Bicyclic Guanidine-Catalyzed Enantioselective Phospha-Michael Reactions: Synthesis of Chiral β-Aminophosphine Oxides and β-Aminophosphines

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Supplementary Information

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1. General procedures and methods.

$^1$H, $^{13}$C and $^{31}$P NMR spectra were recorded on a Bruker ACF300 (300MHz), DPX300 (300MHz) or AMX500 (500MHz) spectrometer. Chemical shifts are reported in parts per million (ppm). The residual solvent peak was used as an internal reference. Low resolution mass spectra were obtained on a VG Micromass 7035 spectrometer in EI mode, a Finnigan/MAT LCQ spectrometer in ESI mode. High resolution mass spectra were obtained on a Finnigan/MAT 95XL-T spectrometer and Shimadzu-IT-TOF spectrometer. Infrared spectra were recorded on a BIO-RAD FTS 165 FTIR spectrometer. Enantiomeric excesses were determined by chiral HPLC analysis on Jasco HPLC units, including a Jasco DG-980-50 Degasser, a LG-980-02 Ternary Gradient Unit, a PU-980 Intelligent HPLC Pump, UV-975 Intelligent UV/VIS Detectors, and an AS-950 Intelligent Sampler. Optical rotations were recorded on a Jasco DIP-1000 polarimeter. Melting points were determined on a BÜCHI B-540 melting point apparatus. Analytical thin layer chromatography (TLC) was performed with Merck pre-coated TLC plates, silica gel 60F-254, layer thickness 0.25 mm. Flash chromatography separations were performed on Merck 60 (0.040 - 0.063mm) mesh silica gel. Diethyl ether and THF were freshly distilled from sodium/benzophenone before use. CH$_2$Cl$_2$ were freshly distilled from calcium hydride. All distilled solvents were stored under N$_2$. All other reagents and solvents are of commercial grade and were used as supplied without further purification, unless otherwise stated.

2. Experimental protocols: Standard bicyclic guanidine catalyzed reactions between diaryl phosphine oxide and nitroalkenes.

To a 50 ml RBF containing catalyst 1 (1.8 mg, 0.008 mmol, 10 mol %) and a stirring bar, di(1-naphthyl) phosphine oxide 2f (24.2 mg, 0.08 mmol), anhydrous diethyl ether (25ml), were added in this sequence and stirred under -40 °C for one hour. 4-Chloro-β-nitrostyrene (73.4 mg, 0.4 mmol, 5eq.) was added to the reaction mixture and stirred at -40 °C for 12 hours. Solvent was removed from the reaction mixture and loaded onto a short silica gel column. This was followed by flash chromatography (gradient elution with hexane/EA mixtures; 10/1 to 2/1). Adduct 4a (36.5mg) was obtained as a white solid in 94% yield and 96% ee.
3. Characterization of the Michael adducts

(3a) (2-Nitro-1-phenylethyl)diphenyl phosphine oxide

White solid. mp 204.3-205.1 °C. 64% yield, 60% ee; after recrystallization from MeOH, 96% ee. [α]D27 -58.7 (c 0.45, CHCl3).

1H NMR (300 MHz, CDCl3, ppm): δ 4.37-4.45 (m, 1H), 4.72-4.78 (m, 1H), 5.05-5.15 (m, 1H), 7.19-8.01 (m, 15H). 13C NMR (75 MHz, CDCl3, ppm): δ 45.4, 46.3, 75.7, 75.8, 128.2, 128.4, 128.8, 129.2, 129.4 (two peaks), 129.5, 130.7, 130.9, 131.0, 131.1, 131.2, 131.6, 131.7, 132.0, 132.1, 132.7 (two peaks). 31P NMR (121MHz, CDCl3, ppm): δ 30.5. IR (KBr) 708, 1185, 1551, 3060 cm⁻¹. LRMS (ESI) m/z 374.0 (M+Na⁺), HRMS (ESI) m/z 374.0932 (M+Na⁺), calc. for C20H18NO3PNa 374.0917.

The ee was determined by chiral HPLC; CHIRALCEL IA (4.6 mm i.d. x 250 mm); hexane/2-propanol 70/30; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 9.1 min and 14.4 min.
(3b) (2-Nitro-1-phenylethyl)di-4-fluorophenyl phosphine oxide

White solid. mp 186.4-187.7 °C. 92% yield, 60% ee; after recrystallization from tBuOMe/CH₂Cl₂ mixture, >99% ee. [α]D²⁷ -142.4 (c 0.71, CHCl₃). ¹H NMR (300 MHz, CDCl₃, ppm): δ 4.31-4.40 (m, 1H), 4.71-4.79 (m, 1H), 5.03-5.13 (m, 1H), 6.94-8.02 (m, 13H). ¹³C NMR (75 MHz, CDCl₃, ppm): δ 45.6, 46.5, 75.5, 75.6, 115.7, 115.8, 115.9, 116.1, 116.7, 116.9, 117.0, 117.2, 128.5, 128.9, 129.3, 129.4, 131.4, 133.4, 133.5, 133.6 (two peaks), 133.7, 133.9, 163.4, 163.9, 166.7, 167.3. ³¹P NMR (121MHz, CDCl₃, ppm): δ 29.6. IR (KBr) 758, 1162, 1594, 3077 cm⁻¹. HRMS (ESI) m/z 410.0731 (M+Na⁺), calc. for C₂₀H₁₆F₂NO₃PNa 410.0734.

