), 138.5 (d, J = 2.7 Hz), 134.1 (s), 134.0 (s), 132.9 (d, J = 6.9 Hz), 132.1 (d, J = 6.4 Hz), 128.7 (s), 128.6 (s), 128.5 (s), 128.5 (s), 128.5 (s), 128.3 (s), 127.5 (d, J = 8.2 Hz), 127.4 (s), 127.2 (d, J = 2.7 Hz), 126.1 (d, J = 3.7 Hz), 124.9 (s), 124.9 (s), 65.8 (d, J = 6.0 Hz), 65.1 (d, J = 6.0 Hz), 54.8 (d, J = 164 Hz), 51.1 (d, J = 17 Hz); ³¹P-NMR (162 MHz, CDCl₃) δ 23.2; HRMS (ES) m/z for C₂₆H₂₅N₃O₇PS [M+H]⁺ calcd. 554.1151, found 554.1160.

4r: Reaction was performed on a 0.50 mmol scale at 4 °C for 48 h using 10 mol% **1b** (0.0287 g, 0.0500 mmol), **3h** (0.176 g, 0.500 mmol), **2r** (0.0921 g, 0.500 mmol), and diethyl ether (1.2 mL). The product was purified via flash chromatography on silica gel (60:40 hexanes:ethyl acetate) to provide **4r** as a very viscous pale yellow oil (0.231 g, 0.431 mmol, 86%) in 81% *ee*. Chiral HPLC (Chiralpak AD, 70:30

hexane:IPA, 1.0 mL/min, λ = 208 nm) t_R (minor) = 18.1 min, t_R (major) = 21.8 min; $[\alpha]_D^{25}$ = +27.8° (c = 1.0, CHCl₃); IR (thin film, cm⁻¹) 3405 (m), 3300 (s), 3065 (m), 2944 (m), 1530 (s), 1449 (m), 1343 (s), 1229 (s), 1198 (m), 1086 (s), 1026 (s); ¹H-NMR (500 MHz, CDCl₃) δ 9.14 (1H, brs, N-H), 8.14 (1H, d, J = 7.8 Hz, ArH), 8.06 (1H, dd, J = 8.3, 1.0 Hz, ArH), 7.73-7.64 (2H, m, ArH), 7.58-7.41 (3H, m, ArH), 7.32-7.20 (6H, m, ArH), 6.83-6.78 (1H, m, ArH), 6.18-6.14 (2H, m, ArH), 5.63 (1H, dd, J = 15, 7.8 Hz, O-CH₂), 5.52 (1H, dd, J = 15, 6.8 Hz, O-CH₂), 5.34 (1H, dd, J = 15, 7.3 Hz, O-CH₂), 5.20 (1H, dd, J = 15, 7.8 Hz, O-CH₂), 4.26 (1H, d, J = 21 Hz, P-CH), 3.86 (1H, d, J = 13 Hz, N-CH₂), 3.63 (1H, d, J = 13 Hz, N-CH₂), 2.27 (1H, brs, N-H); ¹³C-NMR (101 MHz, CDCl₃) δ 146.7 (s), 146.5 (s), 139.2 (s), 134.3 (s), 134.2 (s), 133.1 (d, J = 7.3 Hz), 133.0 (d, J = 6.4 Hz), 128.8 (s), 128.6 (s), 128.6 (s), 128.4 (s), 128.4 (s), 128.3 (s), 127.2 (s), 125.0 (s), 124.9 (s), 124.3 (d, J = 4.6 Hz), 119.4 (s), 110.2 (d, J = 10.2 Hz), 108.3 (s), 65.9 (d, J = 5.5 Hz), 65.8 (d, J = 5.5 Hz), 52.9 (d, J = 162 Hz), 51.1 (d, J = 18 Hz); ³¹P-NMR (162 MHz, CDCl₃) δ 24.6; HRMS (ES) m/z for C₂₆H₂₆N₄O₇P [M+H]⁺ calcd. 537.1539, found 537.1536.

