Supplementary information for

Bifunctional Iminophosphorane Organocatalysts for Enantioselective Synthesis: Application to the Ketimine Nitro-Mannich Reaction

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2. Supplementary Methods

2.1. General information

Solvents and Reagents
Concentration under reduced pressure was performed by rotary evaporation at the appropriate pressure and temperature. Reagents used were obtained from commercial suppliers or purified according to standard procedures. Petroleum ether (PE) refers to distilled light petroleum of fraction 30 - 40 °C. Anhydrous toluene, tetrahydrofuran, dichloromethane and diethyl ether were dried by filtration through activated alumina (powder ~150 mesh, pore size 58 Å, basic, Sigma-Aldrich) columns. Dimethyl sulfoxide and dimethylformamide were used as supplied. Deuterated solvents were used as supplied.

Chromatography
Reactions were monitored by thin layer chromatography (TLC) using Merck silica gel 60 F254 plates and visualized by fluorescence quenching under UV light. In addition, TLC plates were stained with potassium permanganate solution. Chromatographic purification was performed on VWR 60 silica gel 40 - 63 μm using technical grade solvents that were used as supplied.

Instrumentation
Melting points were obtained on a Leica Galen III Hot-stage melting point apparatus and microscope and on a Kofler hot block and are reported uncorrected. NMR spectra were recorded on a Bruker Spectrospin spectrometer operating at 200, 400 or 500 MHz (1H acquisitions), 50, 100 or 125 MHz (13C acquisitions), 162 or 202 MHz (31P acquisitions) and 376 or 470 MHz (19F acquisitions). Chemical shifts (δ) are reported in ppm with the solvent resonance as the internal standard (e.g. Chloroform δ 7.27 ppm for 1H and 77.0 ppm for 13C). Coupling constants (J) are reported in hertz (Hz). Data are reported as follows: multiplicity [s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, ddd = doublet of doublets of doublets, td = triplet of doublets, m = multiplet, br = broad], coupling constants in Hz, integration. Two-dimensional spectroscopy (COSY, HSQC and HMBC) was used to assist in the assignment and the data is not reported. High-resolution mass spectra (ESI) were recorded on Bruker Daltonics MicroTOF mass spectrometer. Infrared spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer as a thin film. Only selected maximum absorbances are reported. Optical rotations were recorded using a Perkin Elmer 341 polarimeter; [α]D values are reported in 10⁻¹ deg cm² g⁻¹; concentrations (c) are quoted in g/100 mL; D refers to the D-line of sodium (589 nm); temperatures (T) are given in degrees Celsius.
(°C). (+) and (−) compound number prefixes indicate the sign of the optical rotation. The enantiomeric excesses were determined by HPLC analysis on an Agilent 1200 Series instrument employing a chiral stationary phase column specified in the individual experiment and by comparing the samples with the appropriate racemic mixtures.

2.2. Synthesis and characterization of catalysts 4a, 4d - 4i precursors

In the preparation of catalysts 4d, 4e, 4f and 4a azide precursors (13, 17, 22 and 2), the amino alcohols 9, 14, 18 and 32 (See Supplementary Figures 1, 2, 3 and 5) were synthesized by the reduction of the corresponding commercial natural or unnatural amino acid according to a literature procedure. Compounds 23, 37 and 42 are commercially available.

Unless otherwise stated, all synthesized azides were concentrated under reduced pressure by rotary evaporation inside a fume cupboard behind a blast shield at T < 25 °C.

Synthesis of catalyst 4d precursor (See Supplementary Figure 1)

Compounds 10 and 11 were synthesized according to literature procedures and their physical and spectroscopic properties are in agreement to those reported.

tert-Butyl [(2S)-1-azido-3-phenylpropan-2-yl]carbamate, 12

To a solution of compound 11 (1.25 g, 3.08 mmol) in DMF (10 mL), NaN₃ (220 mg, 3.39 mmol) was added at rt and the resulting suspension was stirred at 45 °C for 7 h. After cooling to rt, H₂O (15 ml) was added to the reaction mixture and it was extracted with Et₂O (3 x 40 mL). The combined organics were dried over Na₂SO₄, filtered and concentrated. The resulting crude was purified by flash column chromatography (PE/Et₂O 7:3) to yield 12 (460 mg, 54%) as a colorless solid.

[α]D²⁴ = - 9.4 (c = 0.98, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ ppm 1.44 (s, 9H), 2.79 (dd, J = 13.5, 8.0 Hz, 1H), 2.88 (dd, J = 13.5, 6.2 Hz, 1H), 3.31 (dd, J = 12.4, 4.5 Hz, 1H), 3.42 (dd, J = 12.4, 4.0 Hz, 1H), 3.98 (br s, 1H), 4.69 (m, 1H), 7.17 - 7.28 (m, 3H), 7.28 - 7.36 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 28.6, 38.4, 51.6, 53.4, 80.0, 127.0, 128.9, 129.5, 137.4, 155.3; IR
\[ \nu_{\text{max}}/\text{cm}^{-1} \, 3339, \, 2978, \, 2098, \, 1496, \, 1366, \, 1165; \, \text{MP} \, 60 \, ^\circ\text{C}; \, \text{HRMS} \, (\text{ESI+}): \text{calcd. for} \, C_{14}H_{20}N_{4}NaO_{2} \, [\text{M+Na}]^{+} \, 299.1478, \, \text{found} \, 299.1471. \]

1-[(2S)-1-Azido-3-phenylpropan-2-yl]-3-[3,5-bis(trifluoromethyl)phenyl]thiourea, 13

![Structure of 13](image)

An ice-cooled round-bottom flask containing compound 12 (386 mg, 1.40 mmol) under inert atmosphere was placed behind a blast-shield. A solution of 2 M HCl in Et₂O (15.0 mL, 30.0 mmol) was added carefully dropwise and the resulting solution was stirred at rt for 24 h. 2 M NaOH solution was added until pH 14, the aqueous phase was extracted with Et₂O (3 x 20 mL) and the combined organic were dried over Na₂SO₄, filtered and concentrated (CAUTION: solvents were evaporated under a stream of N₂ behind a blast-shield). The crude aminoazide was dissolved in THF (5.0 mL), 3,5-bis(trifluoromethyl)phenyl isothiocyanate (0.250 mL, 1.49 mmol) was added and the solution was stirred at rt for 16 h. After evaporation of the solvents, the crude product was purified by flash column chromatography (PE/Et₂O 8:2 to 7:3) to obtain 13 (447 mg, 71% over 2 steps) as a colorless solid.

\[ [\alpha]_{D}^{24} \, = \, + \, 3.3 \, (c \, = \, 0.84, \, \text{CHCl}_3); \, ^{1}H \, \text{NMR} \, (500 \, \text{MHz, CDCl}_3) \, \delta \, \text{ppm} \, 2.86 \, (dd, \, J \, = \, 13.8, \, 8.2 \, \text{Hz, 1H}), \, 3.06 \, (dd, \, J \, = \, 13.8, \, 6.6 \, \text{Hz, 1H}), \, 3.48 \, (dd, \, J \, = \, 12.5, \, 3.4 \, \text{Hz, 1H}), \, 3.72 \, (dd, \, J \, = \, 12.5, \, 4.3 \, \text{Hz, 1H}), \, 4.87 \, (br \, s, \, 1H), \, 6.24 \, (br \, s, \, 1H), \, 7.19 - 7.38 \, (m, \, 5H), \, 7.69 \, (s, \, 2H), \, 7.76 \, (s, \, 1H), \, 8.36 \, (br \, s, \, 1H); \, ^{13}C \, \text{NMR} \, (125 \, \text{MHz, CDCl}_3) \, \delta \, \text{ppm} \, 37.4, \, 52.3, \, 55.4, \, 119.7 - 119.9 \, (m), \, 122.6 \, (q, \, J_{CF} = 272.7 \, \text{Hz}), \, 124.0 - 124.1 \, (m), \, 127.2, \, 128.9, \, 129.1, \, 133.2 \, (q, \, J_{CF} = 34.3 \, \text{Hz}), \, 136.2, \, 138.2, \, 180.0; \, ^{19}F \, \text{NMR} \, (376.5 \, \text{MHz, CDCl}_3) \, \delta \, \text{ppm} \, -63.0; \, \text{IR} \, \nu_{\text{max}}/\text{cm}^{-1} \, 3247, \, 2105, \, 1529, \, 1382, \, 1277, \, 1175, \, 1133; \, \text{MP} \, 96 - 98 \, ^\circ\text{C}; \, \text{HRMS} \, (\text{ESI+}): \text{calcd. for} \, C_{18}H_{15}F_{6}N_{5}NaS \, [\text{M+Na}]^{+} \, 470.0845, \, \text{found} \, 470.0839. \]

**Synthesis of catalyst 4e precursor** (See Supplementary Figure 2)

Compounds 15⁴ and 16⁵ were synthesized according to literature procedures and their physical and spectroscopic properties are in agreement to those reported.⁴
1-[(2S)-1-Azido-3-methylbutan-2-yl]-3-[3,5-bis(trifluoromethyl)phenyl]thiourea, 17

To a solution of azide 16 (322 mg, 0.920 mmol) in THF (4.5 mL) was added diethylamine (1.90 mL, 18.2 mmol) and the resulting solution was stirred at rt for 16 h. After evaporation of the solvents by a stream of N₂, the residue was dissolved in toluene (4.0 mL), concentrated under a stream of N₂ and this procedure was repeated 4 times. The resulting crude was dissolved in THF (4.0 mL), 3,5-bis(trifluoromethyl)phenyl isothiocyanate (0.410 mL, 2.28 mmol) was added and the solution was stirred at rt for 16 h. After evaporation of the solvents, the crude product was purified by flash column chromatography (PE/Et₂O 9:1 to 8:2) to obtain 17 (194 mg, 53% over 2 steps) as a colorless solid.

\[ [\alpha]_D^{23} = -6.4 (c = 1.00, \text{CHCl}_3); \]

\[^1^H\text{NMR} (500\text{ MHz, CDCl}_3) \delta \text{ppm} 0.99 (d, J = 6.6 \text{ Hz, } 3\text{H}), 1.02 (d, J = 6.6 \text{ Hz, } 3\text{H}), 1.93 (dq, J = 14.3, 6.9 \text{ Hz, } 1\text{H}), 3.60 (dd, J = 12.6, 4.4 \text{ Hz, } 1\text{H}), 3.79 (dd, J = 12.6, 4.1 \text{ Hz, } 1\text{H}), 4.42 (br s, 1H), 6.19 (br s, 1H), 7.75 (s, 1H), 7.81 (s, 2H), 8.29 (br s, 1H);

\[^1^3^C\text{NMR} (125\text{ MHz, CDCl}_3) \delta \text{ppm} 19.0, 19.3, 29.7, 52.0, 60.0, 119.6 - 119.8 (m), 122.7 (q, J_{CF} = 272.7 \text{ Hz}), 123.8 - 124.0 (m), 133.3 (q, J_{CF} = 34.3 \text{ Hz}), 138.5, 180.6; \]

\[^1^9^F\text{NMR} (470\text{ MHz, CDCl}_3) \delta \text{ppm} -63.1; \]

\[^{IR} \nu_{\max}/\text{cm}^{-1} 3248, 2111, 1536, 1383, 1276, 1129; \]

\[^{MP} 112 - 115 \degree\text{C}; \]

\[^{HRMS} (ESI+): \]

calcld. for C_{14}H_{15}F_{6}N_{5}NaS [M+Na]^+ 422.0845, found 422.0831.

**Synthesis of catalyst 4f precursor** (See Supplementary Figure 3)

Compounds 19⁶ and 20⁷ were synthesized according to literature procedures and their physical and spectroscopic properties are in agreement to those reported.

**tert-Butyl [(1R)-2-azido-1-phenylethyl]carbamate, 21⁸**

To a stirred solution of tosylate 20 (5.53 g, 14.1 mmol) in DMF (47 mL) was added NaN₃ (1.01 g, 15.6 mmol) at rt. The reaction mixture was warmed to 45 °C and stirring was maintained for 14 h. The reaction mixture was cooled to rt then diluted with H₂O (100 mL) and Et₂O (60 mL). The aqueous phase was extracted with Et₂O (2 x 30 mL) and the combined organics were washed with brine (50 mL), dried over MgSO₄, filtered and concentrated. The crude product was purified by flash column chromatography (PE to PE/EtOAc 9:1) to obtain 21 (2.83 g, 76%) as a colorless solid.
$[\alpha]_D^{24} = -7.5 \ (c = 1.32, \text{CHCl}_3); \ ^1H\ \text{NMR} \ (400 \text{ MHz, CDCl}_3) \ \delta \text{ ppm } 1.45 \ (s, 9\text{H}), \ 3.55 - 3.69 \ (m, \ 2\text{H}), \ 4.89 \ (br \ s, \ 1\text{H}), \ 5.15 \ (d, \ J = 7.6 \text{ Hz, } 1\text{H}), \ 7.28 - 7.43 \ (m, \ 5\text{H}); \ ^13C\ \text{NMR} \ (100 \text{ MHz, CDCl}_3) \ \delta \text{ ppm } 28.3, \ 54.1, \ 55.6, \ 80.1, \ 126.5, \ 128.0, \ 128.8, \ 139.3, \ 155.1; \ \text{IR} \ \nu_{\max}/\text{cm}^{-1} \ 2970, \ 2093, \ 1738, \ 1512, \ 1443, \ 1366, \ 1216; \ \text{MP} \ 82 - 84 \degree \text{C}; \ \text{HRMS} \ (\text{ESI+}): \ \text{calcd. for } \text{C}_{13}\text{H}_{18}\text{N}_4\text{NaO}_2 \ [\text{M+Na}]^+ \ 285.1322, \ \text{found } 285.1312.

1-[(1R)-2-Azido-1-phenylethyl]-3-[3,5-bis(trifluoromethyl)phenyl]thiourea, 22

An ice-cooled round-bottom flask containing compound 21 (1.50 g, 5.73 mmol) under inert atmosphere was placed behind a blast-shield. TFA (6.00 mL, 78.0 mmol) was added carefully dropwise and the resulting solution was stirred at rt for 3 h. TFA was evaporated under a stream of N2, the residue diluted with H2O (10 mL) and Et2O (20 mL) and solid NaOH was added after cooling to 0 °C until pH 14. The aqueous phase was extracted with Et2O (2 x 10 mL) and the combined organics were dried over MgSO4, filtered and concentrated (CAUTION: solvents were evaporated under a stream of N2 behind a blast-shield). The crude aminoazide was dissolved in THF (20 mL), 3,5-bis(trifluoromethyl)phenyl isothiocyanate (1.20 mL, 6.30 mmol) was added and the solution was stirred at rt for 8 h. After evaporation of the solvents, the crude product was purified by flash column chromatography (PE to PE/EtOAc 9:1) to yield 22 (2.01 g, 81% over 2 steps) as a colorless solid.

$[\alpha]_D^{24} = +16.8 \ (c = 1.14, \text{CHCl}_3); \ ^1H\ \text{NMR} \ (400 \text{ MHz, CDCl}_3) \ \delta \text{ ppm } 3.78 \ (dd, \ J = 12.6, \ 5.1 \text{ Hz, } 1\text{H}), \ 3.90 \ (dd, \ J = 12.6, \ 4.8 \text{ Hz, } 1\text{H}), \ 5.69 \ (br \ s, \ 1\text{H}), \ 6.93 \ (br \ s, \ 1\text{H}), \ 7.28 - 7.43 \ (m, \ 5\text{H}), \ 7.72 \ (s, \ 1\text{H}), \ 7.77 \ (s, \ 2\text{H}), \ 8.54 \ (br \ s, \ 1\text{H}); \ ^13C\ \text{NMR} \ (125 \text{ MHz, CDCl}_3) \ \delta \text{ ppm } 54.9, \ 57.7, \ 119.6 \ (spt, \ J_{CF} = 3.2 \text{ Hz}), \ 122.7 \ (q, \ J_{CF} = 273.0 \text{ Hz}), \ 123.8 \ (m), \ 126.6, \ 128.7, \ 129.2, \ 133.0 \ (q, \ J_{CF} = 33.6 \text{ Hz}), \ 137.4, \ 138.6, \ 180.2; \ ^19F\ \text{NMR} \ (376 \text{ MHz, CDCl}_3) \ \delta \text{ ppm } -63.1; \ \text{IR} \ \nu_{\max}/\text{cm}^{-1} \ 3214, \ 3031, \ 2102, \ 1542, \ 1470, \ 1382, \ 1334, \ 1280, \ 1169, \ 1126; \ \text{MP} \ 136 - 137 \degree \text{C}; \ \text{HRMS} \ (\text{ESI+}): \ \text{calcd. for } \text{C}_{17}\text{H}_{13}\text{F}_6\text{N}_5\text{NaS} \ [\text{M+Na}]^+ \ 456.0688, \ \text{found } 456.0695.
Synthesis of catalyst 4g precursor (See Supplementary Figure 4)

Compounds 24,9 25,10 and 2611 were synthesized according to literature procedures and their physical and spectroscopic properties are in agreement to those reported.

*tert*-Butyl [(2R)-3-hydroxy-1,1-diphenylpropan-2-yl]carbamate, 28

![Chemical Structure of 28]

To a solution of compound 26 (3.05 g, 7.96 mmol) in formic acid (150 mL) was added Pd(OH)$_2$ on carbon (1:4 catalyst/substrate by weight). The resulting suspension was stirred under a H$_2$ atmosphere at 60 °C for 48 h. The catalyst was removed by filtration and the solvent was evaporated. The resulting crude product was dissolved in H$_2$O/MeOH (1:1, 200 mL), NaOH (3.00 g, 75.0 mmol) was added and the suspension was heated at reflux for 12 h. MeOH was removed *in vacuo*, the aqueous layer was extracted with CHCl$_3$/isopropanol (3:1) (4 × 60 mL) and the combined organics were dried over Na$_2$SO$_4$, filtered and concentrated to give 1.57 g of crude amino alcohol 27. This compound was dissolved in CH$_2$Cl$_2$ (35 mL), NEt$_3$ (1.00 mL, 7.60 mmol) and Boc$_2$O (1.51 g, 6.91 mmol) were added and the reaction mixture was stirred at rt for 16 h. After evaporation of the solvents, the crude reaction mixture was purified by flash column chromatography (PE/EtOAc 4:1) to obtain 28 (1.95 g, 75% over 2 steps) as a colorless solid.

[$\alpha$]$_D^{23}$ = -28.4 (c = 1.12, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm 1.35 (s, 9H), 2.54 (br s, 1H), 3.47 (dd, $J = 11.1, 4.5$ Hz, 1H), 3.67 (dd, $J = 11.1, 3.0$ Hz, 1H), 4.18 (d, $J = 10.9$ Hz, 1H), 4.50 (br s, 1H), 4.75 (d, $J = 8.6$ Hz, 1H), 7.15 - 7.23 (m, 2H), 7.26 - 7.31 (m, 4H), 7.32 - 7.37 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 28.2, 52.5, 54.8, 63.5, 79.6, 126.5, 126.7, 128.0, 128.4, 128.5, 128.8, 141.4, 142.0, 156.0; IR $\nu_{\text{max}}$/cm$^{-1}$ 3411, 1686, 1495, 1366, 1166, 1048; MP 108 - 111 °C; HRMS (ESI+): calcd. for C$_{20}$H$_{25}$NNaO$_3$ [M+Na]$^+$ 350.1727, found 350.1724.

(2R)-2-[(tert-Butoxycarbonyl)amino]-3,3-diphenylpropyl4-methylbenzenesulfonate, 29

![Chemical Structure of 29]

To a solution of compound 28 (1.40 g, 4.28 mmol) in CH$_2$Cl$_2$ (19 mL), NEt$_3$ (1.50 mL, 11.2 mmol) and TsCl (1.17 g, 6.15 mmol) were added and the reaction mixture was stirred at rt for 16 h. After evaporation of the solvents, the crude reaction mixture was purified by flash column chromatography (PE/EtOAc 4:1) to yield 29 (1.70 g, 83%) as a colorless solid.
\([\alpha]_D^{23} = -24.8 \text{ (c = 1.12, CHCl}_3\); \(\textsuperscript{1}H\) NMR (500 MHz, CDCl\(_3\)) \(\delta\) ppm 1.30 (s, 9H), 2.44 (s, 3H), 3.78 (d, \(J = 9.1\) Hz, 1H), 4.04 - 4.17 (m, 2H), 4.56 - 4.68 (m, 2H), 7.10 - 7.21 (m, 6H), 7.22 - 7.33 (m, 6H), 7.71 (d, \(J = 8.2\) Hz, 2H); \(\textsuperscript{13}C\) NMR (125 MHz, CDCl\(_3\)) \(\delta\) ppm 21.6, 28.1, 51.9, 52.2, 70.3, 79.7, 126.7, 126.9, 127.9, 127.9, 128.1, 128.5, 128.8, 129.8, 132.3, 140.6, 140.9, 144.8, 155.0; IR \(\nu_{\text{max}}/\text{cm}^{-1}\) 1710, 1496, 1364, 1176; MP 137 - 139 °C; HRMS (ESI+): calcd. for C\(_{27}\)H\(_{31}\)NNaO\(_5\)S \([\text{M+Na}^+]\) 504.1815, found 504.1810.

tert-Butyl [(2\(R\)-3-azido-1,1-diphenylpropan-2-yl)carbamate, 30

Na\(_3\) (150 mg, 2.28 mmol) was added to a solution of compound 29 (1.00 g, 2.08 mmol) in DMF (7 mL) and the reaction mixture was stirred at 50 °C for 16 h. After cooling to rt, H\(_2\)O (10 mL) was added and it was extracted with Et\(_2\)O (3 x 40 mL). The combined organics were dried over Na\(_2\)SO\(_4\), filtered and concentrated. The resulting crude mixture was purified by flash column chromatography (PE/Et\(_2\)O 9:1) to obtain 30 (545 mg, 74%) as a colorless solid.