The ee was determined by chiral HPLC; CHIRALCEL AD-H (4.6 mm i.d. x 250 mm); hexane/2-propanol 70/30; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 7.4 min and 9.9 min.
(3c) (2-Nitro-1-phenylethyl)di-4-phenylphenyl phosphine oxide

White solid. mp 236.9-238.5 °C. 85% yield, 50% ee; after recrystallization from MeOH, 91% ee. \( [\alpha]_D^{27} \) -64.5 (c 0.10, CHCl₃). \( ^1\text{H NMR} \) (300 MHz, CDCl₃, ppm): \( \delta \) 4.43-4.52 (m, 1H), 4.80-4.88 (m, 1H), 5.11-5.21 (m, 1H), 7.23-8.10 (m, 23H). \( ^{13}\text{C NMR} \) (75 MHz, CDCl₃, ppm): \( \delta \) 45.6, 46.5, 75.8, 75.9, 126.9, 127.0, 127.2, 127.3, 127.9, 128.0, 128.3, 128.4, 128.5, 128.9 (two peaks), 129.1, 129.2, 129.3, 129.5, 129.6, 131.5, 131.6, 131.7, 131.8, 139.5, 144.8, 145.7. \( ^{31}\text{P NMR} \) (121 MHz, CDCl₃, ppm): \( \delta \) 30.6. IR (KBr) 761, 1176, 1552, 3030 cm\(^{-1}\). HRMS (ESI) m/z 504.1722 (M+H\(^+\)), calc. for C\(_{32}\)H\(_{27}\)NO\(_3\)P 504.1729.

The ee was determined by chiral HPLC; CHIRALCEL AD-H (4.6 mm i.d. x 250 mm); hexane/2-propanol 70/30; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 20.9 min and 34.5 min.
(3d) (2-Nitro-1-phenylethyl)di-2-ethylphenyl phosphine oxide

Colorless oil. 77% yield, 75% ee. \([\alpha]_D^{27} -36.1 (c 0.50, \text{CHCl}_3)\). 

**1H NMR (300 MHz, CDCl₃, ppm):** \(\delta\) 0.76 (t, \(J=7.4\text{Hz}, 3\text{H}\)), 0.92 (t, \(J=7.4\text{Hz}, 3\text{H}\)), 2.34-2.47 (m, 1H), 2.68-2.78 (m, 1H), 2.80-2.91 (m, 2H), 4.62-4.69 (m, 1H), 5.05-5.12 (m, 1H), 5.20-5.30 (m, 1H), 7.00-7.95 (m, 13H).

**13C NMR (125 MHz, CDCl₃, ppm):** \(\delta\) 15.0, 15.3, 26.5, 26.6, 27.1, 27.2, 44.5, 45.0, 76.5, 76.6, 125.2, 125.3, 126.0, 126.1, 128.1 (two peaks), 128.5, 128.6, 129.3, 129.4 (two peaks), 129.7, 129.8, 130.2 (two peaks), 130.6, 131.3, 131.4, 132.0 (three peaks), 132.1, 132.2 (two peaks), 132.6 (two peaks), 148.4, 148.5, 149.7, 149.8. 

**31P NMR (121MHz, CDCl₃, ppm):** \(\delta\) 35.0. IR (film) 771, 1217, 1524, 3021 cm⁻¹. LRMS (ESI) m/z 408.0 (M+H⁺), HRMS (ESI) m/z 408.1745 (M+H⁺), calc. for C₂₄H₂₇NO₃P 408.1729.

The ee was determined by chiral HPLC; CHIRALCEL IA (4.6 mm i.d. x 250 mm); hexane/2-propanol 90/10; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 11.2min and 12.6min.

(3e) (2-Nitro-1-phenylethyl)di-2-naphthyl phosphine oxide

White solid. mp 229.1-230.4 °C. 92% yield, 65% ee; after recrystallization from MeOH, 99% ee. \([\alpha]_D^{27} -73.5 (c 0.34, \text{CHCl}_3)\). 

**1H NMR (300 MHz, CDCl₃, ppm):** \(\delta\) 4.61-4.69 (m, 1H), 4.79-4.87 (m, 1H), 5.13-5.23 (m, 1H), 7.17-8.68 (m, 19H).

**13C NMR (75 MHz, CDCl₃, ppm):** \(\delta\) 45.4, 46.2, 75.9, 76.0, 125.1, 125.2, 125.3, 125.4, 126.5, 126.9, 127.5, 127.7, 127.8, 127.9 (two peaks), 128.1, 128.2, 128.3 (two peaks), 128.4, 128.8 (two peaks), 129.0, 129.2, 129.4, 129.5 (two peaks), 131.7, 131.8, 132.1, 132.6, 132.8, 133.6, 133.7, 133.9, 134.0, 134.5, 134.6, 134.9, 135.0. 

**31P NMR (121MHz, CDCl₃, ppm):** \(\delta\) 30.8. IR 745, 1175, 1540, 3055 cm⁻¹. LRMS (ESI) m/z 452.1 (M+H⁺), HRMS (ESI) m/z 452.1410 (M+H⁺), calc. for C₂₈H₂₃NO₃P 452.1410.
The ee was determined by chiral HPLC; CHIRALCEL ADH (4.6 mm i.d. x 250 mm); hexane/2-propanol 70/30; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 48.9 min and 57.8 min.