VI. Deprotection.

5a (representative experimental procedure for hydrogenolytic deprotection): A 100-mL round bottomed flask was charged with **4a** (0.252 g, 0.459 mmol, 98% *ee*), methanol (7.5 mL), and Pd/C (10% w/w) (0.0978 g, 0.0919 mmol, 0.20 equivalents) and sealed with a rubber septum. The head-space was evacuated and back-filled with nitrogen. The head-space was evacuated and back-filled with hydrogen three times and then stirred under a balloon of hydrogen for 24 h. The reaction mixture was concentrated *in vacuo*. The crude solid was suspended in ethyl acetate (5 mL) and vacuum filtered. The light gray solid residue was washed with ethyl acetate (65 mL). The collection flask was replaced, and the solid was washed with deionized water (70 mL). The aqueous solution was vacuum filtered a second time to remove any trace Pd/C and then concentrated *in vacuo* to provide the product **5a** as a white solid (0.0745 g, 0.398 mmol, 87%) in 97% *ee*. Chiral HPLC (Chiralcel OD, 95:05 hexane:IPA, 1.0 mL/min, λ = 208 nm) t_R (minor) = 19.2 min, t_R (major) = 30.2 min (as

N-Cbz dimethyl phosphonate derivative); $[\alpha]_D^{23} = +17.1^\circ$ ($c = 0.96$, 1N NaOH_{aq}) (lit.⁵ $[\alpha]_D^{20} = +18.2$ ($c = 0.7$, 1 N NaOH_{aq})); mp = 280-283°C (lit.⁵ = 284-285°C); IR (KBr, cm⁻¹) 3219 (m), 3003 (s), 2922 (s), 1620 (m), 1539 (m), 1267 (m), 1188 (s), 1067 (s), 916 (s); ¹H-NMR (500 MHz, 0.5 M NaOD_{aq}) δ 7.34-7.17 (5H, m, ArH), 3.71 (1H, d, $J = 16$ Hz, P-CH); ¹³C-NMR (126 MHz, 0.5 M NaOD_{aq}) δ 145.5 (s), 128.6 (s), 128.2 (s), 126.8 (s), 56.1 (d, $J = 131$ Hz); ³¹P-NMR (162 MHz, CDCl₃) δ 18.7; HRMS (ES) m/z for C₇H₁₁NO₃P [M+H]⁺ calcd. 188.0476, found 188.0483.

5b: Reaction was performed on a 0.42 mmol scale using **4b** (0.227 g, 0.419 mmol, 96% *ee*), methanol (7.0 mL), and Pd/C (10% w/w) (0.0893 g, 0.0838 mmol, 0.20 equiv) for 24 h. The aqueous washes were concentrated *in vacuo* to provide the product **5b** as a white solid (0.0678 g, 0.374 mmol, 89%) in 96% *ee*. Chiral HPLC (Chiralcel OD, 95:05 hexane:IPA, 1.0 mL/min, $\lambda = 208$ nm) t_R (minor) = 9.9 min, t_R (major) = 14.4 min (as *N*-Cbz dimethyl phosphonate derivative); $[\alpha]_D^{24} = -15.5^\circ$ ($c = 0.78$, 1N NaOH_{aq}); mp = 263-266°C; IR (KBr, cm⁻¹) 3133 (s), 3092 (s), 2969 (s), 2880 (s), 2683 (w), 1526 (m), 1217 (s), 1165 (w), 1059 (s), 1026 (m), 932 (m); ¹H-NMR (500 MHz, 0.5 M NaOD_{aq}) δ 2.60 (1H, dd, $J = 14, 2.4$ Hz, P-CH), 1.71-1.61 (1H, m, CH(CH₂CH₃)₂), 1.48-1.36 (2H, m, CH₂CH₃), 1.28-1.16 (1H, m, CH₂CH₃), 1.05-0.94 (1H, m, CH₂CH₃), 0.79 (3H, dd, $J = 8.5, 6.9$ Hz, CH₃), 0.78 (3H, dd, $J = 7.3, 6.1$ Hz, CH₃); ¹³C-NMR (126 MHz, 0.5 M NaOD_{aq}) δ 51.6 (d, $J = 138$ Hz), 42.5 (s), 23.3 (d, $J = 10$ Hz), 21.8 (s), 12.1 (s), 11.9 (s); ³¹P-NMR (162 MHz, CDCl₃) δ 22.7; HRMS (ES) m/z for C₆H₁₇NO₃P [M+H]⁺ calcd. 182.0946, found 182.0941.