\([\alpha]_D^{23} = -44.1 \text{ (c = 1.15, CHCl}_3\); \(\textsuperscript{1}H\) NMR (500 MHz, CDCl\(_3\)) \(\delta\) ppm 1.35 (br s, 9H), 3.23 (dd, \(J = 12.3, 3.5\) Hz, 1H), 3.53 (d, \(J = 11.3\) Hz, 1H), 4.10 (d, \(J = 10.7\) Hz, 1H), 4.48 - 4.67 (m, 2H), 7.13 - 7.25 (m, 2H), 7.25 - 7.39 (m, 8H); \(\textsuperscript{13}C\) NMR (125 MHz, CDCl\(_3\)) \(\delta\) ppm 28.2, 52.7, 53.3, 79.7, 126.7, 127.0, 128.0, 128.2, 128.6, 129.0, 140.9, 141.5, 155.2; IR \(\nu_{\text{max}}/\text{cm}^{-1}\) 2099, 1689, 1511, 1298, 1166; MP 125 - 127 °C; HRMS (ESI+): calcd. for C\(_{20}\)H\(_{25}\)N\(_4\)O\(_2\) \([\text{M+H}^+]\) 353.1972, found 353.1972.

1-[(2\(R\)-3-Azido-1,1-diphenylpropan-2-yl)-3-[3,5-bis(trifluoromethyl)phenyl]urea, 31

An ice-cooled round-bottom flask containing compound 30 (214 mg, 0.607 mmol) under inert atmosphere was placed behind a blast-shield. TFA (0.700 mL, 9.42 mmol) was added carefully dropwise and the resulting solution was stirred at rt for 3 h. TFA was evaporated under a stream of N\(_2\), the residue dissolved in Et\(_2\)O (3.0 mL) and aq. 2 M NaOH solution added until pH 14. The aqueous phase was extracted with Et\(_2\)O (3 x 30 mL) and the combined organics were dried over Na\(_2\)SO\(_4\), filtered and concentrated (CAUTION: solvents were evaporated under a stream of N\(_2\) behind a blast-shield). The crude aminoazide was dissolved in THF (2.5 mL), 3,5-bis(trifluoromethyl)phenyl isothiocyanate (0.110 mL, 0.595 mmol) was added
and the solution was stirred at rt for 16 h. After evaporation of the solvents, the crude product was purified by flash column chromatography (PE/Et₂O 9:1) to obtain 31 (274 mg, 86% over 2 steps) as a colorless foam.

\[ [\alpha]_D^{23} = -103.2 \ (c = 1.00, \text{CHCl}_3); \text{ } \int \text{H NMR} \ (500 \text{ MHz, CDCl}_3) \delta \text{ ppm} 3.28 (\text{dd}, \ J = 12.6, 2.2 \text{ Hz, 1H}), 3.91 (\text{dd}, \ J = 12.6, 3.3 \text{ Hz, 1H}), 4.22 (\text{d}, \ J = 11.3 \text{ Hz, 1H}), 5.47 - 5.56 (m, 1H), 5.91 - 6.05 (m, 1H), 7.20 - 7.38 (m, 12H) 7.73 (s, 1 H) 8.54 (br s, 1H); \text{ } \int \text{C NMR} \ (125 \text{ MHz, CDCl}_3) \delta \text{ ppm} 51.8, 52.8, 57.0, 120.0 - 120.2 (m), 122.5 (q, \ J_{\text{CF}} = 272.7 \text{ Hz}), 124.2 - 124.4 (m), 127.3, 127.4, 127.7, 128.0, 129.1, 129.2, 133.3 (q, \ J_{\text{CF}} = 34.3 \text{ Hz}), 137.7, 140.1, 140.5, 179.7; \text{ } \int \text{F NMR} \ (376.5 \text{ MHz, CDCl}_3) \delta \text{ ppm} -62.9; \text{ } \text{IR} \nu_{\text{max}}/\text{cm}^{-1} 2101, 1495, 1275, 1173, 1130; \text{ } \text{MP} \ 50 - 53 \degree \text{C}; \text{ } \text{HRMS} \ (\text{ESI+}): \text{calcd. for C}_{24}\text{H}_{19}\text{F}_6\text{N}_5\text{NaS} [\text{M+Na}]^+ 546.1158, \text{found 546.1158.}

Synthesis of catalyst 4a precursor (See Supplementary Figure 5)

Compounds 33, 34, 35 were synthesized according to literature procedures and their physical and spectroscopic properties are in agreement to those reported.

**1-tet-Butyl [(2S)-1-azido-3,3-dimethylbutan-2-yl] carbamate, 36**

To a suspension of diamine 35 (1.25 g, 5.79 mmol), K₂CO₃ (1.36 g, 9.84 mmol) and CuSO₄·5H₂O (0.015 g, 0.058 mmol) in MeOH (30 mL) at 0 °C behind a blast-shield was added diazotransfer reagent N₂SO₂Im·HCl 14 (1.44 g, 6.94 mmol) portionwise. Stirring at rt was maintained for 14 h and then the volatiles were removed under a stream of N₂. The reaction mixture was diluted with H₂O (25 mL) and Et₂O (25 mL). The aqueous layer was extracted with Et₂O (2 x 20 mL) and the combined organics were washed with brine, dried over MgSO₄, filtered and concentrated. The crude product was purified by flash column chromatography (PE/EtOAc 9:1) to yield 36 (1.20 g, 85%) as a colorless solid.

\[ [\alpha]_D^{24} = -46.6 \ (c = 0.91, \text{CHCl}_3); \text{ } \int \text{H NMR} \ (400 \text{ MHz, CDCl}_3) \delta \text{ ppm} 0.92 (s, 9H), 1.44 (s, 9H), 3.20 (dd, \ J = 12.6, 8.3 \text{ Hz, 1H}), 3.45 (dd, \ J = 12.6, 3.3 \text{ Hz, 1H}), 3.54 - 3.67 (m, 1H), 4.57 (d, \ J = 9.9 \text{ Hz, 1H}); \text{ } \int \text{C NMR} \ (125 \text{ MHz, CDCl}_3) \delta \text{ ppm} 26.5, 28.3, 34.1, 51.9, 58.2, 79.4, 155.7; \text{ } \text{IR} \nu_{\text{max}}/\text{cm}^{-1} 2970, 2095, 1700, 1519, 1367, 1247, 1171, 1054; \text{ } \text{MP} \ 58 - 60 \degree \text{C. HRMS} \ (\text{ESI+}): \text{calcd. for C}_{11}\text{H}_{22}\text{N}_4\text{NaO}_2 [\text{M+Na}]^+ 265.1635, \text{found 265.1634.}
1-[(2S)-1-Azido-3,3-dimethylbutan-2-yl]-3-[3,5-bis(trifluoromethyl)phenyl]thiourea, 2

An ice-cooled round-bottom flask containing compound 36 (1.50 g, 6.19 mmol) under inert atmosphere was placed behind a blast-shield. TFA (6.00 mL, 78.3 mmol) was added carefully dropwise and the resulting solution was stirred at rt for 3 h. TFA was evaporated under a stream of N₂, the residue dissolved in Et₂O (20 mL) and aq. 2 M NaOH solution added until pH 14. The aqueous phase was extracted with Et₂O (2 x 20 mL) and the combined organics were dried over MgSO₄, filtered and concentrated (CAUTION: solvents were evaporated under N₂ stream behind a blast-shield). The crude aminoazide was dissolved in THF (21 mL), 3,5-bis(trifluoromethyl)phenyl isothiocyanate (1.10 mL, 6.02 mmol) was added dropwise and the solution was stirred at rt for 12 h. Volatiles were removed under vacuum and the crude product was purified by flash column chromatography (PE to PE/EtOAc 9:1) to obtain 2 (2.24 g, 88% over 2 steps) as a colorless solid.

The ee was determined by HPLC analysis (Chiralpak IA, hexane/isopropanol 95:5, λ 220 nm, 1.0 mL/min): t (minor) = 6.42 min., t (major) = 7.75 min (> 99%).

$[\alpha]_D^{23} = -13.5 \text{ (c = 1.05, CHCl₃)}$; $^1$H NMR (500 MHz, CD₃OD) δ ppm 0.93 (s, 9H), 3.32 (dd, $J = 12.9, 8.2$ Hz, 1H), 3.51 (dd, $J = 12.9, 3.8$ Hz, 1H), 4.57 - 4.69 (m, 1H), 7.53 (s, 1H), 8.14 (s, 2H); $^{13}$C NMR (125 MHz, CD₃OD) δ ppm 27.3, 35.8, 52.7, 62.8, 117.8 - 118.1 (m), 123.7 - 124.0 (m), 124.9 (q, $J_{CF} = 271.9$ Hz), 132.8 (q, $J_{CF} = 33.3$ Hz), 143.4, 184.1; $^{19}$F NMR (376 MHz, CDCl₃) δ ppm - 64.5; IR νmax/cm⁻¹ 2968, 2104, 1537, 1472, 1383, 1278, 1176, 1134; MP 164 - 167 °C; HRMS (ESI+): calcd. for C₁₅H₁₇F₆N₅NaS [M+Na]⁺ 436.1001, found 436.0992.

Synthesis of racemic catalyst (±)-4a precursor (See Supplementary Figure 8)

Compound 46 was synthesized according to a literature procedure and its spectroscopic properties are in agreement to those reported.¹⁵

tert-Butyl (1-azido-3,3-dimethylbutan-2-yl)carbamate, (±)-36

To a stirred solution of 46 (49.0 mg, 0.202 mmol) in MeOH/THF (3:1, 2.0 mL) at 0 °C was added NiCl₂·6H₂O (48.0 mg, 0.202 mmol) and NaBH₄ (38.2 mg, 0.98 mmol) in 1.0 mL of MeOH/THF (3:1).

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¹⁵ Enantiomeric excess of catalyst 4a precursor was measured to check that no racemisation took place during its synthesis from commercial l-tert-leucine (ee: 99% (GLC)).
1.01 mmol) [CAUTION: Hydrogen Gas Release]. The resulting black suspension was stirred at 0 °C for 30 mins. The reaction was quenched with sat. aq. NH₄Cl (1 mL) and extracted with CH₂Cl₂ (3 x 5 mL). The combined organics were dried over Na₂SO₄, filtered and concentrated. The resulting crude diamine (±)-35 was dissolved in MeOH (1.0 mL), and K₂CO₃ (46.2 mg, 0.340 mmol) and CuSO₄·5H₂O (0.5 mg, 0.002 mmol) were added sequentially. After cooling the suspension to 0 °C and placing it behind a blast-shield, diazotransfer reagent N₃SO₂Im·HCl (49.7 mg, 0.240 mmol) was added portionwise. Stirring at rt was maintained for 16 h and after the volatiles were removed under a stream of N₂, the reaction mixture was diluted with H₂O (1 mL) and Et₂O (1 mL). The aqueous layer was extracted with Et₂O (2 x 5 mL) and the combined organics were dried over Na₂SO₄, filtered and concentrated. After evaporation of the solvents, the crude product was purified by flash column chromatography (PE/EtOAc 9:1) to obtain (±)-36 (20 mg, 41% over 2 steps) as a colorless solid. Its spectroscopic properties are in agreement to those of 36.

1-(1-Azido-3,3-dimethylbutan-2-yl)-3-[3,5-bis(trifluoromethyl)phenyl]thiourea, (±)-2

Racemic catalyst precursor (±)-2 was synthesized as a colorless solid from compound (±)-36 in 60% yield over 2 steps following the same experimental procedure as that reported for the synthesis of 2. Its spectroscopic properties are in agreement to those of 2. MP = 150 - 153 °C.

Synthesis of catalyst 4h precursor (See Supplementary Figure 6)

Compounds 38 and 39 were synthesized according to literature procedures and their physical and spectroscopic properties are in agreement to those reported.¹⁶

(1S, 2S)-2-Azido-1,2-diphenylethanamine, 40

To a solution of 39 (240 mg, 0.910 mmol) in THF (4.5 mL) under inert atmosphere, PPh₃ (239 mg, 0.910 mmol) was added and the resulting solution was stirred at 50 °C for 3 h. Subsequently H₂O (0.170 mL, 9.10 mmol) was added and the mixture was stirred at 50 °C for 24 h. After evaporation of the solvents, Et₂O (2 mL) was added and the precipitated triphenylphosphine oxide was filtered off. The filtrate was concentrated and the crude
product was purified by flash column chromatography (PE/Et\textsubscript{2}O 2:3) to obtain 40 (180 mg, 83%) as a colorless oil.

$[\alpha]_D^{24} = + 85.3$ (c = 0.91, CHCl\textsubscript{3}); \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) $\delta$ ppm 2.07 (br s, 2H), 4.13 (d, $J = 7.6$ Hz, 1H), 4.65 (d, $J = 7.6$ Hz, 1H), 7.10 - 7.29 (m, 10H); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) $\delta$ ppm 61.2, 73.2, 127.4, 127.6, 127.7, 127.8, 128.2, 128.4, 137.1, 140.8; IR $\nu$\textsubscript{max}/cm\textsuperscript{-1} 2098, 1247; HRMS (ESI+): calcd. for C\textsubscript{14}H\textsubscript{15}N\textsubscript{4}[M+H]\textsuperscript{+} 239.1291, found 239.1288.

1-[(1S,2S)-2-Azido-1,2-diphenylethyl]-3-[3,5-bis(trifluoromethyl)phenyl]thiourea, 41

![Structure of 41](image)

To a solution of aminoazide 40 (66.0 mg, 0.277 mmol) in THF (1.0 mL) under inert atmosphere, 3,5-bis(trifluoromethyl)phenyl isothiocyanate (0.051 mL, 0.277 mmol) was added dropwise and the solution was stirred at rt for 16 h. After evaporation of the solvents, the crude product was purified by flash column chromatography (PE/EtOAc 4:1) to yield 41 (120 mg, 86%) as a colorless solid.

$[\alpha]_D^{24} = + 24.4$ (c = 1.10, CHCl\textsubscript{3}); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) $\delta$ ppm 4.99 (d, $J = 5.1$ Hz, 1H), 5.75 (br s, 1H), 7.02 (br s, 1H), 7.14 - 7.44 (m, 10H), 7.68 (s, 1H), 7.74 (s, 1H), 8.49 (br s, 1H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) $\delta$ ppm 62.9, 69.5, 119.5 - 119.7 (m), 122.7 (q, $J_{CF} = 273.2$ Hz), 123.8 - 124.0 (m), 126.9, 127.0, 128.4, 128.8, 128.9, 133.0 (q, $J_{CF} = 32.7$ Hz), 135.7, 137.5, 138.5, 180.3; \textsuperscript{19}F NMR (376 MHz, CDCl\textsubscript{3}) $\delta$ ppm - 63.0; IR $\nu$\textsubscript{max}/cm\textsuperscript{-1} 3245, 2108, 1527, 1381, 1277, 1176, 1133; MP 147 - 150 °C; HRMS (ESI+): calcd. for C\textsubscript{23}H\textsubscript{17}F\textsubscript{6}N\textsubscript{5}NaS [M+Na]\textsuperscript{+} 532.1001, found 532.1006.

Synthesis of catalyst 4i precursor (See Supplementary Figure 7)

Compound 43 was synthesized according to a literature procedure and its physical and spectroscopic properties are in agreement to those reported.\textsuperscript{17}

tert-Butyl [(1R,2R)-2-azidocyclohexyl]carbamate, 44

![Structure of 44](image)

To an ice-cooled round-bottom flask containing a solution of diamine 43 (152 mg, 0.710 mmol), K\textsubscript{2}CO\textsubscript{3} (167 mg, 1.20 mmol) and CuSO\textsubscript{4}•5H\textsubscript{2}O (2.0 mg, 0.0071 mmol) in MeOH (3.5 mL) behind a blast-shield was added the
diazotransfer reagent N\textsubscript{3}SO\textsubscript{2}Im-HCl (176 mg, 0.852 mmol) portionwise. Stirring at rt was maintained for 16 h and after the volatiles were removed under a stream of N\textsubscript{2}, the reaction mixture was diluted with H\textsubscript{2}O (5 mL) and Et\textsubscript{2}O (5 mL). The aqueous layer was extracted with Et\textsubscript{2}O (2 x 15 mL) and the combined organic extracts dried over Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated. After evaporation of the solvents, the crude product was purified by flash column chromatography (PE/EtOAc 9:1) to obtain 44 (150 mg, 80%) as a colorless solid.

\[\alpha\]_D\textsuperscript{24} = - 15.8 (c = 0.95, CHCl\textsubscript{3}); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \delta ppm 1.13 - 1.40 (m, 4H), 1.44 (s, 9H), 1.62 - 1.79 (m, 2H), 1.97 - 2.07 (m, 2H), 3.05 - 3.16 (m, 1H), 3.31 - 3.47 (m, 1H), 4.55 - 4.68 (m, 1H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \delta ppm 24.0, 24.3, 28.3, 30.7, 32.2, 53.9, 64.3, 79.6, 155.4; IR \nu\textsubscript{max}/cm\textsuperscript{-1} 3347, 2929, 2102, 1679, 1528, 1366, 1264, 1171; MP 90 - 93 °C; HRMS (ESI+): calcd. for C\textsubscript{11}H\textsubscript{20}N\textsubscript{4}NaO\textsubscript{2} [M+Na\textsuperscript{+}] 263.1478, found 263.1472.

1-[(1R,2R)-2-Azidocyclohexyl]-3-[3,5-bis(trifluoromethyl)phenyl]thiourea, 45

![Image of the chemical structure]

An ice-cooled round-bottom flask containing 44 (76.0 mg, 0.288 mmol) under inert atmosphere was placed behind a blast-shield. TFA (0.700 mL, 9.14 mmol) was added carefully dropwise and the resulting solution was stirred at rt for 2 h. TFA was evaporated under a stream of N\textsubscript{2}, the residue dissolved in Et\textsubscript{2}O (3 mL) and aq. 2 M NaOH solution added until pH 14. The aqueous phase was extracted with Et\textsubscript{2}O (3 x 10 mL) and the combined organics were dried over Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated (CAUTION: solvents were evaporated under a stream of N\textsubscript{2} behind a blast-shield). The crude aminoazide was dissolved in THF (1.5 mL), 3,5-bis(trifluoromethyl)phenyl isothiocyanate (0.060 mL, 0.317 mmol) was added dropwise and the solution was stirred at rt for 16 h. After evaporation of the solvents, the crude product was purified by flash column chromatography (PE/Et\textsubscript{2}O 4:1) to yield 45 (100 mg, 84% over 2 steps) as a colorless solid.

\[\alpha\]_D\textsuperscript{24} = - 42.3 (c = 1.10, CHCl\textsubscript{3}); \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) \delta ppm 1.16 - 1.43 (m, 3H), 1.47 - 1.61 (m, 1H), 1.68 - 1.93 (m, 2H), 2.13 - 2.35 (m, 2H), 3.23 - 3.36 (m, 1H), 4.00 (br s, 1H), 6.47 (br s, 1H), 7.69 (s, 1H), 7.89 (s, 2H), 8.70 (s, 1H); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) \delta ppm 23.8, 24.1, 30.4, 31.7, 58.2, 64.5 (br s), 119.1, 122.8 (q, J\textsubscript{CF} = 272.7 Hz), 123.8, 132.6 (q, J\textsubscript{CF} = 33.4 Hz), 139.5, 180.8; \textsuperscript{19}F NMR (376 MHz, CDCl\textsubscript{3}) \delta ppm - 63.0; IR \nu\textsubscript{max}/cm\textsuperscript{-1} 3237, 2098, 1542, 1382,
2.3. Synthesis and characterization of catalysts 4j - 4q precursors

General procedure A for the synthesis of catalysts 4j - 4q precursors

An ice-cooled round-bottom flask containing aminoazide 36 (100 mg, 0.410 mmol) under N₂ atmosphere was placed behind a blast-shield. TFA (0.500 mL) was carefully added dropwise and the resulting solution was stirred at rt for 1 h. TFA was evaporated under a stream of N₂, the residue dissolved in Et₂O and aq. 2 M NaOH solution added until pH 14. The aqueous phase was extracted with Et₂O and the combined organics were dried over Na₂SO₄, filtered and concentrated (CAUTION: solvents were evaporated under a stream of N₂ behind a blast-shield). The crude aminoazide was then taken to the next step as specified in each of the following procedures.

1-[(2S)-1-Azido-3,3-dimethylbutan-2-yl]-3-[3,5-bis(trifluoromethyl)phenyl]urea, 51, catalyst 4j precursor

Crude aminoazide obtained as described in general procedure A was dissolved in THF (2.0 mL), 3,5-bis(trifluoromethyl)phenyl isocyanate (0.085 mL, 0.492 mmol) was added and the resulting mixture was stirred at rt for 16 h. After evaporation of the volatiles under a stream of N₂, the crude reaction mixture was purified by flash column chromatography (PE/Et₂O 4:1) to obtain 51 (106 mg, 65% over 2 steps) as a colorless solid.

\[ [\alpha]_D^{23} = -29.9 \text{ (c = 0.90, CHCl}_3) \]; \text{IH NMR (500 MHz, CDCl}_3) \delta \text{ ppm} 0.96 (s, 9H), 3.29 (dd, J = 12.6, 8.2 Hz, 1H), 3.60 (dd, J = 12.6, 3.8 Hz, 1H), 3.84 (m, 1H), 5.46 (br s, 1H), 7.46 (s, 1H), 7.69 (m, 1H), 7.81 (s, 2H); \text{C NMR (125 MHz, CDCl}_3) \delta \text{ ppm} 26.5, 34.1, 52.3, 57.9, 116.0 - 116.2 (m), 118.7 - 118.9 (m), 123.0 (q, J\text{CF} = 272.7 \text{ Hz}), 132.2 (q, J\text{CF} = 33.4 \text{ Hz}), 140.2, 155.4; \text{F NMR (470 MHz, CDCl}_3) \delta \text{ ppm} -63.1; \text{IR } \nu_{\text{max}}/\text{cm}^{-1} \text{ 3338, 2968, 2102, 1650, 1570, 1388, 1277, 1175, 1133; MP 164 - 166 °C; HRMS (ESI+): calcd. for C}_{15}H_{13}F_{6}N_{5}NaO [M+Na]^+ 420.1230, found 420.1224.}
1-[(2S)-1-Azido-3,3-dimethylbutan-2-yl]-3-[4-(trifluoromethyl)phenyl]thiourea, 52, catalyst 4k precursor

Crude aminoazide obtained as described in general procedure A was dissolved in THF (2.0 mL), 4-trifluoromethylphenyl isothiocyanate (100 mg, 0.492 mmol) was added and the resulting mixture was stirred at rt for 16 h. After evaporation of the volatiles under a stream of N₂, the crude reaction mixture was purified by flash column chromatography (PE/Et₂O 4:1) to obtain 52 (86 mg, 61% over 2 steps) as a colorless oil.

\[ \alpha \] = + 27.1 (c = 0.86, CHCl₃); \(^1\)H NMR (500 MHz, CDCl₃) δ ppm 0.98 (s, 9H), 3.43 (dd, \( J = 12.6, 6.0 \) Hz, 1H), 3.75 (dd, \( J = 12.6, 4.3 \) Hz, 1H), 4.64 (br s, 1H), 6.25 (d, \( J = 7.9 \) Hz, 1H), 7.41 (d, \( J = 7.2 \) Hz, 2H), 7.70 (d, \( J = 8.5 \) Hz, 2H), 8.67 (br s, 1H); \(^13\)C NMR (125 MHz, CDCl₃) δ ppm 27.0, 34.6, 51.3, 61.9, 123.6 (q, \( J_{\text{CF}} = 271.8 \) Hz), 124.2, 127.2 - 127.6 (m), 128.7 (q, \( J_{\text{CF}} = 33.4 \) Hz), 139.4, 180.7; \(^19\)F NMR (376 MHz, CDCl₃) δ ppm - 62.4; IR \( \nu_{\text{max}}/\text{cm}^{-1} \) 3237, 2965, 2086, 1537, 1321, 1163, 1116, 1065; HRMS (ESI+): calcd. for C₁₄H₁₈F₃N₅NaS \([\text{M+Na}]^+\) 368.1127, found 368.1116.