(3f) (2-Nitro-1-phenyl)ethyl)di-1-naphthyl phosphine oxide

White solid. mp 203.8-205.7 °C. 94% yield, 91% ee; after recrystallization 95% ee. [α]$_D^{26}$ -86.7 (c 0.55, CHCl$_3$). $^1$H NMR (300 MHz, CDCl$_3$, ppm): δ 4.86-4.94 (m, 1H), 5.14-5.22 (m, 1H), 5.32-5.40 (m, 1H), 7.00-8.77 (m, 19H). $^{13}$C NMR (75 MHz, CDCl$_3$, ppm): δ 45.2, 46.1, 76.5, 76.6, 123.9, 124.1, 124.4, 124.6, 125.7, 125.8, 126.2, 126.4, 126.5, 126.6, 126.8, 127.2, 127.5, 127.8, 128.0, 128.1, 128.5 (two peaks), 128.6, 128.7, 129.1, 129.3, 129.4, 130.6, 130.8, 131.9 (two peaks), 132.3, 132.4, 133.2, 133.3, 133.4, 133.5, 133.6, 133.7, 133.8, 133.9, 134.0, 134.2, 134.3. $^{31}$P NMR (121MHz, CDCl$_3$, ppm): δ 36.7. (KBr) 773, 1161, 1550, 3044 cm$^{-1}$. LRMS (ESI) m/z 452.2 (M+H$^+$), HRMS (ESI) m/z 452.1435 (M+H$^+$), calc. for C$_{28}$H$_{23}$NO$_3$P 452.1416.
The ee was determined by chiral HPLC; CHIRALCEL AD-H (4.6 mm i.d. x 250 mm); hexane/2-propanol 70/30; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 26.9 min and 34.8 min.

(4a) (2-Nitro-1-(4-chlorophenyl)ethyl)di-1-naphthyl phosphine oxide

White solid. mp 237.2-238.8 °C. 94% yield, 96% ee; after recrystallization >99% ee. [α]D 24 -88.2 (c 3.59, CHCl₃).

1H NMR (300 MHz, CDCl₃, ppm): δ 4.82-4.90 (m, 1H), 5.12-5.19 (m,1H), 5.26-5.35 (m, 1H), 6.97-8.76 (m, 18H).

13C NMR (300 MHz, CDCl₃, ppm): δ 44.7, 45.5, 76.3, 76.4, 124.0, 124.2, 124.4, 125.6 (two peaks), 126.2, 126.3, 126.5 (two peaks), 127.0, 127.3, 127.5, 127.9, 128.3, 128.7, 129.2, 130.5, 130.6, 130.7 (two peaks), 132.3, 132.4, 133.3, 133.4, 133.6 (two peaks), 133.8, 134.1, 134.2 (two peaks), 134.4.

31P NMR (121MHz, CDCl₃, ppm): δ 36.6. IR (KBr): 768, 1158, 1550, 3051 cm⁻¹. LRMS (ESI) m/z 486.2 (M+H⁺), HRMS (ESI) m/z 486.1050 (M+H⁺), calc. for C₂₈H₂₂ClO₃P 486.1026.
The ee was determined by chiral HPLC; CHIRALCEL AD-H (4.6 mm i.d. x 250 mm); hexane/2-propanol 60/40; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 19.8 min and 64.4 min.

(4b) (2-Nitro-1-(2-nitrophenyl)ethyl)di-1-naphthyl phosphine oxide

White solid. mp 176.2-177.7 °C. 96% yield, 92% ee; after recrystallization 95% ee. [α]_D^{26} -80.8 (c 1.38, CHCl_3). ¹H NMR (300 MHz, CDCl₃, ppm): δ 4.79-4.87 (m, 1H), 5.15-5.22 (m, 1H), 5.28-5.38 (m, 1H), 6.87-8.74 (m, 18H).

¹³C NMR (75 MHz, CDCl₃, ppm): δ 44.9, 45.8, 76.0, 76.1, 124.0, 124.2, 124.4, 124.6, 125.6, 125.7, 126.4, 126.6 (two peaks), 127.0, 127.2, 127.5 (two peaks), 127.9, 128.2, 128.3, 128.6, 129.2, 129.4, 129.5, 129.6 (two peaks), 130.4, 130.6, 132.1, 132.2, 133.3, 133.4, 133.6, 133.7, 133.8, 133.9 (two peaks), 134.1, 134.2, 134.3 (two peaks), 134.4 (two peaks). ³¹P NMR (121 MHz, CDCl₃, ppm): δ 37.2. (KBr) 772, 1158, 1554, 3058 cm⁻¹. LRMS (ESI) m/z 486.1 (M+H⁺), HRMS (ESI) m/z 486.1047. (M+H⁺), calc. for C_{28}H_{22}ClNO₃P 486.1026.
The ee was determined by chiral HPLC; CHIRALCEL AD-H (4.6 mm i.d. x 250 mm); hexane/2-propanol 70/30; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 19.7 min and 27.2 min.