5f (*R*)-Leu^P: Reaction was performed on a 1.31 mmol scale using **4f** (0.689 g, 1.31 mmol, 99% *ee*), methanol (20 mL), and Pd/C (10% w/w) (0.279 g, 0.262 mmol, 0.20 equiv) for 72 h. The aqueous washes were concentrated *in vacuo* to provide the product **5f** as a white solid (0.204 g, 1.22 mmol, 93%) in 98% *ee*. Chiral HPLC (Chiralcel OD, 95:05 hexane:EtOH, 1.0 mL/min, $\lambda = 208$ nm) t_R (minor) = 10.7 min, t_R (major) = 12.7 min (as *N*-Cbz dimethyl phosphonate derivative); $[\alpha]_D^{24} = -29.0^\circ$ ($c = 1.0$, 1N NaOH_{aq}) (lit.⁶ $[\alpha]_D^{25} = -29.5$ ($c = 1$, 1N NaOH_{aq})); mp = 280-282°C (lit.⁶ mp = 285-286°C); IR (KBr, cm⁻¹) 3084 (m), 2961 (s), 2872 (s), 1535 (s), 1248 (m), 1180 (s), 1028 (s), 926 (s); ¹H-NMR (500 MHz, 0.5 M NaOD_{aq}) δ 2.52 (1H, dt, $J = 11, 2.9$ Hz, P-CH), 1.72-1.61 (1H, m, CH(CH₃)₂), 1.41-1.30 (1H, m, CH₂), 1.29-1.19 (1H, m, CH₂), 0.83 (3H, d, $J = 6.8$ Hz, CH₃), 0.77 (3H, d, $J = 6.3$ Hz, CH₃); ¹³C-NMR (126 MHz, 0.5 M NaOD_{aq}) δ 48.3 (d, $J = 138$ Hz), 41.4 (s), 24.8 (d, $J = 13$ Hz), 24.1 (s), 21.0 (s); ³¹P-NMR (162 MHz, CDCl₃) δ 23.0; HRMS (ES) m/z for C₁₀H₂₉N₂O₆P₂ [2M+H]⁺ calcd. 335.1501, found 335.1505.

VII. General Procedure for Generating *N*-Cbz Dimethyl Phosphonate Derivative for %*ee* Determination by Chiral HPLC.

7a (representative procedure for derivatization of **5** for %*ee* analysis): A 4-mL glass vial was charged with **5a** (0.0113 g, 0.0638 mmol, 1 equivalent) and a magnetic stir bar. The vial was sealed with a septum cap and a nitrogen line was connected. DI water (0.30 mL) and dioxane (0.30 mL) were added. Triethylamine (84 μ L, 0.603 mmol, 10 equivalents) was added and the stirring solution became homogeneous. Finally, benzyl chloroformate (43 μ L, 0.302 mmol, 5 equivalents) was added drop-wise. After 16 h, the reaction mixture was transferred to a 30 mL separatory funnel with a saturated aqueous solution of sodium carbonate (3mL, to litmus blue) and washed with diethyl ether (2 X 7 mL). The aqueous solution was acidified to pH<1 (litmus red) by the drop-wise addition of a concentrated solution of hydrochloric acid. The phosphonic acid precipitated out of solution and was extracted into ethyl acetate (3 X 7 mL). The combined ethyl acetate solution was dried over sodium sulfate, filtered, and concentrated *in vacuo* to yield crude **6a** (0.0183 g, 0.0570 mmol, 94%) as a white solid. This crude material was transferred to a 4-mL glass vial equipped with a magnetic stir bar, septum cap and nitrogen line. Methanol (0.55 mL) and

dichloromethane (0.10 mL) were added. A 2.0 M solution of (trimethylsilyl)diazomethane in hexanes (0.17 mL, 0.34 mmol, 6 equivalents) was added drop-wise over 30 seconds. After 30 minutes, the reaction was concentrated *in vacuo*. The crude residue was purified by flash chromatography on silica gel (25:75 hexanes:ethyl acetate) to provide **7a** (0.0079 g, 0.0226 mmol, 40%, 37% from **5a**) as a white solid which was used directly for *%ee* determination by chiral HPLC.