1-[(2S)-1-Azido-3,3-dimethylbutan-2-yl]-3-(4-nitrophenyl)thiourea, 53, catalyst 4l precursor

Crude aminoazide obtained as described in general procedure A was dissolved in THF (2.0 mL), 4-nitrophenyl isothiocyanate (88.6 mg, 0.492 mmol) was added and the resulting mixture was stirred at rt for 16 h. After evaporation of the volatiles under a stream of N₂, the crude reaction mixture was purified by flash column chromatography (PE/Et₂O 1:1) to obtain 53 (82 mg, 62% over 2 steps) as a yellow solid.

\[ \alpha \] = + 10.9 (c = 1.22, CHCl₃); \(^1\)H NMR (400 MHz, CDCl₃) δ ppm 1.01 (s, 9H), 3.46 (dd, \( J = 12.7, 6.8 \) Hz, 1H), 3.75 (dd, \( J = 12.7, 3.3 \) Hz, 1H), 4.68 (br s, 1H), 6.57 (d, \( J = 9.6 \) Hz, 1H), 7.54 (d, \( J = 7.6 \) Hz, 2H), 8.22 (d, \( J = 8.8 \) Hz, 2H), 9.00 (br s, 1H); \(^13\)C NMR (100 MHz, CDCl₃) δ ppm 26.9, 34.6, 51.2, 61.9, 122.7, 125.4, 143.1, 144.2, 180.5; IR \( \nu_{\text{max}}/\text{cm}^{-1} \) 3331, 2964, 2101, 1597, 1513, 1300, 1259, 1177, 1110; MP 107 - 110 °C; HRMS (ESI+): calcd. for C₁₃H₁₈N₆NaO₂S \([\text{M+Na}]^+\) 345.1104, found 345.1107.
1-[(2S)-1-Azido-3,3-dimethylbutan-2-yl]-3-(4-methoxyphenyl)thiourea, 54, catalyst 4m precursor

Crude aminoazide obtained as described in general procedure A was dissolved in THF (2.0 mL), 4-methoxyphenyl isothiocyanate (0.068 mL, 0.49 mmol) was added and the resulting mixture was stirred at rt for 16 h. After evaporation of the volatiles under a stream of N₂, the crude reaction mixture was purified by flash column chromatography (PE/Et₂O 3:2) to obtain 54 (80 mg, 63% over 2 steps) as a thick colorless oil.

\[ \{\alpha\}_D^{23} = +36.5 \ (c = 1.08, \text{CHCl}_3) \]

\[ ^1H \text{ NMR} \ (500 \text{ MHz, CDCl}_3) \delta \text{ ppm} 0.89 \ (s, 9H), 3.34 \ (dd, J = 12.9, 5.7 \text{ Hz}, 1H), 3.65 \ (dd, J = 12.9, 4.4 \text{ Hz}, 1H), 3.83 \ (s, 3H), 4.50 - 4.62 \ (m, 1H), 5.87 \ (d, J = 9.5 \text{ Hz}, 1H), 6.96 \ (d, J = 9.1 \text{ Hz}, 2H), 7.19 \ (d, J = 9.1 \text{ Hz}, 2H), 8.00 \ (s, 1H); \]

\[ ^{13}C \text{ NMR} \ (125 \text{ MHz, CDCl}_3) \delta \text{ ppm} 26.9, 34.5, 51.3, 55.5, 61.7, 115.3, 127.9, 128.0, 159.1, 181.6; \]

\[ \text{IR } \nu_{\text{max}}/\text{cm}^{-1} 3300, 2962, 2095, 1508, 1240; \]

\[ \text{HRMS (ESI+): calcd. for C}_{14}H_{21}N_5NaOS [M+Na]^+ 330.1359, \text{ found 330.1358}. \]

1-[(2S)-1-Azido-3,3-dimethylbutan-2-yl]-3-(4-methylphenyl)thiourea, 55, catalyst 4n precursor

Crude aminoazide obtained as described in general procedure A was dissolved in THF (2.0 mL), \( p \)-tolyl isothiocyanate (73.4 mg, 0.492 mmol) was added and the resulting mixture was stirred at rt for 16 h. After evaporation of the volatiles under a stream of N₂, the crude reaction mixture was purified by flash column chromatography (PE/Et₂O 4:1) to obtain 55 (76 mg, 63% over 2 steps) as a colorless oil.

\[ \{\alpha\}_D^{23} = +49.5 \ (c = 1.01, \text{CHCl}_3) \]

\[ ^1H \text{ NMR} \ (400 \text{ MHz, CDCl}_3) \delta \text{ ppm} 0.90 \ (s, 9H), 2.36 \ (s, 3H), 3.35 \ (dd, J = 12.9, 5.8 \text{ Hz}, 1H), 3.65 \ (dd, J = 12.9, 4.3 \text{ Hz}, 1H), 4.47 - 4.67 \ (m, 1H), 6.02 \ (d, J = 9.3 \text{ Hz}, 1H), 7.13 \ (d, J = 8.1 \text{ Hz}, 2H), 7.24 \ (d, J = 8.1 \text{ Hz}, 2H) 8.28 \ (br s, 1H); \]

\[ ^{13}C \text{ NMR} \ (100 \text{ MHz, CDCl}_3) \delta \text{ ppm} 21.0, 26.9, 34.5, 51.3, 61.6, 125.6, 130.7, 132.8, 137.8, 181.0; \]

\[ \text{IR } \nu_{\text{max}}/\text{cm}^{-1} 3300, 2963, 2908, 1513; \]

\[ \text{HRMS (ESI+): calcd. for C}_{14}H_{21}N_5NaS [M+Na]^+ 314.1410, \text{ found 314.1413}. \]
1-[(2S)-1-Azido-3,3-dimethylbutan-2-yl]-3-phenylthiourea, 56, catalyst 4o precursor

Crude aminoazide obtained as described in general procedure A was dissolved in THF (2.0 mL), phenyl isothiocyanate (0.059 mL, 0.49 mmol) was added and the resulting mixture was stirred at rt for 16 h. After evaporation of the volatiles under a stream of N₂, the crude reaction mixture was purified by flash column chromatography (PE/Et₂O 4:1) to obtain 56 (84 mg, 73% over 2 steps) as a colorless solid.

\[ [\alpha]_D^{23} = +35.1 \text{ (c = 1.02, CHCl₃); } ^{1}H \text{ NMR (400 MHz, CDCl₃)} \delta ppm 0.91 \text{ (s, 9H), 3.36 (dd, } J = 12.8, 5.8 \text{ Hz, 1H), 3.67 (dd, } J = 12.8, 4.2 \text{ Hz, 1H), 4.59 (br s, 1H), 6.09 (d, } J = 9.3 \text{ Hz, 1H), 7.26 (d, } J = 7.6 \text{ Hz, 2H), 7.29 - 7.36 \text{ (m, 1H), 7.40 - 7.50 \text{ (m, 2H), 8.48 (br s, 1H); } ^{13}C \text{ NMR (100 MHz, CDCl₃)} \delta ppm 26.9, 34.5, 51.3, 61.7, 125.5, 127.6, 130.2, 135.6, 180.9; IR } \nu_{\text{max}}/\text{cm}^{-1} \text{ 3259, 2963, 2098, 1596, 1532, 1497, 1450, 1296; MP 60 - 62 °C; HRMS (ESI+): calcd. for C}_{13}H_{19}N_{5}NaS [M+Na]^{+} 300.1253, found 300.1258.}

N-[(2S)-1-Azido-3,3-dimethylbutan-2-yl]-3,5-bis(trifluoromethyl)benzamide, 57, catalyst 4p precursor

Crude aminoazide obtained as described in general procedure A was dissolved in Et₂O (1.4 mL). NEt₃ (0.066 mL, 0.47 mmol) was added, the reaction mixture was cooled to 0 °C and 3,5-bis(trifluoromethyl)benzoyl chloride (0.083 mL, 0.45 mmol) was added. The reaction mixture was allowed to warm to rt and stirring was maintained for 5 h. After evaporation of the volatiles under a stream of N₂, the crude reaction mixture was purified by flash column chromatography (PE to PE/EtOAc 9:1) to obtain 57 (135 mg, 85% over 2 steps) as a colorless solid.

\[ [\alpha]_D^{23} = +16.4 \text{ (c = 1.00, CHCl₃); } ^{1}H \text{ NMR (400 MHz, CDCl₃)} \delta ppm 1.04 \text{ (s, 9H), 3.45 (dd, } J = 12.9, 8.5 \text{ Hz, 1H), 3.67 (dd, } J = 12.9, 3.8 \text{ Hz, 1H), 4.23 (dd, } J = 8.3, 3.8 \text{ Hz, 1H), 7.94 (s, 1H), 8.16 \text{ (s, 2H); } ^{13}C \text{ NMR (100 MHz, CDCl₃)} \delta ppm 26.7, 34.4, 51.4, 57.2, 122.8 (q, } J_{CF} = 272.4 \text{ Hz), 124.9 - 125.1 \text{ (m), 127.2 - 127.4 \text{ (m), 132.1 (q, } J_{CF} = 34.0 \text{ Hz), 136.6, 165.1; } ^{19}F \text{ NMR (376 MHz, CDCl₃)} \delta ppm – 63.0; IR } \nu_{\text{max}}/\text{cm}^{-1} \text{ 2972, 2378, 2089, 1634, 1615, 1474, 1445, 1371, 1338, 1278, 1175, 1130, 906, 705, 682; MP 116 - 122 °C; HRMS (ESI+): calcd. for C}_{15}H_{16}F_{6}N_{4}NaO [M+Na]^{+} 405.1121, found 405.1116.\]
N-[(2S)-1-Azido-3,3-dimethylbutan-2-yl]-4-methylbenzenesulfonamide, 58, catalyst 4q precursor

Crude aminoazide obtained as described in general procedure A was dissolved in Et₂O (1.4 mL). NEt₃ (0.066 mL, 0.47 mmol) was added, the reaction mixture was cooled to 0 °C and 4-toluenesulfonyl chloride (86.5 mg, 0.454 mmol) was added. The reaction mixture was allowed to warm to rt and stirring was maintained for 5 h. After evaporation of the volatiles under a stream of N₂, the crude reaction mixture was purified by flash column chromatography (PE to PE/EtOAc 9:1) to obtain 58 (30 mg, 25% over 2 steps) as a pale yellow solid.

\[ \alpha \]D²⁵ = -39.4 (c = 0.87, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ ppm 0.90 (s, 9H), 2.43 (s, 3H), 3.13 (ddd, J = 9.6, 4.8, 4.8 Hz, 1H), 3.26 (dd, J = 12.9, 4.8 Hz, 1H), 3.31 (dd, J = 12.9, 4.8 Hz, 1H), 4.92 (d, J = 9.6 Hz, 1H), 7.31 (d, J = 8.1 Hz, 2H), 7.80 (d, J = 8.3 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 21.5, 26.9, 34.5, 51.9, 61.1, 127.0, 129.6, 138.2, 143.4; IR νmax/cm⁻¹ 3292, 2964, 2102, 1438, 1326, 1159, 1089, 964, 814, 669; MP 81 - 84 °C; HRMS (ESI+): calcd. for C₁₃H₂₀N₄NaO₂S [M+Na]⁺ 319.1199, found 319.1198.

2.4. Synthesis and characterization of catalysts 4a, 4b and 4c

1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(2S)-3,3-dimethyl-1-[(triphenylphosphoranylidene)amino]butan-2-yl]thiourea, 4a

To azide 2 (300 mg, 0.726 mmol) in Et₂O (1.8 mL) under argon atmosphere was added triphenylphosphine (190 mg, 0.726 mmol) at rt. Stirring was maintained at rt for 26 h and the reaction mixture was then concentrated in vacuo to afford a colorless foam. Pentane (4 mL) was added under N₂ and the mixture stirred vigorously for 2 h. The resultant suspension was filtered and the precipitate dried in vacuo to obtain compound 4a (344 mg, 73%) as a colorless solid.

\[ \alpha \]D²⁴ = -64.4 (c = 1.40, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ ppm 0.96 (s, 9H), 3.04 ('q', J = 9.8 Hz, 1H), 3.41 ('t', J = 9.8 Hz, 1H), 3.76 (br s, 1H), 7.32 - 7.80 (m, 19 H); ¹³C NMR (125 MHz, CDCl₃) δ ppm 27.1, 33.7, 48.0, 69.9 (d, JCP = 21.0 Hz), 116.5, 123.2 (q, JCF = 272.8 Hz), 123.4,
128.1, 128.9 (J_{CP} = 12.4 Hz), 130.9 (q, J_{CF} = 33.4 Hz), 132.5 (d, J_{CP} = 9.5 Hz), 143.5, 183.7; \^31P NMR (202 MHz, CDCl\textsubscript{3}) δ ppm 21.9 (br s); \(^{19}F\) NMR (470 MHz, CDCl\textsubscript{3}) δ ppm -62.7; IR ν\textsubscript{max}/cm\textsuperscript{-1} 2970, 1739, 1437, 1367, 1216; MP 96 - 99 °C; HRMS (ESI+): calcd. for C\textsubscript{33}H\textsubscript{33}F\textsubscript{6}N\textsubscript{3}PS [M+H]\textsuperscript{+} 648.2032, found 648.2024.

1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(2S)-3,3-dimethyl-1-[[tris(4-methoxyphenyl)phosphoranylidene]amino]butan-2-yl]thiourea, 4b

To azide 2 (500 mg, 1.21 mmol) in Et\textsubscript{2}O (3.0 mL) under an argon atmosphere was added tris(4-methoxyphenyl)phosphine (426 mg, 1.21 mmol) at rt. Stirring was maintained at rt for 24 h and the reaction mixture was concentrated under a stream of N\textsubscript{2} until 1 mL of solvent remained. Pentane (1 mL) was added and the resultant thick precipitate was filtered. The precipitate was washed with pentane/Et\textsubscript{2}O 1:1 (1 mL) and dried \textit{in vacuo} to obtain compound 4b (786 mg, 88%) as a colorless solid.

[\alpha]_D^{24} = -54.4 (c = 1.02, CHCl\textsubscript{3}); \(^1H\) NMR (500 MHz, CDCl\textsubscript{3}) δ ppm; 0.95 (s, 9H), 2.91 (q, J = 9.9 Hz, 1H), 3.23 (dd, J = 8.7, 5.5 Hz, 1H), 3.85 (s, 9H), 4.07 (br s, 1H), 6.99 (dd, J = 8.7, 2.0 Hz, 6H), 7.24 (s, 1H), 7.27 (s, 2H), 7.40 - 7.70 (m, 7H); \(^{13}C\) NMR (125 MHz, CDCl\textsubscript{3}) δ ppm 27.1, 33.6 (br s), 47.1 (br s), 55.5, 65.1 (br s), 113.8 - 114.1 (m), 115.1 (d, J\textsubscript{CP} = 14.3 Hz), 123.7 (q, J\textsubscript{CF} = 272.8 Hz), 123.9 (br s), 130.5 (q, J\textsubscript{CF} = 32.0 Hz), 134.9 (d, J\textsubscript{CP} = 11.4 Hz), 163.8, 181.7 (br s); \(^31P\) NMR (202 MHz, CDCl\textsubscript{3}) δ ppm 29.8 (br s); \(^{19}F\) NMR (470 MHz, CDCl\textsubscript{3}) δ ppm - 63.0; IR ν\textsubscript{max}/cm\textsuperscript{-1} 2959, 1595, 1558, 1503, 1393, 1277, 1256, 1173, 1121; MP 148 - 150 °C; HRMS (ESI+): calcd. for C\textsubscript{36}H\textsubscript{39}F\textsubscript{6}N\textsubscript{3}PS [M+H]\textsuperscript{+} 738.2348, found 738.2343.
1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(1R)-1-phenyl-2-[[tris(4-methoxyphenyl)phosphoranylidene]amino]ethyl]thiourea, 4c

To azide 25 (500 mg, 1.16 mmol) in Et₂O (3.0 mL) under argon atmosphere was added tris(4-methoxyphenyl)phosphine (407 mg, 1.16 mmol) at rt. Stirring was maintained at rt for 24 h and the reaction mixture was then concentrated under a stream of N₂ until a thick precipitate was obtained. The precipitate was filtered, washed with Et₂O (1 mL) and dried in vacuo to obtain compound 4c (786 mg, 90%) as a colorless solid.

$[\alpha]_D^{25} = -40.8$ (c = 1.00, CHCl₃); $^1$H NMR (500 MHz, CDCl₃) δ ppm 3.14 - 3.30 (m, 1H), 3.31 - 3.50 (m, 1H), 3.84 (s, 9H), 5.36 (br s, 1H), 6.95 (dd, $J = 8.8, 1.9$ Hz, 6H), 7.24 - 7.36 (m, 7H), 7.46 - 7.54 (dd, $J = 11.3, 8.8$ Hz, 6H), 7.59 - 7.78 (br s, 2H); $^{13}$C NMR (125 MHz, CDCl₃) δ ppm 52.8 - 53.0 (m), 55.5, 62.4 (br s), 115.0 (d, $J_{CP} = 13.4$ Hz), 123.5, 123.6 (q, $J_{CF} = 272.8$ Hz), 124.1 (br s), 127.0, 127.8 - 128.1 (m), 128.8, 130.6 (q, $J_{CF} = 32.4$ Hz), 134.7 (d, $J_{CP} = 11.4$ Hz), 140.4 (br s), 163.7; $^{31}$P NMR (162 MHz, CDCl₃) δ ppm 27.4 (br s); $^{19}$F NMR (376 MHz, CDCl₃) δ ppm -62.6; IR ν max/cm⁻¹ 2972, 1595, 1502, 1275, 1176, 1118, 1026; MP 136 - 142 °C; HRMS (ESI+): calcd. for C₃₈H₃₂F₆N₃O₃PS [M+H]⁺ 758.2035, found 758.2028.

2.5. $pK_{BH^+}$ Measurement of iminophosphorane salts 1a·HCl and 1b·HCl in CD₃CN

Synthesis and characterization of iminophosphorane salt 1a·HCl

NaN₃ (877 mg, 13.5 mmol) was added to a solution of bromocyclohexane (2.00 g, 12.3 mmol) in DMSO (41 mL) and the reaction mixture was stirred at 60 °C for 16 h. After cooling to rt, H₂O (40 mL) was added and it was extracted with Et₂O (3 x 40 mL). The combined organics were dried over MgSO₄, filtered and concentrated under a stream of N₂. The resulting crude was dissolved in Et₂O (25 mL) under argon atmosphere and triphenylphosphine (3.22 g, 12.3 mmol) was added. Stirring was maintained at rt for 20 h, a solution of 2 M HCl in Et₂O (18.0 mL, 36.0 mmol) was added and the resulting solution was stirred at rt for 1 h. After evaporation of the solvents, the resulting crude was purified by flash column
chromatography (CH₂Cl₂ to CH₂Cl₂/MeOH 9:1) to obtain 1a·HCl (1.10 g, 23% over 3 steps) as a colorless solid.

1H NMR (400 MHz, CD₃CN) δ ppm 0.93 - 1.13 (m, 3H), 1.42 - 1.51 (m, 1H), 1.59 - 1.80 (m, 6H), 2.65 - 2.79 (m, 1H), 7.60 - 7.70 (m, 6H), 7.76 - 7.93 (m, 9H), 8.24 (t, J = 9.4 Hz, 1H); 13C NMR (100 MHz, CD₃CN) δ ppm 26.1, 26.5, 36.3, 36.4, 54.7 (d, JCP = 2.4 Hz), 123.8 (d, JCP = 102.5 Hz), 130.9 (d, JCP = 13.5 Hz), 135.1 (d, JCP = 11.1 Hz), 136.0 (d, JCP = 9.6 Hz); 31P NMR (162 MHz, CD₃CN) δ ppm 35.6; IR νmax/cm⁻¹ 3397, 2932, 2851, 1438, 1113, 1082; MP 194 - 198 °C; HRMS (ESI+): calcd. for C₂₄H₂₇NO₃P [M]⁺ 360.1876, found 360.1869.

**Synthesis and characterization of iminophosphorane 1a**

![PS-BEMP](image)

PS-BEMP (63.0 mg, 2.2 mmol/g, 0.138 mmol) was added to a solution of iminophosphorane salt 1a·HCl (50.0 mg, 0.126 mmol) in CH₂Cl₂ (1.0 mL) under argon atmosphere. The reaction mixture was stirred at rt for 1 h and then filtered, concentrated under a stream of N₂ and dried under vacuum to obtain 1a (43.0 mg, 95%) as a colorless oil.