![Chromatogram](image)

**purified by silica gel column**

![Chromatogram](image)

**purified by recrystallization after flash chromatography**

(4c) (2-Nitro-1-(2-chlorophenyl)ethyl)di-1-naphthyl phosphine oxide

White solid. mp 249.3-250.5 °C. 98% yield, 93% ee; after recrystallization 99% ee. \([\alpha]_{D}^{25}\) -102.4 (c 2.99, CHCl₃). ¹H NMR (300 MHz, CDCl₃, ppm): δ 5.14-5.21 (m, 1H), 5.29-5.38 (m, 1H), 5.63-5.72 (m, 1H), 6.87-8.79 (m, 18H). ¹³C NMR (75 MHz, CDCl₃, ppm): δ 40.4, 41.3, 76.2, 76.3, 123.8, 124.0, 124.4, 124.6, 125.7, 126.1, 126.2, 126.6, 126.7, 126.9 (two peaks), 127.1, 127.4, 127.5, 127.9, 128.2, 128.3, 129.2 (two peaks), 129.5 (two peaks), 130.2 (two peaks), 130.3 (two peaks), 130.9, 131.0, 132.4, 132.5, 133.1, 133.2, 133.5, 133.6 (two peaks), 133.7, 133.9, 134.0, 134.1 (two peaks), 134.3, 134.4, 134.7, 134.8. ³¹P NMR (121MHz, CDCl₃, ppm): δ 38.9. IR (KBr) 764, 1161, 1565, 2923 cm⁻¹. LRMS (ESI) m/z 486.1 (M+H⁺), HRMS (ESI) m/z 486.1044 (M+H⁺), calc. for C₂₈H₂₂ClNO₃P 486.1026.
The ee was determined by chiral HPLC; CHIRALCEL AD-H (4.6 mm i.d. x 250 mm); hexane/2-propanol 60/40; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 20.5 min and 31.1 min.

Purified by silica gel column

Purified by recrystallization after flash chromatography

(4d) (2-Nitro-1-(4-bromophenyl)ethyl)di-1-naphthyl phosphine oxide

White solid. mp 250.7-252.1 °C. 99% yield; 93% ee, after recrystallization >99% ee. [α]$_D^{26}$ -61.3 (c 1.30, CHCl$_3$). $^1$H NMR (300 MHz, CDCl$_3$, ppm): δ 4.80-4.89 (m, 1H), 5.11-5.19 (m, 1H), 5.26-5.35 (m, 1H), 7.12-8.76 (m, 18H). $^{13}$C NMR (75 MHz, CDCl$_3$, ppm): δ 44.8, 45.6, 76.2, 76.3, 122.4, 122.5, 124.0, 124.2, 124.4, 124.6, 125.6 (two peaks), 126.1, 126.3, 126.5 (two peaks), 126.9, 127.4, 127.5, 127.9, 128.2, 128.8, 129.2, 130.6, 130.8, 130.9, 131.0 (two peaks), 131.7, 132.3, 132.4, 133.3, 133.4 (two peaks), 133.6 (two peaks), 133.8, 134.1, 134.2 (two peaks), 134.4. $^{31}$P NMR (121MHz, CDCl$_3$, ppm): δ 36.6. IR (KBr) 770, 1158, 1549, 3052 cm$^{-1}$. LRMS (ESI) m/z 552.0 (M+Na$^+$), HRMS (ESI) m/z 552.0332 (M+Na$^+$)
554.0317 (M+Na$^+$), calc. for C$_{28}$H$_{21}^{79}$BrNO$_3$PNa 552.0335 and C$_{28}$H$_{21}^{81}$BrNO$_3$PNa 554.0314.

The ee was determined by chiral HPLC; CHIRALCEL AD-H (4.6 mm i.d. x 250 mm); hexane/2-propanol 50/50; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 20.1 min and 63.6 min.

(4e) (2-Nitro-1-(3-nitrophenyl)ethyl)di-1-naphthyl phosphine oxide

White solid. mp 196.3-198.0 °C. 95% yield, 96% ee; after recrystallization 96% ee. [α]$_D$ -124.6 (c 2.59, CHCl$_3$). $^1$H NMR (300 MHz, CDCl$_3$, ppm): δ 4.94-5.02 (m, 1H), 5.23-5.30 (m, 1H), 5.36-5.46 (m, 1H), 7.16-8.72 (m, 18H). $^{13}$C NMR (75 MHz, CDCl$_3$, ppm): δ 45.1, 45.9, 75.6, 75.7, 123.0, 124.1, 124.3, 124.4, 124.5, 124.6, 125.4 (two peaks), 125.7, 126.4, 126.5, 126.6, 127.0, 127.1, 127.5, 127.7, 128.1, 128.7, 129.2, 129.4, 130.3, 130.4, 132.1, 132.2, 133.2, 133.3, 133.6 (two peaks), 133.7, 133.9 (two peaks), 134.1, 134.2, 134.4 (two peaks), 134.5, 134.9, 135.0, 147.7. $^{31}$P NMR (121MHz, CDCl$_3$, ppm):
ppm): \( \delta 37.4 \). IR (KBr) 732, 1157, 1556, 3064 cm\(^{-1}\). LRMS (ESI) m/z 497.1 (M+H\(^{+}\)), HRMS (ESI) m/z 497.1291 (M+H\(^{+}\)) calc. for C\(_{28}\)H\(_{22}\)N\(_{2}\)O\(_{5}\)P 497.1266

The ee was determined by chiral HPLC; CHIRALCEL AD-H (4.6 mm i.d. x 250 mm); hexane/2-propanol 70/30; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 26.3 min and 50.1 min.