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Chiral HPLC: Pirkle Covalent L-Leucine, 95:05 Hex:IPA, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
82.11	16128328	50.66
88.72	15707217	49.34
Totals	31835545	100.00

98 % ee

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
87.93	31992751	98.99
100.13	327830	1.01
Totals	32320581	100.00

**Chiral HPLC: Chiralcel OD, 97:03 Hex:EtOH, 1.0 ml/min, 208 nm
racemic**

SPD-10Avp Ch1-208nm Results		
Retention Time	Area	Area Percent
28.57	39348849	49.89
35.05	39522276	50.11
Totals	78871125	100.00

96 % ee

SPD-10Avp Ch1-208nm Results		
Retention Time	Area	Area Percent
28.64	1594678	2.11
34.83	74151150	97.89
Totals	75745828	100.00

Chiral HPLC: Chiralcel OD, 97:03 Hex:EtOH, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
38.86	19659064	50.05
45.44	19621581	49.95
Totals	39280645	100.00

90 % ee

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
41.67	3236470	4.95
49.51	62143407	95.05
Totals	65379877	100.00

Chiral HPLC: Chiralcel OD, 95:05 Hex:EtOH, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results			
Retention Time	Area	Area Percent	
22.30	51079939	49.83	
28.82	51423601	50.17	
Totals	102503540	100.00	

90 % ee

SPD-10Avp Ch1-208nm Results			
Retention Time	Area	Area Percent	
20.80	2960389	4.97	
26.36	56664704	95.03	
Totals	59625093	100.00

Chiral HPLC: Chiralcel OD, 95:05 Hex:EtOH, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results			
Retention Time	Area	Area Percent	
18.98	35576033	49.89	
25.27	35730747	50.11	
Totals	71306780	100.00	

93 % ee

SPD-10Avp Ch1-208nm Results			
Retention Time	Area	Area Percent	
19.65	3511188	3.72	
26.02	90866874	96.28	
Totals	94378062	100.00

Chiral HPLC: Chiralcel OD, 97:03 Hex:EtOH, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
46.49	11054504	49.90
53.42	11098358	50.10
Totals	22152862	100.00

82 % ee

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
48.35	2431411	8.91
55.06	24851774	91.09
Totals	27283185	100.00

4f after recrystallization to 99% ee

Chiral HPLC: Chiralcel OD, 97:03 Hex:EtOH, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results			
	Retention Time	Area	Area Percent
	46.49	11054504	49.90
	53.42	11098358	50.10
	Totals	22152862	100.00

99 % ee

SPD-10Avp Ch1-208nm Results			
	Retention Time	Area	Area Percent
	48.49	450591	0.72
	54.81	62011750	99.28
	Totals	62462341	100.00

Chiral HPLC: Chiralpak AD, 70:30 Hex:IPA, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results			
Retention Time	Area	Area Percent	
34.36	15546682	49.91	
53.17	15604766	50.09	
Totals	31151448	100.00	

98 % ee

SPD-10Avp Ch1-208nm Results			
Retention Time	Area	Area Percent	
35.25	134994947	99.25	
55.16	1017013	0.75	
Totals	136011960	100.00

Chiral HPLC: Chiralpak AD, 70:30 Hex:IPA, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
59.23	33425814	50.01
68.10	33412829	49.99

Totals	66838643	100.00
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96 % ee

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
58.38	73305868	98.12
66.30	1405048	1.88

Totals	74710916	100.00
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Chiral HPLC: Chiralpak AD, 70:30 Hex:IPA, 1.5 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results		
Retention Time	Area	Area Percent
48.02	14709984	50.30
57.69	14536162	49.70
Totals	29246146	100.00

96 % ee

SPD-10Avp Ch1-208nm Results		
Retention Time	Area	Area Percent
46.57	103679118	98.07
54.22	2043643	1.93
Totals	105722761	100.00