1H NMR (400 MHz, CD₃CN) δ ppm 1.03 - 1.16 (m, 3H), 1.28 - 1.40 (m, 2H), 1.44 - 1.50 (m, 1H), 1.59 - 1.67 (m, 4H), 2.80 - 2.95 (m, 1H), 7.45 - 7.56 (m, 6H), 7.55 - 7.61 (m, 3H), 7.66 - 7.73 (m, 6H); 13C NMR (100 MHz, CD₃CN) δ ppm 26.7, 27.0, 39.6, 39.7, 54.9 (d, JCP = 3.2 Hz), 130.0 (d, JCP = 12.0 Hz), 132.3 (d, JCP = 96.0 Hz), 133.2 (d, JCP = 3.2 Hz), 133.9 (d, JCP = 9.6 Hz); 31P NMR (162 MHz, CD₃CN) δ ppm 9.4; HRMS (ESI+): calcd. for C₂₄H₂₇NOP [M+H]⁺ 360.1876, found 360.1862.

**pKₐ Measurement of 1a·HCl in CD₃CN**

1a·HCl (20.0 mg, 0.050 mmol) and tetramethylguanidine (6.3 μL, 0.050 mmol) were dissolved in CD₃CN. The 13C NMR and 31P NMR were measured and the chemical shift of the CH-N=PPh₃ and CH-N=PPh₃ were used to estimate the equilibrium ratio and the equilibrium constant of the reaction. The equilibrium constant was then used, with the known pKₐ of TMG in CD₃CN (pKₐ = 23.3) to determine the estimated pKₐ of 1a·HCl. The experiment was repeated three times. Representative 13C NMR and 31P NMR spectra of the experiments are included in Section 5.1.
Estimated $pK_{BH+}$ of 1a·HCl in $\text{CD}_3\text{CN}$

|       | Using $^{13}\text{C}$ NMR | Using $^{31}\text{P}$ NMR |
|-------|---------------------------|---------------------------|
| Exp.1 | 22.7                      | 23.0                      |
| Exp.2 | 22.8                      | 22.9                      |
| Exp.3 | 22.6                      | 23.2                      |
| Average | 22.7                  | 23.0                      |

**Synthesis and characterization of iminophosphorane salt 1b·HCl**

Na$_3$ (219 mg, 3.37 mmol) was added to a solution of bromocyclohexane (500 mg, 3.06 mmol) in DMSO (10 mL) and the reaction mixture was stirred at 60 °C for 16 h. After cooling to rt, H$_2$O (15 mL) was added and it was extracted with Et$_2$O (3 x 20 mL). The combined organics were dried over MgSO$_4$, filtered and concentrated under a stream of N$_2$. The resulting crude was dissolved in Et$_2$O (12 mL) under argon atmosphere and tris(4-methoxyphenyl)phosphine (560 mg, 1.59 mmol) was added. Stirring was maintained at rt for 20 h, a solution of 2 M HCl in ether (4.60 mL, 9.20 mmol) was added and the resulting solution stirred at rt for 1 h. After evaporation of the solvents, the resulting crude was purified by flash column chromatography (CH$_2$Cl$_2$/MeOH 20:1) to obtain 1b·HCl (850 mg, 57% over 3 steps) as a colorless foam.

$^1\text{H}$ NMR (400 MHz, CD$_3$CN) δ ppm 0.94 - 1.10 (m, 3H), 1.42 - 1.51 (m, 1H), 1.59 - 1.74 (m, 6H), 2.58 - 2.77 (m, 1H), 3.87 (s, 9H), 6.75 (t, $J = 9.6$ Hz, 1H), 7.09 - 7.19 (m, 6H), 7.69 - 7.79 (m, 6H);

$^{13}\text{C}$ NMR (100 MHz, CD$_3$CN) δ ppm 26.2, 26.5, 36.4, 36.4, 54.2 (d, $J_{CP} = 1.6$ Hz), 56.9, 115.0 (d, $J_{CP} = 111.3$ Hz), 116.4 (d, $J_{CP} = 14.3$ Hz), 137.0 (d, $J_{CP} = 12.7$ Hz), 165.7 (d, $J_{CP} = 3.2$ Hz);

$^{31}\text{P}$ NMR (162 MHz, CD$_3$CN) δ ppm 34.1; IR $\nu_{\max}$/cm$^{-1}$ 3300, 2934, 2843, 1593, 1503, 1262, 1113;

MP 89 - 93 °C; HRMS (ESI+): calcd. for C$_{27}$H$_{33}$NO$_3$P [M]$^+$ 450.2193, found 450.2181.
Synthesis and characterization of iminophosphorane 1b

PS-BEMP (51.5 mg, 2.2 mmol/g, 0.113 mmol) was added to a solution of iminophosphorane salt 1b-HCl (50.0 mg, 0.103 mmol) in CH$_2$Cl$_2$ under argon atmosphere. The reaction mixture was stirred at rt for 1h and then filtered, concentrated and dried under vacuum to obtain 1b (45.0 mg, 97%) as a colorless oil.

$^1$H NMR (400 MHz, CD$_3$CN) δ ppm 1.03 - 1.14 (m, 3H), 1.21 - 1.33 (m, 2H), 1.43 - 1.50 (m, 1H), 1.55 - 1.66 (m, 4H), 2.75 - 2.92 (m, 1H), 3.81 (s, 9H), 3.81 (s, 3H), 6.94 - 7.03 (m, 6H), 7.51 - 7.60 (m, 6H); $^{13}$C NMR (100 MHz, CD$_3$CN) δ ppm 26.8, 27.2, 40.1, 40.2, 55.0 (d, $J_{CP}$ = 4.0 Hz), 56.5, 115.2 (d, $J_{CP}$ = 11.9 Hz), 124.8 (d, $J_{CP}$ = 102.5 Hz), 135.5 (d, $J_{CP}$ = 10.3 Hz), 163.5 (d, $J_{CP}$ = 2.4 Hz); $^{31}$P NMR (162 MHz, CD$_3$CN) δ ppm 8.9; HRMS (ESI+): calcd. for C$_{27}$H$_{33}$NO$_3$P [M+H]$^+$ 450.2193, found 450.2179.

$pK_{BH^+}$ Measurement of 1b-HCl in CD$_3$CN$^{18}$

1b-HCl (20.0 mg, 0.041 mmol) and tetramethylguanidine (5.2 μL, 0.04 mmol) were dissolved in CD$_3$CN. The $^{13}$C NMR and $^{31}$P NMR were measured and the chemical shift of the CH-N=PPh$_3$ and CH-N=PPh$_3$ were used to estimate the equilibrium ratio and the equilibrium constant of the reaction $^{18}$. The equilibrium constant was then used, with the known $pK_{BH^+}$ of TMG in CD$_3$CN ($pK_{BH^+}$ = 23.3) $^{19}$ to determine the estimated $pK_{BH^+}$ of 1b-HCl. The experiment was repeated three times. Representative $^{13}$C NMR and $^{31}$P NMR spectra of the experiments are included in Section 5.1.

| Estimated $pK_{BH^+}$ of 1b-HCl in CD$_3$CN |
|--------------------------------------------|
| Using $^{13}$C NMR | Using $^{31}$P NMR |
| Exp.1 | 25.1 | 24.8 |
| Exp.2 | 25.1 | 24.9 |
| Exp.3 | 25.2 | 25.0 |
| Average | **25.1** | **24.9** |
2.6. Synthesis and characterization of N-diphenylphosphinoylketimines 5a - 5q

General procedure B for the preparation of N-diphenylphosphinoylketimines 5a - 5q (See Supplementary Figure 9)

To a solution of NH₂OH·HCl (1.5 equiv.) and NaOAc (1.5 equiv.) in EtOH/H₂O (1:1, 1.8 M) was added the corresponding ketone (1.0 equiv.) at rt, and the reaction mixture refluxed for 20 h. After cooling to rt, the reaction mixture was stored at -20 °C for 24 h. The precipitated oxime was filtered, washed with cold ethanol, vacuum dried and used directly without further purification (in some cases, extraction with CH₂Cl₂ of the aqueous phase after evaporation of the ethanol was performed and the crude oxime used directly without further purification in the next step). To a solution of crude oxime (1.0 equiv.) in CH₂Cl₂/n-hexane (1:1, 0.3 M) under inert atmosphere at -45 °C was added triethylamine (1.1 equiv.) and stirred for 10 min. Subsequently, chlorodiphenylphosphine (1.1 equiv.) was added dropwise over 20 min. via syringe pump. After stirring at -45 °C for 1 h and at rt for 16 h, the solvents were removed under reduced pressure (temperature of H₂O bath below 20 °C). The crude reaction mixture was dissolved in CH₂Cl₂ and washed with H₂O (2 x). The organic phase was dried over Na₂SO₄, filtered and concentrated. The crude product was purified by flash column chromatography (CH₂Cl₂/acetone or PE/EtOAc mixtures) to obtain ketimines 5a - 5q in yields ranging from 37 - 64%.

Ketimines 5a, 20, 5b, 20a,21 5c, 20c 5d, 20a 5e, 20a 5i, 20a,21 5j, 20a,22 5m, 20a,20c,21 5n, 20c,23 5o, 20a and 5p 20a have been reported and characterized previously in the literature. Their physical and spectroscopic properties are in agreement to those reported.

N-[(1E)-1-(Biphenyl-4-yl)ethyldiene]-P,P-diphenylphosphinic amide, 5f

![Structure of 5f](image)

Obtained according to general procedure B using 1-[(1,1'-biphenyl)-4-yl]ethanone on a 7.10 mmol scale. Phosphinoyl ketimine 5f was obtained as a pale yellow solid (1.08 g, 40% over 2 steps).

¹H NMR (400 MHz, CDCl₃) δ ppm 3.00 (d, J = 2.0 Hz, 3H), 7.39 - 7.52 (m, 9H), 7.65 (d, J = 7.4 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H), 7.97 - 8.01 (m, 2H), 8.01 - 8.04 (m, 2H), 8.17 (d, J = 8.4 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 23.0 (d, Jₕₗ = 12.0 Hz), 127.1, 127.2, 128.1, 128.4 (d, Jₕₗ = 12.8 Hz), 128.5, 129.0, 131.4 (d, Jₕₗ = 2.4 Hz), 131.5 (d, Jₕₗ = 9.6 Hz), 134.7 (d, Jₕₗ = 131.8 Hz),
138.2 (d, $J_{CP} = 24.0$ Hz), 140.0, 145.1, 181.1 (d, $J_{CP} = 8.0$ Hz); $^{31}$P NMR (162 MHz, CDCl$_3$) $\delta$ ppm 20.2; IR $\nu_{max}/$cm$^{-1}$ 1630, 1599, 1437, 1277, 1199, 1121, 1107; MP 153 - 154 °C; HRMS (ESI+): calcd. for C$_{26}$H$_{23}$NOP [M+H]$^+$ 396.1512, found 396.1502.

$N$-[(1E)-1-(4-Nitrophenyl)ethylidene]-$P,P$-diphenylphosphinic amide, 5g

Obtained according to general procedure B using 1-(4-nitrophenyl)ethanone on a 8.33 mmol scale. Phosphinoyl ketimine 5g was obtained as a pale yellow solid (1.11 g, 37% over 2 steps).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 3.02 (d, $J = 2.3$ Hz, 3H), 7.44 - 7.54 (m, 6H), 7.96 (dd, $J = 8.0$ Hz), 8.01 - 8.34 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 23.1 (d, $J_{CP} = 12.0$ Hz), 123.6, 128.5 (d, $J_{CP} = 12.0$ Hz), 128.7, 131.4 (d, $J_{CP} = 9.5$ Hz), 131.7 (d, $J_{CP} = 2.4$ Hz), 133.6 (d, $J_{CP} = 131.1$ Hz), 144.4 (d, $J_{CP} = 23.8$ Hz), 149.7, 179.2 (d, $J_{CP} = 7.9$ Hz); $^{31}$P NMR (162 MHz, CDCl$_3$) $\delta$ ppm 19.8; IR $\nu_{max}/$cm$^{-1}$ 3443, 1638, 1520, 1320, 1197, 1120, 1105; MP 122 - 126 °C; HRMS (ESI+): calcd. for C$_{20}$H$_{18}$N$_2$O$_3$P [M+H]$^+$ 365.1050, found 365.1043.

$N$-[(1E)-1-(2-Fluorophenyl)ethylidene]-$P,P$-diphenylphosphinic amide, 5h

Obtained according to general procedure B using 1-(2-fluorophenyl)ethanone on a 6.31 mmol scale. Phosphinoyl ketimine 5h was obtained as a colorless solid (1.36 g, 64% over 2 steps).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 2.97 (dd, $J = 4.0$, 2.0 Hz, 3H), 7.11 (dd, $J = 11.1$, 8.6 Hz, 1H), 7.22 (‘t’, $J = 7.6$ Hz, 1H), 7.37 - 7.53 (m, 7H), 7.89 (td, $J = 7.7$, 1.8 Hz, 1H), 7.94 - 8.04 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 27.2 (d, $J_{CF} = 12.8$, $J_{CF} = 7.2$ Hz), 116.7 (d, $J_{CF} = 23.2$ Hz), 124.2 (d, $J_{CF} = 4.0$ Hz), 128.4 (d, $J_{CF} = 12.0$ Hz), 128.5 - 128.7 (m), 130.3 (d, $J_{CF} = 2.4$ Hz), 131.4 (d, $J_{CF} = 2.4$ Hz), 131.5 (d, $J_{CF} = 9.6$ Hz), 133.3 (d, $J_{CF} = 8.8$ Hz), 134.2 (d, $J_{CF} = 130.2$ Hz), 161.5 (d, $J_{CF} = 254.9$ Hz), 180.9 (dd, $J_{CF} = 7.2$, $J_{FC} = 2.4$ Hz); $^{19}$F NMR (376.5 MHz, CDCl$_3$) $\delta$ ppm - 110.0; IR $\nu_{max}/$cm$^{-1}$ 1640, 1483, 1200, 1122; MP 98 – 100 °C; HRMS (ESI+): calcd. for C$_{20}$H$_{17}$FNNaOP [M+Na]$^+$ 360.0924, found 360.0915.
N-[(1E)-1-(3,4-Dichlorophenyl)ethylidene]-P,P-diphenylphosphinic amide, 5k

Obtained according to general procedure B using 1-(3,4-dichlorophenyl)ethanone on a 4.90 mmol scale. Phosphinoyl ketimine 5k was obtained as a pale yellow solid (1.00 g, 54% over 2 steps).

$^1$H NMR (400 MHz, CDCl$_3$) δ ppm 2.93 (d, $J = 2.0$ Hz, 3H), 7.41 - 7.51 (m, 6H), 7.54 (d, $J = 8.4$ Hz, 1H), 7.88 (dd, $J = 8.4$, 2.1 Hz, 1H), 7.93 - 7.99 (m, 4H), 8.12 (d, $J = 2.1$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 22.9 (d, $J_{CP} = 12.2$ Hz), 127.1, 128.6 (d, $J_{CP} = 12.6$ Hz), 129.9, 130.7, 131.6 (d, $J_{CP} = 9.2$ Hz), 131.8 (d, $J_{CP} = 2.8$ Hz), 133.2, 134.2 (d, $J_{CP} = 131.0$ Hz), 136.9, 139.3 (d, $J_{CP} = 24.6$ Hz), 179.1 (d, $J_{CP} = 7.4$ Hz); $^{31}$P NMR (162 MHz, CDCl$_3$) δ ppm 20.8; IR ν$_{max}$/cm$^{-1}$ 1636, 1437, 1200, 1122, 1107; MP 135 - 136 °C; HRMS (ESI+): calcd. for C$_{20}$H$_{17}$Cl$_2$NOP [M+H]$^+$ 388.0419, found 388.0405.

N-{(2R)-2-[3,5-Bis(trifluoromethyl)phenyl]-1-nitropropan-2-yl}-P,P-diphenylphosphinic amide, 5l

Obtained according to general procedure B using 1-[3,4-bis(trifluoromethyl)phenyl]ethanone on a 3.69 mmol scale. Phosphinoyl ketimine 5l was obtained as a colorless solid (0.92 g, 55% over 2 steps).

$^1$H NMR (400 MHz, CDCl$_3$) δ ppm 3.05 (d, $J = 2.0$ Hz, 3H), 7.42 - 7.59 (m, 6H), 7.90 - 8.01 (m, 4H), 8.05 (s, 1H), 8.46 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 22.9 (d, $J_{CP} = 11.8$ Hz), 123.0 (q, $J_{CP} = 272.8$ Hz), 125.3 - 125.6 (m), 127.5 - 127.7 (m), 128.6 (d, $J_{CP} = 12.7$ Hz), 131.5 (d, $J_{CP} = 9.3$ Hz), 131.9 (d, $J_{CP} = 2.5$ Hz), 132.1 (q, $J_{CP} = 33.8$ Hz), 133.5 (d, $J_{CP} = 130.9$ Hz), 141.3 (d, $J_{CP} = 24.6$ Hz), 178.1 (d, $J_{CP} = 7.1$ Hz); $^{31}$P NMR (162 MHz, CDCl$_3$) δ ppm 21.5; $^{19}$F NMR (376.5 MHz, CDCl$_3$) δ ppm -62.9; MP 120 - 121 °C; IR ν$_{max}$/cm$^{-1}$ 1649, 1279, 1245, 1184, 1134; HRMS (ESI+): calcd. for C$_{22}$H$_{17}$F$_6$NOP [M+H]$^+$ 456.0946, found 456.0924.
N-[(1E)-1-Cyclohexylethyldene]-P,P-diphenylphosphinic amide, 5q

Obtained according to general procedure B using 1-cyclohexylethanone on a 9.88 mmol scale. Phosphinoyl ketimine 5q was obtained as a colorless solid (1.20 g, 37% over 2 steps).

\[ \text{IR } \nu_{\text{max}}/\text{cm}^{-1} \]
\[ 3425, 2928, 2853, 1650, 1437, 1198, 1107 \]

**2.7. Synthesis and characterization of nitro-Mannich addition products 6a - 6q**

**General procedure C for the catalyst optimization studies (Table 1)**

To a stirred solution of the azide precursors to catalysts 4a, 4d – 4r (0.02 mmol) in Et₂O (0.1 mL) in a closed vial was added triphenylphosphine (5.2 mg, 0.020 mmol, 1 eq) and stirred at rt for 24 h. The catalyst formation was confirmed by LRMS and TLC, the volatiles removed under nitrogen stream and to the crude mixture was added ketimine 5a (64 mg, 0.20 mmol) and MeNO₂ (0.215 mL, 4.00 mmol). The reaction was stirred at rt for 24 h and quenched by the addition of 0.05 mL of a 1 M acetic acid solution in CH₂Cl₂ and stirred at rt for 10 min. After evaporation of the solvents, the conversion was measured by \(^1\)H NMR and the ee was determined on an analytical sample of 6a obtained by flash column chromatography (PE/EtOAc).

**General procedure D for the synthesis of racemic nitro-Mannich addition products**

To a stirred suspension of the corresponding ketimine 5a - 5q (0.200 mmol) in MeNO₂ (0.215 mL, 4.00 mmol), BEMP (0.017 mL, 0.060 mmol) was added and the resulting solution was stirred at rt until consumption of the starting material. After evaporation of the solvents, the crude reaction mixture was purified by flash column chromatography (PE/EtOAc or CH₂Cl₂/MeOH mixtures used as eluent) to yield the desired racemic nitro-Mannich addition product in yields ranging from 70 - 85%.
General procedure E for the enantioselective nitro-Mannich addition of nitromethane to ketimines 5a - 5q

To a stirred suspension of ketimine 5 (0.200 mmol) in MeNO₂ (0.215 mL, 4.00 mmol) at -15 °C, catalyst 4a (0.020 mmol) was added and the reaction mixture was stirred at -15 °C in a closed vial until disappearance of starting material by TLC or for a maximum of 96 h. The reaction was quenched by addition of 0.05 mL of a 1 M acetic acid solution in CH₂Cl₂ and stirred at rt for 10 min. After evaporation of the solvents the crude reaction mixture was purified by flash column chromatography.

General procedure F for the enantioselective nitro-Mannich addition of nitromethane to ketimines 5a - 5q

To a stirred suspension of ketimine 5 (0.200 mmol) in MeNO₂ (0.215 mL, 4.00 mmol) at 0 °C, catalyst 4a (0.020 mmol) was added and the reaction mixture was stirred at 0 °C in a closed vial until disappearance of starting material by TLC or for a maximum of 48 h. The reaction was quenched by addition of 0.05 mL of a 1 M acetic acid solution in CH₂Cl₂ and stirred at rt for 10 min. After evaporation of the solvents the crude reaction mixture was purified by flash column chromatography.

General procedure G for the ¹H NMR kinetic experiments of the nitro-Mannich addition of nitromethane to ketimine 5a (Figure 2)

To a stirred solution of 2 (6.6 mg, 0.016 mmol) in Et₂O (0.1 mL) in a closed vial was added the corresponding triarylphosphine (0.016 mmol, 1 eq) and stirred at rt for 24 h. The volatiles were removed under nitrogen stream and the catalyst transferred to a NMR tube containing ketimine 5a (52 mg, 0.16 mmol) and mesitylene (22 µL, 0.16 mmol) using d⁸-THF (0.40 mL). To the resulting solution was added MeNO₂ (0.17 mL, 3.2 mmol, 20 eq) and the ¹H NMR spectrum measured every 10 mins over 12 h. Product conversion was measured by integration of the CH₃H₆NO₂ signal against the CH₃ of mesitylene.⁶ The ee was measured on analytical samples from experiments according to General Procedure C with the corresponding triarylphosphine.