(4f) (2-Nitro-1-(2-nitrophenyl)ethyl)di-1-naphthyl phosphine oxide

White solid. mp 206.3-208.1 °C. 99% yield, 96% ee. \([\alpha]_{D}^{25} -77.8 \) (c 3.46, CHCl\(_3\)). \(^1\)H NMR (300 MHz, CDCl\(_3\), ppm): \( \delta 5.16-5.24 \) (m, 1H), 5.36-5.45 (m, 1H), 6.33-6.41 (m, 1H), 7.13-8.77 (m, 18H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\), ppm): \( \delta 38.2, 39.0, 76.2 \) (two peaks), 124.1, 124.3, 124.6, 124.7, 125.2, 125.4, 125.7, 125.8, 126.2, 126.4, 126.5, 126.9, 127.2, 127.6, 128.0, 128.1, 128.2, 128.5, 128.8, 129.2, 130.7, 130.8, 131.1, 131.2, 132.4, 132.6, 133.2, 133.3, 133.5, 133.6, 133.7, 133.8, 134.3 (two peaks), 134.4, 148.9 (two peaks). \(^{31}\)P NMR (121MHz, CDCl\(_3\), ppm): \( \delta 39.3 \). IR (KBr) 775, 1183, 1555, 3081 cm\(^{-1}\). LRMS
(ESI) m/z 519.1 (M+Na\(^+\)), HRMS (ESI) m/z 519.1077 (M+Na\(^+\)), calc. for C\(_{28}\)H\(_{21}\)N\(_2\)O\(_5\)PNa 519.1080.

The ee was determined by chiral HPLC; CHIRALCEL AD-H (4.6 mm i.d. x 250 mm); hexane/2-propanol 60/40; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 28.6 min and 69.1 min.

p\(\underline{4g}\) (2-Nitro-1-(4-methyl-phenyl)ethyl)di-1-naphthyl phosphine oxide

White solid. mp 229.1-229.9 °C. 90% yield, 90% ee; after recrystallization, 96% ee. \([\alpha]_D^{26}\) -68.5 (c 2.73, CHCl\(_3\)). \(^1\)H NMR (300 MHz, CDCl\(_3\), ppm) : \(\delta\) 2.11 (s, 3H), 4.81-4.89 (m, 1H), 5.08-5.16 (m, 1H), 5.28-5.37 (m, 1H), 6.81-8.79 (m, 18H). \(^{13}\)C NMR (75 MHz, CDCl\(_3\), ppm): \(\delta\) 20.9, 45.0, 45.9, 76.6, 76.7, 123.9, 124.1, 124.4, 124.6, 126.0 (two peaks), 126.1, 126.5, 126.6, 126.8, 127.1, 127.6, 127.8, 128.0, 128.6, 128.7, 128.8, 129.1, 129.2, 129.3, 130.8, 130.9, 132.2, 132.4, 133.3, 133.4, 133.6, 133.7, 133.8, 133.9 (two peaks), 134.2, 134.3, 137.9 (two
peaks). $^{31}$P NMR (121MHz, CDCl$_3$, ppm): $\delta$ 36.8. IR 773, 1158, 1550, 3052 cm$^{-1}$. LRMS (ESI) m/z 488.1 (M+Na$^+$), HRMS (ESI) m/z 488.1387 (M+Na$^+$), calc. for C$_{29}$H$_{24}$NO$_3$PNa 488.1386.

The ee was determined by chiral HPLC; CHIRALCEL AD-H (4.6 mm i.d. x 250 mm); hexane/2-propanol 70/30; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 31.4 min and 49.7 min.

(4h) (2-Nitro-1-(2-naphthyl)ethyl)di-1-naphthyl phosphine oxide

White solid. mp 246.1-247.5 °C. 75% yield, 92% ee; after recrystallization, 92% ee. $[\alpha]_D^{27}$ -67.7 (c 0.33, CHCl$_3$). $^1$H NMR (300 MHz, CDCl$_3$, ppm): $\delta$ 5.01-5.09 (m, 1H), 5.18-5.26 (m, 1H), 5.41-5.51 (m, 1H), 7.13-8.80 (m, 21H). $^{13}$C NMR (75 MHz, CDCl$_3$, ppm): $\delta$ 45.4, 46.3, 76.6 (two peaks), 123.9, 124.1, 124.5, 124.6, 125.7 (two peaks), 126.1, 126.2, 126.4, 126.6 (two peaks), 126.8 (two peaks), 126.9, 127.0, 127.3, 127.4, 127.7, 127.9, 128.3, 128.5, 128.7, 128.8, 128.9, 129.2, 129.5, 129.6, 130.9, 131.0, 132.2, 132.3, 132.7, 133.0, 133.2, 133.4.
(two peaks), 133.5, 133.6, 133.8, 133.9, 134.0 (two peaks), 134.3, 134.4. $^{31}$P NMR (121MHz, CDCl$_3$, ppm): $\delta$ 36.9. IR (KBr) 765, 1161, 1565, 2923 cm$^{-1}$. LRMS (ESI) m/z 502.2 (M+H$^+$), HRMS (ESI) m/z 502.1594 (M+H$^+$), calc. for C$_{32}$H$_{25}$NO$_3$P 502.1572.