Chiral HPLC: Pirkle Covalent L-Leucine, 99:01 Hex:EtOH, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results		
Retention Time	Area	Area Percent
121.82	51373316	50.15
130.51	51070149	49.85
Totals	102443465	100.00

92 % ee

SPD-10Avp Ch1-208nm Results		
Retention Time	Area	Area Percent
123.18	157049533	96.12
136.50	6336163	3.88
Totals	163385696	100.00

Chiral HPLC: Chiralpak AD, 70:30 Hex:IPA, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
36.59	63501810	50.73
45.60	61674936	49.27
Totals	125176746	100.00

96 % ee

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
35.47	65635348	98.26
44.02	1161964	1.74
Totals	66797312	100.00

Chiral HPLC: Chiralpak AD, 87:13 Hex:EtOH, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
68.88	37288415	49.93
74.75	37389808	50.07

Totals	74678223	100.00
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98 % ee

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
71.58	1518577	1.11
76.47	135699963	98.89

Totals	137218540	100.00
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Chiral HPLC: Chiralpak AD, 70:30 Hex:IPA, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
39.94	44937310	50.18
62.17	44613811	49.82

Totals	89551121	100.00
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99 % ee

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
38.61	107654959	99.52
58.38	520790	0.48

Totals	108175749	100.00
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Chiral HPLC: Chiralpak AD, 70:30 Hex:IPA, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
59.67	55845540	49.98
73.13	55882584	50.02

Totals	111728124	100.00
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98 % ee

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
57.67	117044577	99.00
70.85	1177568	1.00

Totals	118222145	100.00
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Chiral HPLC: Chiralpak AS, 85:15 Hex:EtOH, 1.5 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
11.94	39008712	50.66
33.89	37998451	49.34

Totals	77007163	100.00
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96 % ee

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
11.78	1693523	2.22
34.44	74471263	97.78

Totals	76164786	100.00
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Chiral HPLC: Chiralpak AD, 70:30 Hex:IPA, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results		
Retention Time	Area	Area Percent
41.73	69586958	50.35
47.03	68607562	49.65
Totals	138194520	100.00

92 % ee

SPD-10Avp Ch1-208nm Results		
Retention Time	Area	Area Percent
41.20	79176926	96.15
46.21	3168525	3.85
Totals	82345451	100.00

Chiral HPLC: Chiralcel OD, 95:05 Hex:EtOH, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
44.57	34695095	50.06
50.57	34617888	49.94
Totals	69312983	100.00

94 % ee

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
44.81	2542692	2.89
50.55	85473129	97.11
Totals	88015821	100.00

Chiral HPLC: Chiralpak AD, 70:30 Hex:IPA, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results		
Retention Time	Area	Area Percent
20.39	24022571	50.11
25.05	23919299	49.89
Totals	47941870	100.00

81 % ee

SPD-10Avp Ch1-208nm Results		
Retention Time	Area	Area Percent
18.10	14602304	9.27
21.82	143004701	90.73
Totals	157607005	100.00

%ee analysis for 5a

Chiral HPLC: Chiralcel OD, 95:05 Hex:IPA, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
19.55	6736672	49.97
32.64	6744031	50.03
Totals	13480703	100.00

97 % ee

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
19.23	774254	1.43
30.21	53519009	98.57
Totals	54293263	100.00

%ee analysis for 5b

Chiral HPLC: Chiralcel OD, 95:05 Hex:IPA, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
9.78	5464457	50.09
14.16	5444236	49.91
Totals	10908693	100.00

96 % ee

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
9.94	218383	1.92
14.40	11179785	98.08
Totals	11398168	100.00

%ee analysis for 5f

Chiral HPLC: Chiralcel OD, 95:05 Hex:EtOH, 1.0 ml/min, 208 nm

racemic

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
10.74	9944761	49.78
12.76	10031496	50.22
Totals	19976257	100.00

98 % ee

SPD-10Avp Ch1-208nm Results

Retention Time	Area	Area Percent
10.69	192377	0.76
12.68	25149372	99.24
Totals	25341749	100.00