⁶The conversion to 6a using cinchonine-derived catalyst I was 0% after 32 h under identical reaction conditions.
N-[(2R)-1-Nitro-2-phenylpropan-2-yl]-P,P-diphenylphosphinic amide, 6a

Obtained according to general procedure E, using N-[(1E)-1-phenylethylidene]-P,P-diphenylphosphinic amide 5a (63.8 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield compound 6a (65 mg, 86%) as a colorless solid. The ee was determined by HPLC analysis (Chiralpak OD-H, hexane/iso-propanol 80:20, λ 220 nm, 1.0 mL/min): t (minor) = 8.09 min, t (major) = 20.25 min (95%).

[^a]$_b$ = - 22.5 (c = 0.50, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm 1.56 (s, 3H), 4.50 (d, J = 4.4 Hz, 1H), 5.06 (d, J = 13.4 Hz, 1H), 5.46 (d, J = 13.4 Hz, 1H), 7.28 - 7.31 (m, 1H), 7.35 - 7.40 (m, 2H), 7.42 - 7.57 (m, 8H), 7.81 - 7.87 (m, 2H), 8.00 - 8.05 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 27.2 (d, J$_{CP}$ = 3.8 Hz), 59.8 (d, J$_{CP}$ = 2.9 Hz), 84.3, 124.6, 127.8, 128.6 (d, J$_{CP}$ = 13.3 Hz), 128.8 (d, J$_{CP}$ = 12.4 Hz), 128.9, 131.0 (d, J$_{CP}$ = 9.5 Hz), 131.9 (d, J$_{CP}$ = 2.8 Hz), 132.0 (d, J$_{CP}$ = 7.6 Hz); $^{31}$P NMR (162 MHz, CDCl$_3$) δ ppm 22.9; IR ν$_{max}$/cm$^{-1}$ 3190, 1546, 1438, 1188, 1121, 1108; MP 161 - 163 °C; HRMS (ESI+): calcd. for C$_{21}$H$_{21}$N$_2$NaO$_3$P [M+Na]$^+$ 403.1182, found 403.1169. Spectroscopic data are consistent with those given in the literature.$^{24}$

N-[(2R)-2-(4-Methylphenyl)-1-nitropropan-2-yl]-P,P-diphenylphosphinic amide, 6b

Obtained according to general procedure F, using N-[(1E)-1-(4-methylphenyl)ethylidene]-P,P-diphenylphosphinic amide 5b (66.6 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield compound 6b (73 mg, 93%) as a colorless foam. The ee was determined by HPLC analysis (Chiralpak OD-H, hexane/iso-propanol 80:20, λ 220 nm, 1.0 mL/min): t (minor) = 7.86 min, t (major) = 30.35 min (89%).

[^a]$_b$ = - 29.1 (c = 0.98, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm 1.54 (s, 3H), 2.32 (s, 3H), 4.49 (d, J = 4.5 Hz, 1H), 5.04 (d, J = 13.4 Hz, 1H), 5.42 (d, J = 13.4 Hz, 1H), 7.16 (d, J = 8.1 Hz, 2H), 7.40 (d, J = 8.3 Hz, 2H), 7.42 - 7.55 (m, 6H), 7.79 - 7.88 (m, 2H), 7.96 - 8.07 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 20.9, 27.2 (d, J$_{CP}$ = 4.0 Hz), 59.7 (d, J$_{CP}$ = 2.4 Hz), 84.5,
124.6, 128.6 (d, \(J_{CP} = 13.6\) Hz), 128.7 (d, \(J_{CP} = 12.8\) Hz), 129.6, 131.0 (d, \(J_{CP} = 9.6\) Hz), 132.0 (‘t’, \(J_{CP} = 3.2\) Hz), 132.2 (d, \(J_{CP} = 9.6\) Hz), 133.8 (d, \(J_{CP} = 131.8\) Hz), 134.0 (d, \(J_{CP} = 125.4\) Hz), 137.6, 140.1 (d, \(J_{CP} = 8.0\) Hz); \(^{31}\)P NMR (162 MHz, CDCl\(_3\)) \(\delta\) ppm 22.7; IR \(\nu_{\text{max}}/\text{cm}^{-1}\) 3195, 1734, 1547, 1438, 1374, 1246, 1189, 1121, 1108; MP 46 - 50 °C; HRMS (ESI+): calcd. for C\(_{22}\)H\(_{23}\)N\(_2\)NaO\(_{4}\)P \([\text{M+Na}]^+\) 417.1339, found 417.1323.

**N-[(2R)-2-(4-Methoxyphenyl)-1-nitropropan-2-yl]-P,P-diphenylphosphinic amide, 6c**

Obtained according to general procedure F, using \(N\)-[(1E)-1-(4-methoxyphenyl)ethylidene]-P,P-diphenylphosphinic amide 5c (69.8 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield compound 6c (78 mg, 95%) as a colorless solid. The ee was determined by HPLC analysis (Chiralpak OD-H, hexane/\(i\)-propanol 80:20, \(\lambda\) 220 nm, 1.0 mL/min): \(t\) (minor) = 10.64 min, \(t\) (major) = 16.78 min (91%).

[\(\text{[a]}\)\(^D\) = -33.0 (c = 1.04, CHCl\(_3\)); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm 1.55 (s, 3H), 3.78 (s, 3H), 4.44 (d, \(J = 4.3\) Hz, 1H), 5.03 (d, \(J = 13.1\) Hz, 1H), 5.38 (d, \(J = 13.1\) Hz, 1H), 6.75 - 6.99 (m, 2H), 7.34 - 7.60 (m, 8H), 7.74 - 7.91 (m, 2H), 7.92 - 8.12 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 27.2 (d, \(J_{CP} = 4.0\) Hz), 55.3, 59.5 (d, \(J_{CP} = 2.4\) Hz), 84.6 (d, \(J_{CP} = 1.6\) Hz), 114.1, 126.1, 128.6 (d, \(J_{CP} = 11.2\) Hz), 128.7 (d, \(J_{CP} = 10.4\) Hz), 131.1 (d, \(J_{CP} = 9.6\) Hz), 131.9 (‘t’, \(J_{CP} = 3.2\) Hz), 132.1 (d, \(J_{CP} = 9.6\) Hz), 133.8 (d, \(J_{CP} = 131.8\) Hz), 134.0 (d, \(J_{CP} = 126.2\) Hz), 134.8 (d, \(J_{CP} = 7.2\) Hz), 159.0 (d, \(J_{CP} = 0.8\) Hz); \(^{31}\)P NMR (162 MHz, CDCl\(_3\)) \(\delta\) ppm 22.5; IR \(\nu_{\text{max}}/\text{cm}^{-1}\) 3180, 1544, 1510, 1247, 1194, 1179, 1120, 1016; MP 148 - 151 °C; HRMS (ESI+): calcd. for C\(_{22}\)H\(_{23}\)N\(_2\)NaO\(_{4}\)P \([\text{M+Na}]^+\) 433.1288, found 433.1270.

**N-[(2R)-2-(3-Methoxyphenyl)-1-nitropropan-2-yl]-P,P-diphenylphosphinic amide, 6d**

Obtained according to general procedure F, using \(N\)-[(1E)-1-(3-methoxyphenyl)ethylidene]-P,P-diphenylphosphinic amide 5d (69.8 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield compound 6d (72 mg, 88%) as a colorless solid. The ee was determined by HPLC analysis
(Chiralpak OD-H, hexane/iso-propanol 80:20, λ 220 nm, 1.0 mL/min): t (minor) = 10.57 min, t (major) = 18.19 min (91%).

\[ \alpha \] D \text{24} = -27.4 (c = 1.15, CHCl₃); \text{1H NMR} (400 MHz, CDCl₃) δ ppm 1.54 (s, 3H), 3.82 (s, 3H), 4.50 (d, \( J = 4.3 \) Hz, 1H), 5.04 (d, \( J = 13.5 \) Hz, 1H), 5.47 (d, \( J = 13.5 \) Hz, 1H), 6.81 (dd, \( J = 8.2, 2.4 \) Hz, 1H), 7.05 (dd, \( J = 7.8, 1.5 \) Hz, 1H), 7.11 (t, \( J = 2.0 \) Hz, 1H), 7.24 - 7.34 (m, 1H), 7.41 - 7.59 (m, 6H), 7.77 - 7.88 (m, 2H), 7.96 - 8.09 (m, 2H); \text{13C NMR} (125 MHz, CDCl₃) δ ppm 27.2 (d, \( J_{CP} = 3.7 \) Hz), 55.3, 59.8 (d, \( J_{CP} = 2.8 \) Hz), 84.2 (br s), 111.7, 112.3, 116.7, 128.6 (d, \( J_{CP} = 12.9 \) Hz), 128.8 (d, \( J_{CP} = 12.0 \) Hz), 130.0, 131.0 (d, \( J_{CP} = 9.2 \) Hz), 132.0 (d, \( J_{CP} = 2.8 \) Hz), 132.0 (d, \( J_{CP} = 2.8 \) Hz), 132.2 (d, \( J_{CP} = 10.2 \) Hz), 133.7 (d, \( J_{CP} = 132.2 \) Hz), 134.0 (d, \( J_{CP} = 125.8 \) Hz), 144.9 (d, \( J_{CP} = 8.3 \) Hz), 159.9; \text{31P NMR} (202 MHz, CDCl₃) δ ppm 24.0; \text{IR} \nu_{max}/cm⁻¹ 3190, 1549, 1538, 1258, 1183, 1120, 1108; \text{MP} 116 - 118 °C; \text{HRMS} (ESI+): calcd. for \( C_{22}H_{23}N_2NaO_4P \) [M+Na]⁺ 433.1288, found 433.1276.

\text{N-[(2R)-2-(2-Methoxyphenyl)-1-nitropropan-2-yl]-P,P-diphenylphosphinic amide, 6e} 

Obtained according to general procedure F, using \( N\-[(1E)-1-(2-\text{methoxyphenyl})\text{ethylidene}]-P,P\-\text{diphenylphosphinic amide 5e} \) (69.8 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield compound 6e (51 mg, 62%) as a colorless foam. The ee was determined by HPLC analysis (Chiralpak OD-H, hexane/iso-propanol 80:20, λ 220 nm, 1.0 mL/min): t (minor) = 8.37 min, t (major) = 15.33 min (93%).

\[ \alpha \] D \text{33} = -31.0 (c = 0.89, CHCl₃); \text{1H NMR} (400 MHz, CDCl₃) δ ppm 1.75 (s, 3H), 3.83 (s, 3H), 5.00 (d, \( J = 5.8 \) Hz, 1H), 5.23 (d, \( J = 11.6 \) Hz, 1H), 5.35 (d, \( J = 11.6 \) Hz, 1H), 6.93 (d, \( J = 8.1 \) Hz, 1H), 6.97 - 7.06 (m, 1H), 7.25 - 7.36 (m, 1H), 7.38 - 7.56 (m, 7H), 7.77 - 7.97 (m, 4H); \text{13C NMR} (100 MHz, CDCl₃) δ ppm 23.0 (d, \( J_{CP} = 3.2 \) Hz), 55.4, 59.5 (d, \( J_{CP} = 2.4 \) Hz), 84.3 (d, \( J_{CP} = 1.6 \) Hz), 111.8, 121.4, 127.3, 128.5 (d, \( J_{CP} = 12.8 \) Hz), 128.7 (d, \( J_{CP} = 12.8 \) Hz), 129.5 (d, \( J_{CP} = 6.4 \) Hz), 129.7, 131.0 (d, \( J_{CP} = 9.6 \) Hz), 131.8 (d, \( J_{CP} = 2.4 \) Hz), 131.9 (d, \( J_{CP} = 2.4 \) Hz), 132.1 (d, \( J_{CP} = 9.6 \) Hz), 134.1 (d, \( J_{CP} = 131.8 \) Hz), 134.5 (d, \( J_{CP} = 126.2 \) Hz), 156.4; \text{31P NMR} (162 MHz, CDCl₃) δ ppm 21.7; \text{IR} \nu_{max}/cm⁻¹ 2924, 1543, 1492, 1461, 1436, 1374, 1236, 1198, 1188, 1119; \text{MP} 56 - 58 °C; \text{HRMS} (ESI+): calcd. for \( C_{22}H_{23}N_2NaO_4P \) [M+Na]⁺ 433.1288, found 433.1273.
\[ \text{N-[(2R)-2-(Biphenyl-4-yl)-1-nitropropan-2-yl]-P,P-diphenylphosphinic amide, 6f} \]

 Obtained according to general procedure F, using \( \text{N-[(1E)-1-(biphenyl-4-yl)ethylidene]-P,P-diphenylphosphinic amide 5f} \) (79.0 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield compound 6f (84 mg, 92%) as a colorless solid. The ee was determined by HPLC analysis (Chiralpak AD, hexane/\textit{iso}-propanol 80:20, \( \lambda \) 240 nm, 1.0 mL/min): t (major) = 17.03 min, t (minor) = 23.58 (90%).

\[ [\alpha]_D^{24} = -43.2 \text{ (c = 1.13, CHCl}_3) \]; \( ^1\text{H NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \text{ ppm} \): 1.61 (s, 3H), 4.55 (d, \( J = 4.5 \text{ Hz, 1H} \)), 5.11 (d, \( J = 13.4 \text{ Hz, 1H} \)), 5.47 (d, \( J = 13.4 \text{ Hz, 1H} \)), 7.32 - 7.40 (m, 1H), 7.41 - 7.62 (m, 14H), 7.85 (d, \( J = 12.4 \text{ Hz, 1H} \)), 7.87 (d, \( J = 12.4 \text{ Hz, 1H} \)), 8.03 (d, \( J = 12.1 \text{ Hz, 1H} \)), 8.04 (d, \( J = 12.1 \text{ Hz, 1H} \)); \( ^{13}\text{C NMR} \) (100 MHz, CDCl\(_3\)) \( \delta \text{ ppm} \): 27.2 (d, \( J = 13.4 \text{ Hz} \)), 88.4 (d, \( J_{\text{CP}} = 1.6 \text{ Hz} \)), 125.3, 127.1, 127.6, 128.7 (d, \( J_{\text{CP}} = 11.2 \text{ Hz} \)), 128.8 (d, \( J_{\text{CP}} = 11.2 \text{ Hz} \)), 128.8, 131.1 (d, \( J_{\text{CP}} = 9.6 \text{ Hz} \)), 132.0 (‘t’, \( J_{\text{CP}} = 3.2 \text{ Hz} \)), 132.2 (d, \( J_{\text{CP}} = 9.6 \text{ Hz} \)), 133.7 (d, \( J_{\text{CP}} = 131.0 \text{ Hz} \)), 134.0 (d, \( J_{\text{CP}} = 126.2 \text{ Hz} \)), 140.2, 140.8, 141.9 (d, \( J_{\text{CP}} = 8.0 \text{ Hz} \)); \( ^{31}\text{P NMR} \) (162 MHz, CDCl\(_3\)) \( \delta \text{ ppm} \): 22.7; \( \text{IR } v_{\text{max/cm}}^{-1} \): 3141, 1547, 1439, 1413, 1372, 1186, 1119, 1107, 1009; \( \text{MP} \) 120 - 122 °C; \( \text{HRMS (ESI)} \): calcd. for \( C_{27}H_{25}N_2NaO_3P [M+Na]^+ \) 479.1495, found 479.1492.

\[ \text{N-[(2R)-1-Nitro-2-(4-nitrophenyl)-propan-2-yl]-P,P-diphenylphosphinic amide, 6g} \]

 Obtained according to general procedure E, using \( \text{N-[(1E)-1-(4-nitrophenyl)ethylidene]-P,P-diphenylphosphinic amide 5g} \) (72.8 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield compound 6g (78 mg, 92%) as a pale yellow solid. The ee was determined by HPLC analysis (Chiralpak IA, hexane/\textit{iso}-propanol 80:20, \( \lambda \) 240 nm, 1.0 mL/min): t (major) = 27.39 min, t (minor) = 35.83 min (86%).

\[ [\alpha]_D^{24} = -36.9 \text{ (c = 1.06, CHCl}_3) \]; \( ^1\text{H NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \text{ ppm} \): 1.57 (s, 3H), 4.60 (d, \( J = 4.3 \text{ Hz, 1H} \)), 5.10 (d, \( J = 13.6 \text{ Hz, 1H} \)), 5.45 (d, \( J = 13.6 \text{ Hz, 1H} \)), 7.42 - 7.58 (m, 6H), 7.73 (d, \( J = 8.8 \text{ Hz, 2H} \)), 7.77 - 7.85 (m, 2H), 7.93 - 8.00 (m, 2H), 8.18 (d, \( J = 8.8 \text{ Hz, 2H} \)); \( ^{13}\text{C NMR} \)
(100 MHz, CDCl₃) δ ppm 26.9 (d, J₀CP = 4.0 Hz), 59.8 (d, J₀CP = 1.6 Hz), 83.9 (d, J₀CP = 1.6 Hz), 124.0, 126.1, 128.8 (d, J₀CP = 6.4 Hz), 128.9 (d, J₀CP = 6.4 Hz), 131.1 (d, J₀CP = 9.6 Hz), 131.9 (d, J₀CP = 9.6 Hz), 132.3 (d, J₀CP = 3.2 Hz), 133.1 (d, J₀CP = 130.2 Hz), 133.4 (d, J₀CP = 126.2 Hz), 147.3, 150.2 (d, J₀CP = 6.4 Hz); ³¹P NMR (162 MHz, CDCl₃) δ ppm 23.1; IR νmax/cm⁻¹ 3176, 1733, 1550, 1519, 1438, 1349, 1247, 1186, 1121; MP 138 - 142 °C; HRMS (ESI+): calcd. for C₂₁H₂₀N₃NaO₅P [M+Na]+ 448.1033, found 448.1018.

N-[(2R)-2-(2-Fluorophenyl)-1-nitropropan-2-yl]-P,P-diphenylphosphinic amide, 6h

Obtained according to general procedure E, using N-[(1E)-1-(2-fluorophenylethylidene)-P,P-diphenylphosphinic amide 5h (67.4 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.0 mmol). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 3:1) to yield compound 6h (71 mg, 89%) as a colorless solid. The ee was determined by HPLC analysis (Chiralpak OD-H, hexane/iso-propanol 80:20, λ 220 nm, 1.0 mL/min): t (minor) = 6.98 min, t (major) = 15.44 min (94%).

[α]D²³ = - 37.1 (c = 1.14, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ ppm 1.69 (s, 3H), 4.50 (d, J = 4.1 Hz, 1H), 5.25 (d, J = 12.9 Hz, 1H), 5.31 (dd, J = 12.9, 0.9 Hz, 1H), 7.04 (ddd, J = 12.9, 8.2, 0.9 Hz, 1H), 7.20 (td, J = 7.6, 0.9 Hz, 1H), 7.28 - 7.34 (m, 1H), 7.43 - 7.56 (m, 6H), 7.71 (tg, J = 8.2, 1.4 Hz, 1H), 7.81 - 7.89 (m, 2H), 7.93 - 8.01 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ ppm 23.8 ('t', J₀CF = J₀CP = 2.9 Hz), 58.8 - 58.9 (m), 84.3 (dd, J₀CF = 7.6, J₀CP = 1.9 Hz), 116.7 (d, J₀CF = 23.8 Hz), 124.8 (d, J₀CF = 2.9 Hz), 127.9 (d, J₀CF = 2.9 Hz). 128.7 (d, J₀CP = 13.4 Hz), 128.8 (d, J₀CP = 12.4 Hz), 129.3 (d, J₀CF = 10.5, J₀CP = 6.7 Hz), 130.2 (d, J₀CF = 8.6 Hz), 131.1 (d, J₀CF = 9.5 Hz), 132.0 (d, J₀CP = 2.9 Hz), 132.0 (d, J₀CP = 9.5 Hz), 132.1 (d, J₀CP = 2.9 Hz), 133.6 (d, J₀CP = 130.7 Hz), 134.0 (d, J₀CP = 126.8 Hz), 159.6 (d, J₀CF = 245.1 Hz); ³¹P NMR (162 MHz, CDCl₃) δ ppm 22.2; ¹⁹F NMR (376.5 MHz, CDCl₃) δ ppm -112.2; IR νmax/cm⁻¹ 3158, 1548, 1483, 1439, 1373, 1279, 1259, 1181, 1107, 1070, 1019; MP 120 - 126 °C; HRMS (ESI+): calcd. for C₂₁H₂₀F₂N₂O₅P [M+Na]+ 421.1088, found 421.1081.
N-[(2R)-2-(4-Chlorophenyl)-1-nitropropan-2-yl]-P,P-diphenylphosphinic amide, 6i

Obtained according to general procedure F, using N-[(1E)-1-(4-chlorophenyl)ethylidene]-P,P-diphenylphosphinic amide 5i (70.6 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield compound 6i (75 mg, 90%) as a colorless solid. The ee was determined by HPLC analysis (Chiralpak OD-H, hexane/isopropanol 80:20, λ 220 nm, 1.0 mL/min): t (minor) = 7.39 min, t (major) = 10.56 min (90%).

[α]D23 = - 37.9 (c = 1.00, CHCl3); 1H NMR (400 MHz, CDCl3) δ ppm 1.53 (s, 3H), 4.51 (d, J = 4.3 Hz, 1H), 5.02 (d, J = 13.4 Hz, 1H), 5.37 (d, J = 13.4 Hz, 1H), 7.30 (d, J = 8.3 Hz, 2H), 7.41 - 7.57 (m, 8H), 7.80 (d, J = 12.1 Hz, 1H), 7.82 (d, J = 12.1 Hz, 1H), 7.96 (d, J = 12.1 Hz, 1H), 7.98 (d, J = 12.1 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ ppm 27.1 (d, JCP = 4.0 Hz), 59.5 (d, JCP = 2.4 Hz), 84.2, 126.4, 128.7 (d, JCP = 8.8 Hz), 128.8 (d, JCP = 8.8 Hz), 129.0, 131.1 (d, JCP = 9.6 Hz), 132.0 (d, JCP = 9.6 Hz), 132.0 - 132.1 (m), 133.5 (d, JCP = 131.0 Hz), 133.7 (d, JCP = 126.2 Hz), 133.8, 141.5 (d, JCP = 7.2 Hz); 31P NMR (162 MHz, CDCl3) δ ppm 22.7; IR νmax/cm⁻¹ 3185, 1548, 1494, 1438, 1374, 1248, 1186, 1107; MP 152-154 °C; HRMS (ESI+): calcd. for C21H20ClN2NaO3P [M+Na]+ 437.0792, found 437.0781.