The ee was determined by chiral HPLC; CHIRALCEL AD-H (4.6 mm i.d. x 250 mm); hexane/2-propanol 60/40; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 23.6 min and 37.1 min.

\[\text{purified by silica gel column}\]

\[\text{purified by recrystalization after flash chromatography}\]

(6a) (2-Methyl-2-nitro-1-phenylethyl)di-1-naphthyl phosphine oxide

White solid. mp 197.4-198.7 °C. 70% yield, 90% ee, 95:5 dr. $^1$H NMR (300 MHz, CDCl$_3$, ppm): $\delta$ 1.73 (d, $J=6.8$ Hz, 3H), 4.93-5.04 (m, 1H), 5.10 (dd, $J=2.9$, 11.7 Hz, 1H), 7.19-8.96 (m, 19H). $^{13}$C NMR (75 MHz, CDCl$_3$, ppm): $\delta$ 15.3, 48.7, 49.6, 82.8, 82.9, 123.8, 124.0, 124.7, 124.8, 125.7, 125.8, 126.0 (two peaks), 126.3, 126.6, 127.3, 127.4, 127.5, 127.8, 128.3, 128.7 (two peaks), 128.9, 129.3, 131.0, 131.1, 131.3, 131.9, 132.0, 132.2, 132.3, 133.2 (two peaks), 133.8 (two peaks), 134.0, 134.1. $^{31}$P NMR (121MHz, CDCl$_3$, ppm): $\delta$ 36.5. IR (KBr) 775, 1158, 1553, 3060
cm⁻¹. LRMS (ESI) m/z 488.1 (M+Na⁺), HRMS (ESI) m/z 488.1386 (M+Na⁺), calc. for C₂₉H₂₄O₃NPNa 488.1386.

The ee was determined by chiral HPLC; CHIRALCEL IA (4.6 mm i.d. x 250 mm); hexane/2-propanol 85/15; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 16.5 min and 20.0 min; 25.1 min and 35.8 min.

(6b) (2-Ethyl-2-nitro-1-phenylethyl)di-1-naphthyl phosphine oxide

White solid. mp 214.2-215.5 °C. 70% yield, 93% ee, 95:5 dr. ¹H NMR (300 MHz, CDCl₃, ppm): δ 0.75 (t, J=7.3 Hz, 3H), 1.78-1.94 (m, 1H), 2.53-2.65 (m, 1H), 4.75-4.86 (m, 2H), 6.74-8.98 (m, 19H). ¹³C NMR (75 MHz, CDCl₃, ppm): δ 11.0, 23.2, 49.4, 50.3, 89.8, 89.9, 123.8, 124.0, 124.6, 124.8, 125.8 (two peaks), 125.9, 126.0, 126.1, 126.3, 126.6, 127.3, 127.5, 127.8, 128.3, 128.6, 128.7, 128.9, 129.3, 130.8, 130.9, 131.8, 131.9, 132.2, 132.3, 132.8, 133.1, 133.2, 133.4, 133.7, 133.8 (two peaks), 134.1. ³¹P NMR (121MHz, CDCl₃, ppm): δ 36.9. IR (KBr) 772, 1157,
1554, 3055 cm$^{-1}$. LRMS (ESI) m/z 480.0 (M+H$^+$), HRMS (ESI) m/z 480.1726 (M+H$^+$), calc. for C$_{30}$H$_{27}$NO$_3$P 480.1729.

The ee was determined by chiral HPLC; CHIRALCEL AD-H (4.6 mm i.d. x 250 mm); hexane/2-propanol 80/20; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 22.3 min and 39.9 min, 27.9 min and 31.3min.

4. Preparation and characterization of donors

Donor 2a was purchased from Sigma-Aldrich and used without purification. 2b-f were prepared using the literature protocol.\textsuperscript{1} Data for 2b was consistent with data reported in the literature.

(2c) Di-4-phenylphenyl phosphine oxide

White solid. mp 159.7-161.0 °C. $^1$H NMR (300 MHz, CDCl$_3$, ppm): $\delta$ 7.39-7.85 (m, 18H), 8.29 (d, $J$=418.9Hz, 1H). $^{13}$C NMR (75 MHz, CDCl$_3$, ppm): $\delta$ 127.0, 127.2, 127.4, 128.0, 128.7, 129.0, 130.4, 130.9, 131.4, 139.4, 145.1 (two peaks). $^{31}$P NMR (121MHz,


S18
CDCl₃, ppm): δ 21.5. IR (KBr) 760, 1128, 3025 cm⁻¹. LRMS ESI m/z 354.9 (M⁺), HRMS ESI m/z 355.1246 (M+H⁺), calc. for C₂₄H₂₀OP 355.1252.