N-[(2R)-2-(4-Bromophenyl)-1-nitropropan-2-yl]-P,P-diphenylphosphinic amide, 6j

Obtained according to general procedure F, using N-[(1E)-1-(4-bromophenyl)ethylidene]-P,P-diphenylphosphinic amide 5j (79.4 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield compound 6j (77 mg, 84%) as a colorless solid. The ee was determined by HPLC analysis (Chiralpak OD-H, hexane/isopropanol 80:20, λ 220 nm, 1.0 mL/min): t (minor) = 9.15 min, t (major) = 15.56 min (90%).

[α]D24 = - 35.0 (c = 0.75, CHCl3); 1H NMR (400 MHz, CDCl3) δ ppm 1.53 (s, 3H), 4.49 (d, J = 4.3 Hz, 1H), 5.02 (d, J = 13.4 Hz, 1H), 5.38 (d, J = 13.4 Hz, 1H), 7.33 - 7.61 (m, 10H), 7.80 (d, J = 12.4 Hz, 1H), 7.82 (d, J = 12.4 Hz, 1H), 7.96 (d, J = 12.1 Hz, 1H), 7.98 (d, J = 12.1 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ ppm 27.0 (d, JCP = 3.2 Hz), 59.6 (d, JCP = 1.6 Hz), 84.1 (d, JCP = 2.4 Hz), 84.2, 126.4, 128.7 (d, JCP = 8.8 Hz), 128.8 (d, JCP = 8.8 Hz), 129.0, 131.1 (d, JCP = 9.6 Hz), 132.0 (d, JCP = 9.6 Hz), 132.0 - 132.1 (m), 133.5 (d, JCP = 131.0 Hz), 133.7 (d, JCP = 126.2 Hz), 133.8, 141.5 (d, JCP = 7.2 Hz); 31P NMR (162 MHz, CDCl3) δ ppm 22.7; IR νmax/cm⁻¹ 3185, 1548, 1494, 1438, 1374, 1248, 1186, 1107; MP 152-154 °C; HRMS (ESI+): calcd. for C21H20ClN2NaO3P [M+Na]+ 437.0792, found 437.0781.
1.6 Hz), 122.0, 126.7, 128.7 (d, \( J_{CP} = 8.8 \) Hz), 128.8 (d, \( J_{CP} = 8.8 \) Hz), 131.1 (d, \( J_{CP} = 9.6 \) Hz), 132.0 - 132.1 (m), 133.5 (d, \( J_{CP} = 131.0 \) Hz), 133.8 (d, \( J_{CP} = 126.2 \) Hz), 142.1 (d, \( J_{CP} = 7.2 \) Hz); 31P NMR (162 MHz, CDCl3) δ ppm 22.7; IR νmax/cm⁻¹ 3158, 2925, 1545, 1439, 1397, 1373, 1253, 1184, 1150, 1110, 1084, 1007; MP 162 - 164 °C; HRMS (ESI+): calcd. for C21H20⁷⁹BrN₂NaO₃P [M+Na]+ 481.0287, found 481.0297; calcd. for C21H20⁸¹BrN₂NaO₃P [M+Na]+ 483.0268, found 483.0276.

N\-[(2R)-2-(3,4-Dichlorophenyl)-1-nitropropan-2-yl]-P,P-diphenylphosphinic amide, 6k

Obtained according to general procedure F, using N\-[(1E)-1-(3,4-dichlorophenylethylidene)-P,P-diphenylphosphinic amide 5k (77.4 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield compound 6k (82 mg, 92%) as a colorless solid. The ee was determined by HPLC analysis (Chiralpak OD-H, hexane/iso-propanol 80:20, λ 230 nm, 1.0 mL/min): t (minor) = 8.83 min, t (minor) = 15.82 min (87%).

[a]D²⁴ = - 37.0 (c = 1.06, CHCl₃); 1H NMR (500 MHz, CDCl₃) δ ppm 1.55 (s, 3H), 4.47 (d, \( J = 3.5 \) Hz, 1H), 5.02 (d, \( J = 13.5 \) Hz, 1H), 5.39 (d, \( J = 13.5 \) Hz, 1H), 7.34 (dd, \( J = 8.5, 2.2 \) Hz, 1H), 7.40 (d, \( J = 8.2 \) Hz, 1H), 7.43 - 7.58 (m, 6H), 7.60 (d, \( J = 2.2 \) Hz, 1H), 7.79 (d, \( J = 12.0 \) Hz, 1H), 7.80 (d, \( J = 12.0 \) Hz, 1H), 7.95 (d, \( J = 12.1 \) Hz, 1H), 7.96 (d, \( J = 12.1 \) Hz, 1H); 13C NMR (125 MHz, CDCl₃) δ ppm 26.9 (d, \( J_{CP} = 2.8 \) Hz), 59.2 (d, \( J_{CP} = 1.9 \) Hz), 83.9, 124.4, 127.4, 128.7 (d, \( J_{CP} = 8.6 \) Hz), 128.8 (d, \( J_{CP} = 8.6 \) Hz), 130.7, 131.1 (d, \( J_{CP} = 10.5 \) Hz), 131.9 (d, \( J_{CP} = 9.5 \) Hz), 132.1 - 132.2 (m), 133.1, 133.2 (d, \( J_{CP} = 130.6 \) Hz), 133.4 (d, \( J_{CP} = 126.8 \) Hz), 143.2 (d, \( J_{CP} = 6.7 \) Hz); 31P NMR (162 MHz, CDCl₃) δ ppm 23.2; IR νmax/cm⁻¹ 3182, 1733, 1549, 1538, 1374, 1250, 1186, 1122; MP 102 - 105 °C; HRMS (ESI+): calcd. for C21H19Cl2N2NaO₃P [M+Na]+ 471.0403, found 471.0393.

N\-[(2R)-2-[3,5-Bis(trifluoromethyl)phenyl]-1-nitropropan-2-yl]-P,P-diphenylphosphinic amide, 6l

Obtained according to general procedure E, using N\-[(1E)-1-[3,5-bis(trifluoromethyl)phenyl]ethylidene]-P,P-diphenylphosphinic amide 5l
(91.0 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 3:1) to yield compound 6l (98 mg, 95%) as a colorless solid. The ee was determined by HPLC analysis (Chiralpak AD-H, hexane/iso-propanol 95:5, λ 220 nm, 1.0 mL/min): t (major) = 12.04 min, t (minor) = 14.73 min (90%).

\[ \text{[a]}_{D}^{24} = -19.8 \, (c = 0.88, \text{CHCl}_3) \]; \text{^1H NMR (500 MHz, CDCl}_3) \delta ppm 1.65 \, (s, 3H), 4.47 \, (d, J = 4.4 Hz, 1H), 5.14 \, (d, J = 13.6 Hz, 1H), 5.43 \, (d, J = 13.6 Hz, 1H), 7.42 - 7.61 \, (m, 6H), 7.75 - 7.85 \, (m, 3H), 7.92 \, (dd, J = 12.3, 1.6 Hz, 1H), 7.94 \, (d, J = 12.3 Hz, 1H), 7.99 \, (s, 2H); \text{^13C NMR (125 MHz, CDCl}_3) \delta ppm 27.0 \, (d, \text{J}_{CP} = 3.7 Hz), 59.6 \, (d, \text{J}_{CP} = 1.8 Hz), 83.7 \, (d, \text{J}_{CP} = 1.8 Hz), 122.1 - 122.2 \, (m), 123.0 \, (q, \text{J}_{CP} = 272.8 Hz), 125.4 - 125.6 \, (m), 128.9 \, (d, \text{J}_{CP} = 12.9 Hz), 128.9 \, (d, \text{J}_{CP} = 12.0 Hz), 131.1 \, (d, \text{J}_{CP} = 10.2 Hz), 131.8 \, (d, \text{J}_{CP} = 9.2 Hz), 132.2 \, (q, \text{J}_{CP} = 33.3 Hz), 132.3 - 132.4 \, (m), 133.0 \, (d, \text{J}_{CP} = 129.5 Hz), 133.1 \, (d, \text{J}_{CP} = 126.7 Hz), 145.6 \, (d, \text{J}_{CP} = 6.5 Hz); \text{^31P NMR (162 MHz, CDCl}_3) \delta ppm 23.4; \text{^19F NMR (376.5 MHz, CDCl}_3) \delta ppm -62.8; \text{IR} \, \nu_{\text{max}}/\text{cm}^{-1} \, 2925, 1553, 1439, 1371, 1277, 1177, 1129; \text{MP} \, 68 - 70 \, ^\circ\text{C}; \text{HRMS (ESI+): calcd. for C}_{23}\text{H}_{19}\text{F}_6\text{N}_2\text{NaO}_5\text{P [M+Na]^+} 539.0930, \text{found 539.0931.}

\text{N-[(2R)-1-Nitro-2-phenylbutan-2-yl]-P,P-diphenylphosphinic amide, 6m}

Obtained according to general procedure F, using \text{N-[(1E)-1-phenylpropylidene]-P,P-diphenylphosphinic amide 5m (66.6 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield compound 6m (75 mg, 95%) as a colorless solid. The ee was determined by HPLC analysis (Chiralpak OD-H, hexane/iso-propanol 80:20, λ 220 nm, 1.0 mL/min): t (minor) = 6.49 min, t (major) = 19.20 min (92%).

\[ \text{[a]}_{D}^{23} = -4.3 \, (c = 1.05, \text{CHCl}_3) \]; \text{^1H NMR (500 MHz, CDCl}_3) \delta ppm 0.46 \, (t, J = 7.4 Hz, 3H), 2.00 \, (q, J = 7.4 Hz, 2H), 4.33 \, (d, J = 4.7 Hz, 1H), 5.28 \, (d, J = 13.6 Hz, 1H), 5.55 \, (d, J = 13.6 Hz, 1H), 7.21 - 7.27 \, (m, 1H), 7.29 - 7.35 \, (m, 2H), 7.39 - 7.57 \, (m, 8H), 7.75 - 7.83 \, (m, 2H), 7.98 - 8.07 \, (m, 2H); \text{^13C NMR (125 MHz, CDCl}_3) \delta ppm 8.5, 32.2 \, (d, \text{J}_{CP} = 3.8 Hz), 63.7 \, (d, \text{J}_{CP} = 2.8 Hz), 81.3, 125.8, 127.8, 128.5 \, (d, \text{J}_{CP} = 8.6 Hz), 128.6, 128.7 \, (d, \text{J}_{CP} = 8.6 Hz), 131.1 \, (d, \text{J}_{CP} = 9.5 Hz), 131.9 \, (d, \text{J}_{CP} = 2.9 Hz), 131.9 \, (d, \text{J}_{CP} = 2.9 Hz), 132.1 \, (d, \text{J}_{CP} = 9.5 Hz), 133.8 \, (d, \text{J}_{CP} = 131.6 Hz), 133.9 \, (d, \text{J}_{CP} = 125.9 \, Hz), 140.4 \, (d, \text{J}_{CP} = 7.6 Hz); \text{^31P NMR (162 MHz, CDCl}_3) \delta ppm 22.8;
IR $\nu_{\text{max}}$/cm$^{-1}$ 3189, 1548, 1437, 1378, 1243, 1187, 1122, 1107; **MP** 133 - 137 °C; **HRMS** (ESI+): calcd. for C$_{22}$H$_{23}$N$_2$NaO$_3$P [M+Na]$^+$ 417.1339, found 417.1322.

**N-[(1R)-1-(Nitromethyl)-1,2,3,4-tetrahydronaphtalen-1-yl]-P,P-diphenylphosphinic amide, 6n**

Obtained according to general procedure E, using N-[(1E)-3,4-dihydronaphthalen-1(2H)-ylidene]-P,P-diphenylphosphinic amide 5n (69.0 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). $^1$H NMR of the crude reaction mixture after 96 h showed a conversion of 50% for compound 6n. The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield compound 6n (32 mg, 40%) as a colorless solid. The ee was determined by HPLC analysis (Chiralpak OD-H, hexane/iso-propanol 90:10, $\lambda$ 220 nm, 1.0 mL/min): t (major) = 15.23 min, t (minor) = 19.42 min (92%).

$[\alpha]_{D}^{23} = -3.4$ (c = 1.00, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 1.71 - 1.86 (m, 1H), 1.99 - 2.13 (m, 2H), 2.13 - 2.24 (m, 1H), 2.72 (t, $J = 5.9$ Hz, 2H), 3.97 (d, $J = 6.1$ Hz, 1H), 4.89 (d, $J = 11.5$ Hz, 1H), 5.42 (d, $J = 11.5$ Hz, 1H), 6.86 - 7.06 (m, 3H), 7.23 - 7.33 (m, 2H), 7.33 - 7.42 (m, 3H), 7.42 - 7.52 (m, 2H), 7.64 (dd, $J = 12.1$, 1.3 Hz, 1H), 7.65 (d, $J = 12.1$ Hz, 1H), 7.72 (dd, $J = 12.1$, 1.3 Hz, 1H), 7.74 (d, $J = 12.1$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 18.6, 29.1, 33.9 (d, $J_{CP} = 5.6$ Hz), 57.6 (d, $J_{CP} = 3.2$ Hz), 84.6 (d, $J_{CP} = 2.4$ Hz), 126.1, 127.4, 128.1 (d, $J_{CP} = 12.8$ Hz), 128.3, 128.5 (d, $J_{CP} = 12.8$ Hz), 129.6, 131.4 (d, $J_{CP} = 9.6$ Hz), 131.4 (d, $J_{CP} = 2.4$ Hz), 131.6 (d, $J_{CP} = 9.6$ Hz), 131.7 (d, $J_{CP} = 2.4$ Hz), 133.1 (d, $J_{CP} = 130.2$ Hz), 133.9 (d, $J_{CP} = 126.2$ Hz), 134.2 (d, $J_{CP} = 3.2$ Hz), 137.1; $^{31}$P NMR (162 MHz, CDCl$_3$) $\delta$ ppm 21.6; IR $\nu_{\text{max}}$/cm$^{-1}$ 3198, 2940, 1544, 1438, 1375, 1242, 1184, 1120; **MP** 154 - 157 °C; **HRMS** (ESI+): calcd. for C$_{23}$H$_{24}$N$_2$O$_3$P [M+H]$^+$ 407.1519, found 407.1505.

**N-[(2S)-2-(2-Furyl)-1-nitropropan-2-yl]-P,P-diphenylphosphinic amide, 6o**

Obtained according to general procedure F, using N-[(1E)-1-(2-furyl)ethylidene]-P,P-diphenylphosphinic amide 5o (61.8 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield compound...
6o (72 mg, 97%) as a colorless solid. The ee was determined by HPLC analysis (Chiralpak OD-H, hexane/iso-propanol 80:20, λ 220 nm, 1.0 mL/min): t (minor) = 7.19 min, t (major) = 9.51 min (84%).

[α]_D^{24} = -13.2 (c = 1.14, CHCl₃); ^1H NMR (400 MHz, CDCl₃) δ ppm 1.67 (s, 3H), 4.21 (d, J = 6.1 Hz, 1H), 5.05 (d, J = 12.1 Hz, 1H), 5.08 (d, J = 12.1 Hz, 1H), 6.22 - 6.23 (m, 1H), 6.32 (d, J = 2.8 Hz, 1H), 7.21 - 7.24 (m, 1H), 7.36 - 7.56 (m, 6H), 7.72 - 7.82 (m, 2H), 7.83 - 7.94 (m, 2H); ^13C NMR (100 MHz, CDCl₃) δ ppm 23.7 (d, J = 13.4 Hz, 1H), 5.06 (d, J = 13.4 Hz, 1H), 5.40 (d, J = 13.4 Hz, 1H), 7.25 (dd, J = 7.6, 4.8 Hz, 1H), 7.38 - 7.57 (m, 6H), 7.74 - 7.88 (m, 3H), 7.91 - 8.02 (m, 2H), 8.48 (br s, 1H), 8.81 (br s, 1H); ^31P NMR (162 MHz, CDCl₃) δ ppm 22.1; IR ν_max/cm⁻¹ 3178, 1548, 1436, 1373, 1240, 1183, 1163, 1122, 1107, 1009; MP 98 - 100 °C; HRMS (ESI+): calcd. for C₁₉H₁₉N₂NaO₄P [M+Na]^+ 393.0975, found 393.0964.

N-[(2R)-2-(Pyridin-3-yl)-1-nitropropan-2-yl]-P,P-diphenylphosphinic amide, 6p

Obtained according to general procedure F, using N-[(1E)-1-(pyridin-3-yl)ethylidene]-P,P-diphenylphosphinic amide 5p (64.0 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). The crude reaction mixture was purified by flash column chromatography (CH₂Cl₂/MeOH 9:1) to yield compound 6p (74 mg, 97%) as a pale yellow solid. The ee was determined by HPLC analysis (Chiralpak AD-H, hexane/iso-propanol 80:20, λ 220 nm, 1.0 mL/min): t (major) = 15.32 min, t (minor) = 18.29 min (82%).

[α]_D^{23} = -17.8 (c = 0.80, CHCl₃); ^1H NMR (400 MHz, CDCl₃) δ ppm 1.56 (s, 3H), 4.57 (d, J = 4.3 Hz, 1H), 5.06 (d, J = 13.4 Hz, 1H), 5.40 (d, J = 13.4 Hz, 1H), 7.25 (dd, J = 7.6, 4.8 Hz, 1H), 7.38 - 7.57 (m, 6H), 7.74 - 7.88 (m, 3H), 7.91 - 8.02 (m, 2H), 8.48 (br s, 1H), 8.81 (br s, 1H); ^13C NMR (100 MHz, CDCl₃) δ ppm 27.0 (d, J_CP = 3.2 Hz), 38.6 (d, J_CP = 1.6 Hz), 83.8 (d, J_CP = 1.6 Hz), 123.3, 128.6 (d, J_CP = 7.2 Hz), 128.8 (d, J_CP = 7.2 Hz), 131.0 (d, J_CP = 10.4 Hz), 131.9 (d, J_CP = 9.6 Hz), 132.1 (‘t’, J_CP = 3.2 Hz), 132.7, 133.3 (d, J_CP = 131.0 Hz), 133.5 (d, J_CP = 126.2 Hz), 138.4 - 138.5 (m), 146.7, 149.1; ^31P NMR (162 MHz, CDCl₃) δ ppm 22.8; IR ν_max/cm⁻¹ 3158, 1545, 1438, 1416, 1374, 1272, 1184, 1121, 1107; MP 70 - 72 °C; HRMS (ESI+): calcd. for C₂₀H₂₀N₃NaO₅P [M+Na]^+ 404.1134, found 404.1120.
N-[(2R)-2-Cyclohexyl-1-nitropropan-2-yl]-P,P-diphenylphosphinic amide, 6q

Obtained according to general procedure F, using N-[(1E)-1-cyclohexylethidene]-P,P-diphenylphosphinic amide 5q (65.0 mg, 0.200 mmol) and nitromethane (0.215 mL, 4.00 mmol). The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield compound 6q (55 mg, 71%) as a colorless solid. The ee was determined by HPLC analysis (Chiralpak IA, hexane/iso-propanol 90:10, λ 220 nm, 1.0 mL/min): t (minor) = 18.04 min, t (major) = 20.95 min (78%).

[α]D24 = + 18.5 (c = 1.03, CHCl3); 1H NMR (400 MHz, CDCl3) δ ppm 0.94 - 1.10 (m, 3H), 1.11 (s, 3H), 1.14 - 1.27 (m, 2H), 1.39 - 1.52 (m, 1H), 1.63 - 1.71 (m, 1H), 1.72 - 1.89 (m, 3H), 2.07 - 2.15 (m, 1H), 3.43 (d, J = 5.0 Hz, 1H), 4.61 (d, J = 11.7 Hz, 1H), 5.13 (d, J = 11.7 Hz, 1H), 7.39 - 7.57 (m, 6H), 7.74 - 7.85 (m, 2H), 7.90 - 8.01 (m, 2H); 13C NMR (100 MHz, CDCl3) δ ppm 18.5 (d, JCP = 3.2 Hz), 26.1, 26.2, 26.4, 27.0, 27.3, 45.4 (d, JCP = 6.4 Hz), 60.1 (d, JCP = 3.2 Hz), 82.8, 128.4 (d, JCP = 12.8 Hz), 128.6 (d, JCP = 13.6 Hz), 131.1 (d, JCP = 10.4 Hz), 131.8 (d, JCP = 3.2 Hz), 131.8 (d, JCP = 3.2 Hz), 132.1 (d, JCP = 9.6 Hz), 133.9 (d, JCP = 131.8 Hz), 134.2 (d, JCP = 124.6 Hz); 31P NMR (162 MHz, CDCl3) δ ppm 22.0; IR νmax/cm⁻¹ 3212, 2928, 2853, 1543, 1437, 1375, 1184, 1107; MP 144 - 146 °C; HRMS (ESI+): calcd. for C21H25N2Na2O3P [M+Na]⁺ 409.1652, found 409.1644.

2.8. Large scale synthesis of nitro-Mannich addition product 6a

To ketimine 5a (10.0 g, 31.3 mmol) and catalyst 4b (231 mg, 0.313 mmol) under argon was added nitromethane via syringe (16.8 mL, 313 mmol) at rt (21-22 °C). Stirring was maintained for 21 h (an aliquot taken after 20 h showed 98% conversion by 1H NMR analysis and an ee of 86%) and the reaction mixture was quenched by the addition of 1 M AcOH in CH2Cl2 (3.13 mL, 3.13 mmol). Stirring was maintained for 30 minutes, the volatiles were removed in vacuo, and propan-2-ol (50 mL) was added and removed in vacuo to afford a crude yellow solid. To the crude material was
added propan-2-ol (100 mL) and the mixture was heated to reflux. The resulting solution was slowly cooled to rt and crystallization allowed to occur over 18 h. The precipitate was filtered, washed with cold propan-2-ol (20 mL) and dried in vacuo to afford the title compound 6a (8.33 g, 70% yield) as a colorless solid. The ee was determined by HPLC analysis (Chiralpak OD-H, hexane/iso-propanol 80:20, λ 220 nm, 1.0 mL/min): t (minor) = 8.01 min, t (major) = 21.12 min (98%).

\[\alpha\]D \text{24} = - 25.7 (c = 1.02, CHCl3); MP 134 - 137 °C. All spectroscopic data were identical to those given previously for this compound.