(2d) Di-2-ethylphenyl phosphine oxide
White solid. mp 67.6-68.1 °C. ¹H NMR (300 MHz, CDCl₃, ppm): δ 1.04 (t, J=7.5Hz, 6H), 2.72 (q, J=7.5, 15.0Hz, 4H), 7.27-7.73 (m, 8H), 8.27 (d, J=474.8Hz, 1H). ¹³C NMR (75 MHz, CDCl₃, ppm): δ 14.9, 26.3, 26.4, 125.9, 126.0, 128.5, 129.2, 129.3, 129.9, 132.2, 132.3, 132.6 (two peaks), 147.1, 147.3. ³¹P NMR (121MHz, CDCl₃, ppm): δ 17.7. IR (KBr) 754, 1180, 3054 cm⁻¹. LRMS ESI m/z 259.2 (M+H⁺), HRMS ESI m/z 259.1247 (M+H⁺), calc. for C₁₆H₂₀OP 259.1252.

(2e) Di-2-naphthyl phosphine oxide
White solid. mp 90.4-92.0 °C. ¹H NMR (300 MHz, CDCl₃, ppm): δ 7.51-8.40 (m, 14H), 8.33 (d, 1H, J = 480.9Hz). ¹³C NMR (75 MHz, CDCl₃, ppm): δ 124.9, 125.1, 127.0, 127.7, 127.8, 128.3, 128.7, 128.9, 129.0, 132.3, 132.5, 132.7, 132.8, 134.9 (two peaks). ³¹P NMR (121MHz, CDCl₃, ppm): δ 22.3. IR (KBr) 748, 1188, 3050 cm⁻¹. LRMS EI m/z 301.9 (M-H⁺), HRMS EI m/z 302.0847 (M⁺), calc. for C₂₀H₁₅OP 302.0861.

(2f) Di-1-naphthyl phosphine oxide
White solid. mp 164.9-165.6 °C. ¹H NMR (300 MHz, CDCl₃, ppm): δ 7.43-8.41 (m, 14H), 8.89(d, 1H, J = 481.4Hz). ¹³C NMR (75 MHz, CDCl₃, ppm): δ 124.8, 125.0, 125.2, 126.5, 126.7, 127.8, 127.9, 129.1, 132.7, 132.8, 133.0, 133.4, 133.6 (two peaks), 133.7. ³¹P NMR (121MHz, CDCl₃, ppm): δ 19.2. (KBr) 773, 1179, 3045 cm⁻¹. LRMS EI m/z 302.0 (M⁺), HRMS EI m/z 302.0850 (M⁺), calc. for C₂₀H₁₅OP 302.0861.
5. Reduction of adducts

(7) 2-(4-Chlorophenyl)-2-(dinaphthalen-1-ylphosphoryl)ethanamine

In a seal tube containing adduct 4a (46.8 mg, 0.1 mmol), zinc (45.8 mg, 0.7 mmol, 7eq.) and a stirring bar, 0.6 ml MeOH, 0.3ml THF, 0.6 ml 6M HCl, were added in this sequence and refluxed until TLC showed the completion of reaction. After cooling down to room temperature, saturated NaHCO₃ solution was added dropwise until pH=8. The solution was then filtered through Celite and extracted with CH₂Cl₂ (x 3 times). The organic phase was dried with MgSO₄ and the organic solvent was removed. The crude product was loaded onto a short silica gel column. Flash chromatography (gradient elution with CH₂Cl₂/MeOH mixtures; 100/1 to 20/1) led to product 7 (34.2 mg) as a white foam in 89% yield.

mp 99.4-100.5 °C. 89% yield, >99% ee. [α]₂⁷D -20.1 (c 1.00, CHCl₃). ¹H NMR (300 MHz, CDCl₃, ppm): δ 3.42-3.50 (m, 1H), 3.56-3.66 (m, 1H), 3.97-4.04 (m, 1H), 7.04-8.80 (m, 18H). ¹³C NMR (75 MHz, CDCl₃, ppm): δ 43.1, 49.2, 50.0, 123.9, 124.1, 124.3, 124.5, 126.0, 126.5, 126.6, 126.7, 127.0, 127.4, 128.2, 128.5, 128.6, 128.7, 129.0, 129.4, 129.7, 131.2, 131.3, 131.4, 131.6, 131.9, 132.0, 132.8, 132.8, 133.3 (two peaks), 133.5 (two peaks), 133.6, 133.7, 133.8, 133.9, 134.0, 134.1. ³¹P NMR (121MHz, CDCl₃, ppm): δ 37.1. IR (KBr) 772, 1158, 1490, 3055 cm⁻¹. LRMS (ESI) m/z 456.1 (M+H⁺), HRMS (ESI) m/z 456.1285 (M+H⁺), calc. for C₂₈H₂₄ClNOP 456.1279.
The ee was determined by chiral HPLC; CHIRALCEL IA (4.6 mm i.d. x 250 mm); hexane/2-propanol 60/40; flow rate 1.0 ml/min; temp 25 °C; detection UV 210 nm; retention time: 15.8 min and 40.4 min.

(8) 2-(4-Chlorophenyl)-2-(dinaphthalen-1-ylphosphino)ethanamine

In a seal tube containing phosphine oxide 7 (36.5mg, 0.08 mmol), triphenyl phosphine (42.1mg, 0.16 mmol, 2eq.) and a stirring bar, 1ml toluene and distilled Et3N (0.22ml, 1.6mmol, 20eq.) were added and cooled down to 0 °C. HSiCl3 (0.32ml, 3.2mmol, 40eq.) was then added dropwise to the seal tube. After purging with N2, the tube was sealed and refluxed. After 12h, the reaction was cooled down to 0 °C and diluted with 3ml diethyl ether. 1M NaOH aq. solution was added dropwise. The solution was washed with sat. NaHCO3, brine and water in this sequence. After acidifying the organic layer with 1M HCl, the aqueous layer was washed with diethyl ether (x5 times) and extracted with dichloromethane (x3 times) after re-basification with 1M NaOH aq. solution. The organic extracts were dried with MgSO4 and removed to provide the product 8 (24.2 mg) as a white solid in 70 % yield.

White solid. 70% yield, >99% ee. [α]D25 -62.3 (c 0.44, CHCl3). 1H NMR (300 MHz, CDCl3, ppm): δ 2.94-3.05 (m, 1H), 3.10-3.19 (m, 1H), 3.66-3.72 (m, 1H), 6.99-8.85 (m,
18H). $^{13}$C NMR (75 MHz, CDCl$_3$, ppm): $\delta$ 49.3, 45.4, 49.2, 49.3, 125.1, 125.6, 125.8, 125.9, 126.0, 126.4, 126.9, 127.4, 128.3, 128.5, 128.7, 129.3, 129.8, 130.4, 130.5, 131.0, 131.2, 131.9, 132.0, 132.2, 132.8, 133.2, 133.6, 133.8, 134.1, 134.3, 135.6, 135.9, 136.2, 136.5, 137.9, 138.0. $^{31}$P NMR (121 MHz, CDCl$_3$, ppm): $\delta$ -34.8. IR (KBr) 774, 1504, 3050 cm$^{-1}$. HRMS (ESI) m/z 440.1348 (M+H$^+$), calc. for C$_{28}$H$_{24}$ClNP 440.1335.

The ee of 8 was determined by converting back to 7 using H$_2$O$_2$.

6. Determination of relative configuration of 6a through NMR and Chemdraw prediction.

The stable conformations of the diastereomers were predicted by Chem3D Ultra MM2 minimization. The relative stereochemistry of the major diastereoisomer is predicted using the coupling constants of H$^a$ obtained with $^1$H NMR.

**Major diastereoisomer:** H$^a$ $\delta$ 5.10 (dd, $J$=2.9, 11.7 Hz, 1H)

**Minor diastereoisomer:** H$^a$ $\delta$ 4.86 (dd, $J$=8.2, 10.2 Hz)
7. Copy of NMR spectrum

(2c) Di-4-phenylphenyl phosphine oxide
(2d) Di-2-ethylphenyl phosphine oxide

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(2e) Di-2-naphthyl phosphine oxide
(2f) Di-1-naphthyl phosphine oxide
(3a) (2-Nitro-1-phenylethyl)diphenyl phosphine oxide

Supplementary Material (ESI) for Chemical Communications
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(3b) (2-Nitro-1-phenylethyl)di-4-fluorophenyl phosphine oxide
(3c) (2-Nitro-1-phenylethyl)di-4-phenylphenyl phosphine oxide
(3d) (2-Nitro-1-phenylethyl)di-2-ethylphenyl phosphine oxide
(3e) (2-Nitro-1-phenylethyl)di-2-naphthyl phosphine oxide
(3f) (2-Nitro-1-phenyl)ethyl(di-1-naphthyl phosphine oxide

9H normal range AC300 ma29f ux1.31 FuX9041
(4a) (2-Nitro-1-(4-chlorophenyl)ethyl)di-1-naphthyl phosphine oxide

H normal range AC300 ma22fux1.2.1 FuX9032 AI I

Supplementary Material (ESI) for Chemical Communications
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(4b) (2-Nitro-1-(2-nitrophenyl)ethyl)di-1-naphthyl phosphine oxide
(4c) (2-Nitro-1-(2-chlorophenyl)ethyl)di-1-naphthyl phosphine oxide
(4d) (2-Nitro-1-(4-bromophenyl)ethyl)di-1-naphthyl phosphine oxide

Supplementary Material (ESI) for Chemical Communications
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(4e) (2-Nitro-1-(3-nitrophenyl)ethyl)di-1-naphthyl phosphine oxide

\[
\begin{align*}
\text{Integral} & = 1.0006 \\
\text{ppm} & = 0.0102
\end{align*}
\]

Diagram of the compound structure.
(4f) (2-Nitro-1-(2-nitrophenyl)ethyl)di-1-naphthyl phosphine oxide
(4g) (2-Nitro-1-(4-methyl-phenyl)ethyl)di-1-naphthyl phosphine oxide

1H normal range AC300 ap1 6fu x1.1 FuX9080A

Supplementary Material (ESI) for Chemical Communications
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(4h) (2-Nitro-1-(2-naphthyl)ethyl)di-1-naphthyl phosphine oxide
(6a) (2-Methyl-2-nitro-1-phenylethyl)di-1-naphthyl phosphine oxide

1H normal range AC30 0 ap24 fux1.1.1 FuX9 084 B

PO

NO2

Me

PO

NO2

Me
(6b) (2-Ethyl-2-nitro-1-phenylethyl)di-1-naphthyl phosphine oxide
(7) 2-(4-Chlorophenyl)-2-(dinaphthalen-1-ylphosphoryl)ethanamine
(8) 2-(4-chlorophenyl)-2-(dinaphthalen-1-ylphosphino)ethanamine