2.9. Derivatization of addition product 6a and determination of absolute configuration

Conversion of addition product 6a into diamine 7 (See Supplementary Figure 10)

Racemic compounds (±)-47, (±)-48 and (±)-7 were synthesized following the same synthetic route described in Supplementary Figure 10, starting from the racemic addition product (±)-6a (synthesized according to general procedure D).

N-[(2R)-1-Amino-2-phenylpropan-2-yl]-diphenylphosphinic amide, 47

\[
\begin{align*}
\text{HN}^\prime & \quad \text{P(O)Ph}_2 \\
\text{NH}_2 & \quad \text{Ph}
\end{align*}
\]

To a solution of 6a (190 mg, 0.500 mmol; recrystallized to > 99% ee according to procedure in Section 3.8) in MeOH (4 mL) at 0 °C was added NiCl2·6H2O (119 mg, 0.500 mmol) and NaBH4 (94.5 mg, 2.50 mmol) [CAUTION: Hydrogen Gas Release]. The resulting black suspension was stirred at 0 °C for 30 min. The reaction was quenched with sat. aq. NH4Cl (6 mL) and extracted with CH2Cl2 (4 x 15 mL). The combined organics were dried over Na2SO4, filtered and concentrated. The resulting crude product was purified by flash column chromatography (CH2Cl2/MeOH 10:1) to obtain 47 (148 mg, 84%) as a colorless oil.

\[\text{This product was further recrystallized using 32 mL of refluxing propan-2-ol to give 7.50 g (90% yield and 63% overall yield) of 6a in 99.7% ee.}\]
[\alpha]^D_{24} = - 56.4 (c = 1.10, CHCl₃); \textbf{¹H NMR} (500 MHz, CDCl₃) δ ppm 1.51 (s, 3H), 1.87 (br s, 2H), 3.07 (d, J = 12.6 Hz, 1H), 3.18 (d, J = 12.6 Hz, 1H), 4.49 (d, J = 5.7 Hz, 1H), 7.22 - 7.26 (m, 1H), 7.32 - 7.39 (m, 4H), 7.40 - 7.49 (m, 4H), 7.51 - 7.57 (m, 2H), 7.85 - 7.98 (m, 4H); \textbf{¹³C NMR} (125 MHz, CDCl₃) δ ppm 25.6 (d, JCP = 3.8 Hz), 53.9, 60.7, 125.6, 126.7, 128.3 (d, JCP = 12.4 Hz), 128.5 (d, JCP = 13.3 Hz), 128.4, 131.3 (d, JCP = 2.8 Hz), 131.4 (d, JCP = 9.5 Hz), 131.4 (d, JCP = 2.8 Hz), 132.0 (d, JCP = 9.5 Hz), 134.6 (d, JCP = 130.7 Hz), 134.9 (d, JCP = 127.8 Hz), 145.9 (d, JCP = 5.7 Hz); \textbf{³¹P NMR} (162 MHz, CDCl₃) δ ppm 20.5; IR \nu_{max}/\text{cm}⁻¹: 3500 - 2870 (br), 1438, 1383, 1184, 1120, 1109; \textbf{HRMS} (ESI+): calcd. for C₂₁H₂₄N₂O₃P [M+H]⁺ 351.1621, found 351.1610.

Benzylic [(2R)-3-(diphenylphosphoryl)-2-methyl-2-phenylpropyl]carbamate, 48

To a solution of 47 (115 mg, 0.328 mmol) in dioxane (0.3 mL) was added H₂O (1.0 mL) and Na₂CO₃ (104 mg, 0.984 mmol). The resulting suspension was cooled to 0 °C and benzyl chloroformate (0.050 mL, 0.361 mmol) was added dropwise. After stirring for 30 mins at 0 °C and at rt for 16 h, the reaction mixture was diluted with Et₂O (10 mL) and the aqueous phase was extracted with Et₂O (3 x 15 mL). The combined organics were dried over Na₂SO₄, filtered and concentrated. The resulting crude product was purified by flash column chromatography (PE/EtOAc 1:1) to obtain 48 (140 mg, 90%) as a colorless oil.

[\alpha]^D_{24} = - 31.0 (c = 1.03, CHCl₃); \textbf{¹H NMR} (400 MHz, CDCl₃) δ ppm 1.46 (s, 3H), 3.50 (d, J = 13.6 Hz, 1H), 3.60 (d, J = 6.3 Hz, 1H), 3.81 (dd, J = 13.8, 7.2 Hz, 1H), 5.08 (d, J = 12.4 Hz, 1H), 5.12 (d, J = 12.4 Hz, 1H), 6.79 (br s, 1H), 7.24 - 7.54 (m, 16H), 7.83 (d, J = 11.9 Hz, 1H), 7.86 (d, J = 11.6 Hz, 1H), 7.92 (d, J = 11.6 Hz, 1H), 7.94 (d, J = 11.9 Hz, 1H); \textbf{¹³C NMR} (100 MHz, CDCl₃) δ ppm 26.0 (d, JCP = 4.0 Hz), 52.1, 60.9, 66.4, 125.3, 127.2, 127.8, 127.9, 128.3 - 128.4 (m), 128.4 - 128.5 (m), 131.4 (d, JCP = 9.6 Hz), 131.6 - 131.7 (m), 131.9 (d, JCP = 9.6 Hz), 133.5 (d, JCP = 130.2 Hz), 133.7 (d, JCP = 128.6 Hz), 136.7, 145.5 (d, JCP = 5.6 Hz), 157.2; \textbf{³¹P NMR} (162 MHz, CDCl₃) δ ppm 20.9; IR \nu_{max}/\text{cm}⁻¹: 3247, 1714, 1539, 1438, 1256, 1181, 1121; \textbf{HRMS} (ESI+): calcd. for C₂₀H₂₀N₂O₃P [M+Na]⁺ 507.1808, found 507.1796.
Benzyl [(2\text{R})-2-amino-2-phenylpropyl]carbamate, 7

To a solution of 48 (92.0 mg, 0.190 mmol) in MeOH (0.8 mL), 12 M HCl (0.800 mL) was added and the resulting solution stirred at rt for 13 h. After evaporation of the solvents, the residue was dissolved in CH$_2$Cl$_2$ (3 mL) and saturated aq. NaHCO$_3$ was added until pH 7. The combined organics were dried over Na$_2$SO$_4$, filtered and concentrated. The resulting crude product was purified by flash column chromatography (PE/EtOAc 1:4) to obtain 7 (44 mg, 81\%) as a colorless oil. The ee was determined by HPLC analysis (Chiralpak AD-H, hexane/\textit{iso}-propanol 95:5, \lambda 210 nm, 1.0 mL/min): t (major) = 33.28 min, t (minor) = 35.78 min (> 99\%).

$[\alpha]_D^{25}$ = - 12.0 (c = 1.00, CHCl$_3$); \textit{$^1$H NMR} (400 MHz, CDCl$_3$) δ ppm 1.47 (s, 3H), 1.71 (br s, 2H), 3.39 (dd, $J = 13.5, 4.9$ Hz, 1H), 3.53 (dd, $J = 13.5, 7.3$ Hz, 1H), 5.01 (br s, 1H), 5.05 - 5.11 (m, 2H), 7.23 - 7.29 (m, 1H), 7.29 - 7.40 (m, 7H), 7.46 (m, 2H); \textit{$^{13}$C NMR} (125 MHz, CDCl$_3$) δ ppm 28.4, 52.7, 55.7, 66.8, 125.2, 126.9, 128.1 (m), 128.5, 128.5, 136.4, 145.8, 156.8; \textit{IR} $\nu_{\text{max}}$/cm$^{-1}$ 3350, 3032, 2967, 1709, 1517, 1247, 1141; \textit{HRMS} (ESI+): calcd. for C$_{17}$H$_{21}$N$_2$O$_2$ [M+H]$^+$ 285.1598, found 285.1597.

**Conversion of addition product 6a into amino acid 8 and determination of absolute configuration** (See Supplementary Figure 11).

Racemic compounds (±)-49, (±)-50 and (±)-8 were synthesized following the same synthetic route described in Supplementary Figure 11 starting from the racemic addition product (±)-6a (synthesized according to general procedure C).

\((2\text{R})\)-2-Amino-2-phenylpropanoic acid ((\textit{R})-(-)-2-Methyl-2-phenylglycine), 8

A solution of 6a (80.6 mg, 0.212 mmol; recrystallized to > 99\% ee according to procedure in Section 3.8) in \textit{t}-BuOH (1.80 mL) was treated with aqueous buffered KOH (0.5 M in KOH and 1.25 M in K$_2$HPO$_4$, 1.25 mL) at rt. The mixture was stirred for 5 min and aq. KMnO$_4$ solution (0.5 M, 1.70 mL, 0.848 mmol) was added dropwise maintaining the temperature below 25 °C by occasional cooling. After stirring at rt for 3 h the mixture was cooled to 0 °C and saturated aq. Na$_2$SO$_3$ solution (5.0 mL) was added. The mixture
was acidified with 2 M HCl until pH 5 and then extracted with ethyl acetate (4 x 10 mL). The combined organics were dried over Na₂SO₄, filtered and concentrated. The crude acid was dissolved in THF (1 mL), aq. 6 M HCl (1 mL) was added and it was stirred at rt for 16 h. The resulting acidic solution was loaded on DOWEX® 50WX8-200 ion-exchange resin, washed sequentially with H₂O, dioxane, more H₂O and then eluted with 2 M aqueous ammonia. The ammoniac fraction was concentrated in vacuo to afford amino acid 8 (20 mg, 57% yield over 2 steps).

\[ [\alpha]_D^{24} = -72.0 \ (c = 0.10, \ 1 \ \text{N HCl}), \ \text{[lit.] } [\alpha]_D^{25} = -70.0 \ (c = 0.2, \ 1 \ \text{N HCl}), \ \text{[lit.] } [\alpha]_D^{26} = -86.9 \ (c = 0.32, \ 1 \ \text{N HCl}) \]. From the optical rotation, the absolute configuration was determined to be \((R)\). \[ \text{MP > 260 °C (dec.), [lit. MP > 260 °C (dec.).]} \] Spectroscopic data are consistent with those reported in the literature.\(^{25-27}\)

**Methyl (2R)-2-[(tert-butoxycarbonyl)amino]-2-phenylpropanoate, 50\(^{21,28}\)**

to a solution of amino acid 8 (47.0 mg, 0.280 mmol) in MeOH (3 mL), SOCl₂ (0.200 mL) was added dropwise at rt and then the reaction mixture was refluxed for 9 h. After cooling to ambient temperature, the solvent was removed in vacuo and the crude was dissolved in CH₃CN (14 mL). To this mixture, NaHCO₃ (1.76 g, 21.0 mmol) and Boc₂O (244 mg, 1.12 mmol) were added, and then the reaction mixture was heated at 70 °C for 12 h. After cooling to ambient temperature, the precipitate was filtered off and the filtrate was concentrated. The resulting crude was purified by flash column chromatography (PE/Et₂O 10:1) to obtain 50 (51 mg, 65 % over 2 steps) as a colorless oil. The ee was determined by HPLC analysis (Chiralpak IA, hexane/isopropanol 95:5, λ 220 nm, 0.8 mL/min): t (minor) = 8.15 min, t (major) = 9.54 min (> 99%).

\[ [\alpha]_D^{24} = -48.7 \ (c = 0.24, \ \text{CHCl}_3), \ \text{[lit.] } [\alpha]_D^{23} = +44.1 \ (c = 0.62, \ \text{CHCl}_3), \ \text{[lit.] } [\alpha]_D^{27c} \text{ for ent-}53 \ [\alpha]_D^{21} = +44.2 \ (c = 1.44, \ \text{CHCl}_3) \]. \(^{1}H\) NMR (400 MHz, CDCl₃) δ ppm 1.38 (br s, 9H), 2.00 (s, 3H), 3.70 (s, 3H), 5.84 (s, 1H), 7.26–7.38 (m, 3H), 7.40 – 7.47 (m, 2H); \(^{13}C\) NMR (100 MHz, CDCl₃) δ ppm 23.2, 28.2, 52.9, 61.8, 79.8, 125.7, 127.8, 128.5, 141.0, 154.2, 173.6; IR νmax/cm\(^{-1}\) 3427, 2977, 1714, 1486, 1448, 1366, 1248, 1162, 1054; HRMS (ESI+): calcd. for C₁₅H₂₁NNaO₄ [M+Na]+ 302.1363, found 302.1358.
3. Single Crystal X-ray Diffraction Data

Single crystal X-ray diffraction data for catalyst 4b

Compound 4b shown in its dimer form as solved by Crystals.

Compound 4b shown as a monomer for clarity.
Crystal data

C_{36}H_{38}F_{6}N_{3}O_{3}PS  

$V = 3680.66 \pm 7 \text{ Å}^3$

$M_r = 737.74$

Monoclinic, P2$_1$

$T = 150 \text{ K}$  

$
\begin{align*}
\alpha &= 12.8838 (1) \text{ Å} \\
b &= 19.4546 (2) \text{ Å} \\
c &= 15.0458 (2) \text{ Å} \\
\beta &= 102.5816 (4)^\circ
\end{align*}$

Data collection

Nonius KappaCCD diffractometer  

16705 independent reflections

Absorption correction: Multi-scan  

DENZO/SCALEPACK (Otwinski & Minor, 1997)  

14629 reflections with $I > 2.0\sigma(I)$

$T_{\text{min}} = 0.63$, $T_{\text{max}} = 0.96$  

$R_{\text{int}} = 0.057$

98019 measured reflections
Refinement

\[ R(F^2 > 2\sigma(F^2)) = 0.039 \]
\[ wR(F^2) = 0.089 \]
\[ S = 0.97 \]
16705 reflections
902 parameters
1 restraint

H-atom parameters constrained
\[ \Delta \rho_{\text{max}} = 0.37 \text{ e Å}^{-3} \]
\[ \Delta \rho_{\text{min}} = -0.27 \text{ e Å}^{-3} \]
Absolute structure: Flack (1983), 8111 Friedel-pairs
Flack parameter: −0.04 (4)

Table 1

Selected geometric parameters (Å, °)

| Bond          | Length (Å) | Angle (°) |
|---------------|------------|-----------|
| S1—C2        | 1.6802 (19)|           |
| C2—N3        | 1.344 (2)  |           |
| C2—N36       | 1.370 (2)  |           |
| N3—C4        | 1.457 (2)  |           |
| C4—C5        | 1.533 (3)  |           |
| C5—N6        | 1.479 (2)  |           |
| N6—P7        | 1.5935 (17)|           |
| P7—C8        | 1.794 (2)  |           |
| P7—C16       | 1.802 (2)  |           |
| P7—C24       | 1.814 (2)  |           |
| C8—C9        | 1.395 (3)  |           |
| C8—C15       | 1.389 (3)  |           |
| C9—C10       | 1.386 (3)  |           |
| C10—C11      | 1.385 (3)  |           |
| C11—C12      | 1.370 (3)  |           |
| C11—C14      | 1.385 (3)  |           |
| O12—C13      | 1.423 (3)  |           |
| C14—C15      | 1.396 (3)  |           |
| C16—C17      | 1.396 (3)  |           |
| C16—C23      | 1.398 (3)  |           |
| C17—C18      | 1.386 (3)  |           |
| C18—C19      | 1.393 (3)  |           |
| C19—O20      | 1.371 (3)  |           |
| C19—C22      | 1.384 (3)  |           |
| O20—C21      | 1.428 (3)  |           |
| C22—C23      | 1.391 (3)  |           |
| C24—C25      | 1.390 (3)  |           |
| C24—C31      | 1.398 (3)  |           |
| Bond                  | Length (Å) | Bond                  | Length (Å) | Bond                  | Length (Å) |
|----------------------|------------|----------------------|------------|----------------------|------------|
| C25—C26              | 1.393 (3)  | C75—C76              | 1.398 (3)  |
| C26—C27              | 1.381 (3)  | C76—C77              | 1.375 (3)  |
| C27—O28              | 1.369 (3)  | C77—O78              | 1.368 (3)  |
| C27—C30              | 1.398 (3)  | C77—C80              | 1.383 (3)  |
| O28—C29              | 1.427 (3)  | O78—C79              | 1.438 (3)  |
| C30—C31              | 1.380 (3)  | C80—C81              | 1.379 (3)  |
| C32—C33              | 1.539 (3)  | C82—C83              | 1.536 (4)  |
| C32—C34              | 1.523 (3)  | C82—C84              | 1.521 (4)  |
| C32—C35              | 1.523 (3)  | C82—C85              | 1.531 (3)  |
| N36—C37              | 1.388 (3)  | N86—C87              | 1.396 (2)  |
| C37—C38              | 1.397 (3)  | C87—C88              | 1.392 (3)  |
| C37—C42              | 1.396 (3)  | C87—C92              | 1.401 (3)  |
| C38—C39              | 1.378 (3)  | C88—C89              | 1.381 (3)  |
| C39—C40              | 1.387 (3)  | C89—C90              | 1.394 (3)  |
| C39—C47              | 1.493 (3)  | C89—C97              | 1.480 (3)  |
| C40—C41              | 1.380 (3)  | C90—C91              | 1.372 (3)  |
| C41—C42              | 1.400 (3)  | C91—C92              | 1.388 (3)  |
| C41—C43              | 1.494 (3)  | C91—C93              | 1.490 (3)  |
| C43—F44              | 1.336 (3)  | C93—F94              | 1.331 (3)  |
| C43—F45              | 1.330 (3)  | C93—F95              | 1.347 (3)  |
| C43—F46              | 1.337 (3)  | C93—F96              | 1.310 (3)  |
| C47—F48              | 1.329 (3)  | C97—F98              | 1.337 (3)  |
| C47—F49              | 1.319 (3)  | C97—F99              | 1.328 (3)  |
| C47—F50              | 1.348 (4)  | C97—F100             | 1.365 (3)  |
| S1—C2—N3             | 124.94 (15)| S51—C52—N53          | 124.71 (15)|
| S1—C2—N36            | 124.28 (14)| S51—C52—N86          | 124.20 (15)|
| N3—C2—N36            | 110.73 (17)| N53—C52—N86          | 111.04 (17)|
| C2—N3—C4             | 126.60 (16)| C52—N53—C54          | 125.50 (17)|
| N3—C4—C5             | 107.74 (15)| N53—C54—C55          | 107.50 (15)|
| N3—C4—C32            | 111.93 (15)| N53—C54—C82          | 112.41 (16)|
| C5—C4—C32            | 113.50 (16)| C54—C54—C82          | 113.15 (17)|
| C4—C5—N6             | 112.51 (15)| C54—C55—N56          | 112.96 (16)|
| C5—N6—P7             | 115.62 (13)| C55—N56—P57          | 116.40 (13)|
| N6—P7—C8             | 107.10 (9) | N56—P57—C58          | 108.19 (9) |
| N6—P7—C16            | 115.87 (10)| N56—P57—C66          | 116.51 (9) |
| C8—P7—C16            | 104.44 (10)| C58—P57—C66          | 105.87 (9) |
| N6—P7—C24            | 112.61 (9) | N56—P57—C74          | 112.16 (9) |
| C8—P7—C24            | 110.09 (10)| C58—P57—C74          | 109.02 (10)|
| C16—P7—C24           | 106.39 (10)| C66—P57—C74          | 104.75 (9) |
| P7—C8—C9             | 124.58 (16)| P57—C58—C59          | 123.04 (16)|
| P7—C8—C15            | 117.08 (16)| P57—C58—C65          | 118.44 (16)|
| C9—C8—C15            | 118.3 (2)  | C59—C58—C65          | 118.51 (19)|
Table 2
Hydrogen-bond geometry (Å, °)

| D—H···A   | D—H  | H···A  | D···A  | D—H···A |
|-----------|-------|--------|--------|---------|
| C13—H132···O20<sup>i</sup> | 0.97  | 2.51   | 3.228 (3) | 131     |
| N86—H861···N6  | 0.88  | 2.16   | 3.008 (3) | 160     |
| N3—H31···N56  | 0.87  | 2.19   | 3.031 (3) | 162     |
| N53—H531···N6  | 0.91  | 2.15   | 3.010 (3) | 158     |
| N36—H361···N56 | 0.88  | 2.14   | 2.995 (3) | 162     |

Symmetry code: (i) −x, y−1/2, −z+1.
Single crystal X-ray diffraction data for catalyst 4c
Crystal data

C_{38}H_{34}F_{6}N_{3}O_{3}PS

$M_r = 757.73$

Trigonal, $P\bar{3}21$

$a = 22.8761 (1)$ Å

c = 14.2626 (1) Å

$V = 6463.88 (6)$ Å$^3$

$Z = 6$

Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å

$\mu = 0.17$ mm$^{-1}$

$T = 150$ K

$0.44 \times 0.40 \times 0.34$ mm

Data collection

Nonius KappaCCD diffractometer

Absorption correction: Multi-scan

DENZO/SCALEPACK (Otwinowski & Minor, 1997)

$T_{\text{min}} = 0.88, T_{\text{max}} = 0.94$

9789 independent reflections

9025 reflections with $I > 2.0\sigma(I)$

177140 measured reflections

$R_{\text{int}} = 0.062$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.042$

$wR(F^2) = 0.106$

$S = 0.91$

9787 reflections

470 parameters

0 restraints

H-atom parameters constrained

$\Delta\rho_{\text{max}} = 0.25$ e Å$^{-3}$

$\Delta\rho_{\text{min}} = -0.24$ e Å$^{-3}$

Absolute structure: Flack (1983), 4540 Friedel-pairs

Flack parameter: $-0.076 (8)$

Table 3

Selected geometric parameters (Å, °)

| Bond          | Length (Å)   | Bond          | Length (Å)   | Bond          | Length (Å)   |
|---------------|--------------|---------------|--------------|---------------|--------------|
| S1—C2         | 1.6798 (18)  | C24—C31       | 1.386 (3)    |               |              |
| C2—N3         | 1.340 (2)    | C25—C26       | 1.373 (3)    |               |              |
| C2—N38        | 1.374 (2)    | C26—C27       | 1.380 (4)    |               |              |
| N3—C4         | 1.461 (2)    | C27—O28       | 1.364 (2)    |               |              |
| C4—C5         | 1.530 (2)    | C27—C30       | 1.396 (3)    |               |              |
| C4—C32        | 1.528 (2)    | O28—C29       | 1.420 (3)    |               |              |
| C5—N6         | 1.479 (2)    | C30—C31       | 1.389 (3)    |               |              |
| N6—P7         | 1.5914 (15)  | C32—C33       | 1.389 (3)    |               |              |
| P7—C8         | 1.7960 (19)  | C32—C37       | 1.396 (3)    |               |              |
| P7—C16        | 1.809 (2)    | C33—C34       | 1.396 (3)    |               |              |
| P7—C24        | 1.8030 (18)  | C34—C35       | 1.373 (4)    |               |              |
C8—C9  1.391 (3)  C35—C36  1.383 (4)
C8—C15  1.404 (3)  C36—C37  1.391 (3)
C9—C10  1.397 (3)  N38—C39  1.397 (2)
C10—C11  1.384 (3)  C39—C40  1.407 (3)
C11—O12  1.366 (3)  C39—C44  1.385 (3)
C11—C14  1.394 (3)  C40—C41  1.390 (3)
O12—C13  1.430 (3)  C41—C42  1.372 (3)
C14—C15  1.383 (3)  C41—C49  1.497 (3)
C16—C17  1.393 (3)  C42—C43  1.392 (3)
C16—C23  1.400 (3)  C43—C44  1.395 (3)
C17—C18  1.394 (3)  C43—C45  1.497 (4)
C18—C19  1.376 (3)  C45—F46  1.331 (3)
C19—O20  1.373 (3)  C45—F47  1.311 (4)
C19—C22  1.391 (3)  C45—F48  1.329 (4)
O20—C21  1.429 (3)  C49—F50  1.333 (3)
C22—C23  1.374 (3)  C49—F51  1.313 (3)
C24—C25  1.401 (3)  C49—F52  1.351 (4)

S1—C2—N3  123.14 (13)  C25—C26—C27  120.8 (2)
S1—C2—N38  125.79 (14)  C26—C27—O28  115.5 (2)
N3—C2—N38  111.01 (15)  C26—C27—C30  120.29 (19)
C2—N3—C4  125.80 (15)  O28—C27—C30  124.2 (2)
N3—C4—C5  107.81 (14)  C27—O28—C29  117.7 (2)
N3—C4—C32  111.11 (14)  C27—C30—C31  118.4 (2)
C5—C4—C32  112.91 (15)  C30—C31—C24  121.86 (19)
C5—C5—N6  110.06 (15)  C4—C32—C33  119.93 (18)
C5—N6—P7  118.95 (12)  C4—C32—C37  121.31 (17)
N6—P7—C8  106.41 (8)  C33—C32—C37  118.72 (18)
N6—P7—C16  116.04 (9)  C32—C33—C34  120.2 (2)
C8—P7—C16  106.38 (9)  C33—C34—C35  120.5 (2)
N6—P7—C24  112.83 (8)  C34—C35—C36  120.0 (2)
C8—P7—C24  108.61 (9)  C35—C36—C37  119.9 (2)
C16—P7—C24  106.22 (9)  C32—C37—C36  120.7 (2)
P7—C8—C9  123.78 (14)  C32—C37—C36  120.7 (2)
P7—C8—C15  117.37 (14)  C2—N38—C39  131.75 (16)
C9—C8—C15  118.61 (18)  N38—C39—C40  114.83 (16)
C8—C9—C10  121.02 (18)  N38—C39—C44  126.28 (17)
C9—C10—C11  119.48 (19)  C40—C39—C44  118.84 (17)
C10—C11—O12  125.2 (2)  C39—C40—C41  120.24 (19)
C10—C11—C14  120.2 (2)  C40—C41—C42  121.4 (2)
O12—C11—C14  114.5 (2)  C40—C41—C49  120.0 (2)
C11—O12—C13  117.9 (2)  C42—C41—C49  118.5 (2)
C11—C14—C15  120.1 (2)  C41—C42—C43  118.07 (19)
C42—C43—C44  121.9 (2)
Table 4
Hydrogen-bond geometry (Å, °)

|        | D—H  | H···A  | D···A  | D—H···A |
|--------|------|--------|--------|---------|
| C15—H151···C37i | 0.97 | 2.54   | 3.483 (4) | 163     |
| C17—H171···O28ii | 0.94 | 2.46   | 3.293 (4) | 147     |
| N3—H31···N6i    | 0.84 | 2.17   | 2.975 (4) | 161     |
| N38—H381···N6i   | 0.85 | 2.17   | 2.987 (4) | 161     |

Symmetry codes: (i) y, x, −z; (ii) y, x, −z+1.

Low temperature single crystal X-ray diffraction data were collected for 4b and 4c using a Nonius Kappa CCD diffractometer. Intensity data were reduced using Denzo-SMN (with SCALEPACK) including unit cell refinement, inter-frame scaling and corrections for absorption. The structures were solved with SuperFlip and refined with CRYSTALS. Although it was necessary to model disordered solvent in 4b with PLATON/SQUEEZE the final Flack parameter and Bayesian analysis the Bijvoet pairs for both compounds was in agreement with the assignment from the initial amino acid.
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5. Supplementary Data

5.1. Copies of NMR spectra

$^1$H NMR of compound 12 (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 12 (100 MHz, CDCl$_3$)
$^1$H NMR of compound 13 (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 13 (125 MHz, CDCl$_3$)
$^1$H NMR of compound 17 (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 17 (125 MHz, CDCl$_3$)
$^1$H NMR of compound 21 (400 MHz, CDCl$_3$)

\[
\begin{array}{c}
\begin{array}{c}
\text{NHBoc} \\
\text{N}_3
\end{array}
\end{array}
\]

$^{13}$C NMR of compound 21 (100 MHz, CDCl$_3$)
\(^1\)H NMR of compound 22 (400 MHz, CDCl\(_3\))

\[ \text{Chemical Shift (ppm)} \]

\(0.87, 0.93, 1.00, 1.01 \)

\(4.70, 1.80, 0.89 \)

\(\text{AF444 1H JUN12-2012-35.002.001.1R.ESP} \)

\(^{13}\)C NMR of compound 22 (100 MHz, CDCl\(_3\))

\[ \text{Chemical Shift (ppm)} \]

\(192, 184, 176, 168, 160, 152, 144, 136, 128, 120, 112, 104, 96, 88, 80, 72, 64, 56, 48, 40, 32, 24, 16, 8, 0 \)

\(\text{AF444 13C AF444.003.001.1R.ESP} \)
$^1$H NMR of compound 28 (400 MHz, CDCl$_3$)

$^1$C NMR of compound 28 (125 MHz, CDCl$_3$)
$^1$H NMR of compound 29 (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 29 (125 MHz, CDCl$_3$)
$^1$H NMR of compound 30 (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 30 (125 MHz, CDCl$_3$)
$^1$H NMR of compound 31 (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 31 (125 MHz, CDCl$_3$)
$^1$H NMR of compound 36 (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 36 (125 MHz, CDCl$_3$)
$^1$H NMR of compound 2 (500 MHz, CD$_3$OD)

$^{13}$C NMR of compound 2 (125 MHz, CD$_3$OD)
$^1$H NMR of compound 40 (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 40 (125 MHz, CDCl$_3$)
$^1$H NMR of compound 41 (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 41 (100 MHz, CDCl$_3$)
$^1$H NMR of compound 44 (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 44 (100 MHz, CDCl$_3$)
$^1$H NMR of compound 45 (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 45 (125 MHz, CDCl$_3$)
$^1$H NMR of compound 51 (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 51 (125 MHz, CDCl$_3$)
$^1$H NMR of compound 52 (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 52 (125 MHz, CDCl$_3$)
$^1$H NMR of compound 53 (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 53 (100 MHz, CDCl$_3$)
$^1$H NMR of compound 54 (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 54 (125 MHz, CDCl$_3$)
$^1$H NMR of compound 55 (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 55 (100 MHz, CDCl$_3$)
$^1$H NMR of compound 56 (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 56 (100 MHz, CDCl$_3$)
$^1$H NMR of compound 57 (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 57 (100 MHz, CDCl$_3$)
$^1$H NMR of compound 58 (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 58 (100 MHz, CDCl$_3$)
$^1$H NMR of compound 4a (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 4a (125 MHz, CDCl$_3$)
$^1$H NMR of compound 4b (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 4b (125 MHz, CDCl$_3$)
$^1$H NMR of compound 4c (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 4c (125 MHz, CDCl$_3$)
$^1$H NMR of compound 1a·HCl (400 MHz, CD$_3$CN)

$^{13}$C NMR of compound 1a·HCl (100 MHz, CDCl$_3$)
$^1$H NMR of compound 1a (400 MHz, CD$_3$CN)

$^{13}$C NMR of compound 1a (100 MHz, CD$_3$CN)
$^{13}$C NMR for $pK_{BH^+}$ estimation of 1a·HCl in CH$_3$CN (100 MHz, CD$_3$CN)

\[
\text{HN}^\text{+}_2\text{PPh}_3 \text{Cl}^- + \text{NN} \rightleftharpoons \text{CD}_3\text{CN} \quad \text{N}_2\text{PPh}_3 \quad + \quad ^{+}\text{NH}_2\text{Cl}^- 
\]

$^{31}$P NMR for $pK_{BH^+}$ estimation of 1a·HCl in CH$_3$CN (101 MHz, CD$_3$CN)
$^1$H NMR of compound 1b·HCl (400 MHz, CD$_3$CN)

$^{13}$C NMR of compound 1b·HCl (100 MHz, CD$_3$CN)
$^1$H NMR of compound 1b (400 MHz, CD$_3$CN)

$^{13}$C NMR of compound 1b (100 MHz, CD$_3$CN)
$^{13}\text{C} \text{NMR for } pK_{\text{BH}^+} \text{ estimation of } 1\text{b} \cdot \text{HCl} \text{ in CH}_3\text{CN (100 MHz, CD}_3\text{CN)}$

$^{31}\text{P} \text{NMR for } pK_{\text{BH}^+} \text{ estimation of } 1\text{b} \cdot \text{HCl} \text{ in CH}_3\text{CN (162 MHz, CD}_3\text{CN)}$
$^1$H NMR of compound 5f (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 5f (100 MHz, CDCl$_3$)
$^1$H NMR of compound 5g (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 5g (100 MHz, CDCl$_3$)
$^1$H NMR of compound 5h (400 MHz, CDCl$_3$)

N\textsuperscript{+}P(O)Ph$_2$

13C NMR of compound 5h (100 MHz, CDCl$_3$)
$^1$H NMR of compound 5k (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 5k (100 MHz, CDCl$_3$)
$^{1}$H NMR of compound 5l (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 5l (100 MHz, CDCl$_3$)
$^1$H NMR of compound 5q (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 5q (100 MHz, CDCl$_3$)
$^1$H NMR of compound 6a (400 MHz, CDCl$_3$)

\[
\begin{array}{c}
\text{HN}^+ P(O)\text{Ph}_2 \\
\text{Ph} - \text{NO}_2
\end{array}
\]

$^{13}$C NMR of compound 6a (100 MHz, CDCl$_3$)
$^1$H NMR of compound 6b (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 6b (100 MHz, CDCl$_3$)
$^1$H NMR of compound 6c (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 6c (100 MHz, CDCl$_3$)
$^1$H NMR of compound 6d (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 6d (100 MHz, CDCl$_3$)
$^1$H NMR of compound 6e (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 6e (100 MHz, CDCl$_3$)
$^1$H NMR of compound 6f (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 6f (100 MHz, CDCl$_3$)
$^1$H NMR of compound 6g (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 6g (100 MHz, CDCl$_3$)
$^1$H NMR of compound 6h (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 6h (125 MHz, CDCl$_3$)
$^1$H NMR of compound 6i (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 6i (100 MHz, CDCl$_3$)
\(^1\)H NMR of compound \(6j\) (400 MHz, CDCl\(_3\))

\(\text{Chemical Shift (ppm)}\)

\(^{13}\)C NMR of compound \(6j\) (100 MHz, CDCl\(_3\))
$^1$H NMR of compound 6k (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 6k (125 MHz, CDCl$_3$)
\(^1\)H NMR of compound \(6l\) (500 MHz, CDCl\(_3\))

\(^{13}\)C NMR of compound \(6l\) (125 MHz, CDCl\(_3\))
$^1$H NMR of compound 6m (500 MHz, CDCl$_3$)

$^{13}$C NMR of compound 6m (125 MHz, CDCl$_3$)
$^1$H NMR of compound 6n (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 6n (100 MHz, CDCl$_3$)
$^1$H NMR of compound 6o (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 6o (100 MHz, CDCl$_3$)
$^1$H NMR of compound 6p (400 MHz, CDCl$_3$)

$^1$C NMR of compound 6p (100 MHz, CDCl$_3$)
$^1$H NMR of compound 6q (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 6q (100 MHz, CDCl$_3$)
\(^1\)H NMR of compound 47 (500 MHz, CDCl\(_3\))

\[ \text{HN}^+P(O)\text{Ph}_2 \]

\[^{13}\text{C}\) NMR of compound 47 (125 MHz, CDCl\(_3\))

\[ \text{Chemical Shift (ppm)} \]
$^1$H NMR of compound 48 (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 48 (100 MHz, CDCl$_3$)
$^1$H NMR of compound 7 (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 7 (100 MHz, CDCl$_3$)
$^1$H NMR of compound 50 (400 MHz, CDCl$_3$)

$^{13}$C NMR of compound 50 (100 MHz, CDCl$_3$)
5.2. Copies of HPLC traces

HPLC chromatogram of catalyst 4a precursor (2)

(S)-1-(1-azido-3,3-dimethylbutan-2-yl)-3-[3,5-bis(trifluoromethyl)phenyl]thiourea, 2
(Chiralpak IA, hexane/iso-propanol 95:5, 1.0 mL/min)

\[
\begin{align*}
&\text{Racemic} \\
&\text{Enantiomerically enriched (} > 99\% \text{ ee)}
\end{align*}
\]
HPLC chromatograms of nitro-Mannich addition products 6a - 6q

\[ N'-(2R)-1-Nitro-2-phenylpropan-2-yl]-P,P'-diphenylphosphinic amide, 6a \]
(Chiralpak OD-H, hexane/iso-propanol 80:20, 1.0 mL/min)

Racemic

Enantiomerically enriched (95% ee)
\[ N-[(2R)-1-Nitro-2-phenylpropan-2-yl]-P,P'-diphenylphosphinic amide, \textit{6a} \]

(Chiralpak OD-H, hexane/\textit{iso}-propanol 80:20, 1.0 mL/min)

Large scale (Section 2.8)

Racemic

Enantiomerically enriched (98% ee)
$N\text{-}[(2R)-2\text{-}(4\text{-} \text{Methylphenyl})\text{-}1\text{-}\text{nitropropan-2-yl}]\text{-}PP\text{-}\text{diphenylphosphinic amide, 6b}$

(Chiralpak OD-H, hexane/iso-propanol 80:20, 1.0 mL/min)

Racemic

![Chromatogram of racemic compound]

Signal 2: DAD1 B, Sig=220.8 Ref=360,100

| Peak RetTime | Type | Width | Area    | Height | Area % |
|---------------|------|-------|---------|--------|--------|
| 1 7.786       | MN   | 0.5628| 7092.65137 | 210.03007 | 50.0346 |
| 2 30.047      | MN   | 2.0061| 7082.94668 | 58.84536 | 49.9654 |

Enantiomerically enriched (89% ee)

![Chromatogram of enriched enantiomer]

Signal 2: DAD1 B, Sig=220.8 Ref=360,100

| Peak RetTime | Type | Width | Area    | Height | Area % |
|---------------|------|-------|---------|--------|--------|
| 1 7.857       | MN   | 0.5707| 1137.90710 | 33.23180 | 5.3065 |
| 2 30.352      | MN   | 2.0608| 2.0305664  | 164.21861 | 94.6935 |
$N$-[(2R)-2-(4-Methoxyphenyl)-1-nitropropan-2-yl]-$P,P$-diphenylphosphinic amide, 6c
(Chiralpak OD-H, hexane/iso-propanol 80:20, 1.0 mL/min)

Racemic

[Spectrum Image]

Enantiomerically enriched (91% ee)

[Spectrum Image]
$N$-[(2$R$)-2-(3-Methoxyphenyl)-1-nitropropan-2-yl]-$P,P$-diphenylphosphinic amide, 6d

(Chiralpak OD-H, hexane/iso-propanol 80:20, 1.0 mL/min)

Racemic

Enantiomerically enriched (91% ee)
$N\text{-}[\{2R\} - 2\text{-}(2\text{-Methoxyphenyl}) - 1\text{-nitropropan}-2\text{-yl}] - P,P\text{-}diphenylphosphinic \ amide, \ 6e$

(Chiralpak OD-H, hexane/iso-propanol 80:20, 1.0 mL/min)

**Racemic**

**Enantiomerically enriched (93% ee)**
$N$-[(2$R$)-2-(Biphenyl-4-yl)-1-nitropropan-2-yl]-$P,P$-diphenylphosphinic amide, 6f

(Chiralpak AD, hexane/iso-propanol 80:20, 1.0 mL/min)

Enantiomerically enriched (90% ee)
N-[(2R)-1-Nitro-2-(4-nitrophenyl)-propan-2-yl]-P,P'-diphenylphosphinic amide, 6g
(Chiralpak IA, hexane/iso-propanol 80:20, 1.0 mL/min)

Racemic

Enantiomerically enriched (86% ee)
N-[(2R)-2-(2-Fluorophenyl)-1-nitropropan-2-yl]-P,P′- diphenylphosphinic amide, 6h
(Chiralpak OD-H, hexane/iso-propanol 80:20, 1.0 mL/min)

Racemic

Enantiomerically enriched (94% ee)
N-[(2R)-2-(4-Chlorophenyl)-1-nitropropan-2-yl]-P,P'-diphenylphosphinic amide, 6i

(Chiralpak OD-H, hexane/iso-propanol 80:20, 1.0 mL/min)

Racemic

Enantiomerically enriched (90% ee)
N-[(2R)-2-(4-Bromophenyl)-1-nitropropan-2-yl]-P,P'-diphenylphosphinic amide, 6j
(Chiralpak OD-H, hexane/iso-propanol 80:20, 1.0 mL/min)

Racemic

![Chromatogram Image]

| Peak RetTime | Type | Width | Area   | Height  | Area  |
|--------------|------|-------|--------|---------|-------|
| 1            | MM   | 9.101 | 9593.52441 | 230.55899 | 49.6747 |
| 2            | MM   | 15.535 | 9719.15430 | 151.98636 | 50.3253 |

Enantiomerically enriched (90% ee)

![Chromatogram Image]

| Peak RetTime | Type | Width | Area   | Height  | Area  |
|--------------|------|-------|--------|---------|-------|
| 1            | MM   | 9.153 | 155.92751 | 3.69872 | 4.5498 |
| 2            | MM   | 15.562 | 3271.20435 | 49.73556 | 95.4502 |
**N-[(2R)-2-(3,4-Dichlorophenyl)-1-nitropropan-2-yl]-P,P- diphenylphosphinic amide, 6k**

(Chiralpak OD-H, hexane/iso-propanol 80:20, 1.0 mL/min)

Racemic

Enantiomerically enriched (87% ee)
$N-[(2R)-2-[3,5-$Bis(trifluoromethyl)phenyl]-1-nitropropan-2-yl]-P,P-$ diphenylphosphinic amide, 6l (Chiralpak AD-H, hexane/iso-propanol 95:5, 1.0 mL/min)

Enantiomerically enriched (90% ee)
$N$-[(2$R$)-1-Nitro-2-phenylbutan-2-yl]-$P,P$-diphenylphosphinic amide, 6m
(Chiralpak OD-H, hexane/iso-propanol 80:20, 1.0 mL/min)

Racemic

Enantiomerically enriched (92 % ee)
$N-[(1R)-1-(Nitromethyl)-1,2,3,4$-tetrahydronaphthalen-1-yl]$-P,P'$-diphenylphosphinic amide, 6n
(Chiralpak OD-H, hexane/iso-propanol 90:10, 1.0 mL/min)

Racemic

Enantiomerically enriched (92% ee)
$N$-[(2S)-2-(2-Furyl)-1-nitropropan-2-yl]-$P,P$- diphenylphosphinic amide, 60
(Chiralpak OD-H, hexane/iso-propanol 80:20, 1.0 mL/min)

Racemic

Enantiomerically enriched (84% ee)
**N-[(2R)-1-Nitro-2-(pyridin-3-yl)propan-2-yl]-P,P- diphenylphosphinic amide, 6p**

(Chiralpak AD-H, hexane/iso-propanol 80:20, 1.0 mL/min)

Enantiomerically enriched (82% ee)
$N$-[(2R)-2-Cyclohexyl-1-nitropropan-2-yl]-$P,P$-diphenylphosphinic amide, 6q

(Chiralpak IA, hexane/iso-propanol 90:10, 1.0 mL/min)

Racemic

Enantiomerically enriched (78% ee)
HPLC chromatograms of derivatisation products 7 and 50

Benzyl [(2R)-2-amino-2-phenylpropyl]carbamate, 7
(Chiralpak AD-H, hexane/iso-propanol 95:5, 1.0 mL/min)

Racemic

Enantiomerically enriched (> 99% ee)
Methyl (2R)-2-[(tert-butoxycarbonyl)amino]-2-phenylpropanoate, \textbf{50}

(Chiralpak IA, hexane/iso-propanol 95:5, 0.8 mL/min)

\begin{align*}
\text{Racemic} \\
\includegraphics[width=0.5\textwidth]{signal_3.png}
\end{align*}

\begin{align*}
\text{Enantiomerically enriched (}>99\% \text{ ee}) \\
\includegraphics[width=0.5\textwidth]{signal_3_enriched.png}
\end{align*}