Catalytic Asymmetric Deprotonation of Phosphine Boranes and Sulfides as a Route to

P-Stereogenic Compounds

Jonathan J. Gammon, Steven J. Canipa, Peter O’Brien, Brian Kelly and Sven Taylor

Department of Chemistry, University of York, Heslington, York YO10 5DD

Fax: +44 1904 432516; Tel: +44 1904 432535; E-mail: paob1@york.ac.uk

Full Experimental Procedures and Characterisation Data/NMR spectra:

General

Water is distilled water. Et₂O, THF and toluene were freshly distilled from benzophenone ketyl. (−)-Sparteine and diamine 3 were distilled from CaH₂ before use. Petrol refers to the fraction of petroleum ether with a boiling range of 40-60 °C. Brine refers to a saturated aqueous solution. All reactions were carried out under O₂ free Ar using oven-dried and/or flame-dried glassware. Flash column chromatography was carried out using Fluka Silica gel 60 (0.035-0.070 mm particle size). Thin layer chromatography was carried out using Merck F₂₅₄ alumina-backed silica plates. Proton (400 MHz), carbon (100.6 MHz) and phosphorus (109 MHz) NMR spectra were recorded on a Jeol ECX-400 or a Jeol EX 270 instrument with internal deuterium lock. Chemical shifts are quoted as parts per million and referenced to CHCl₃ (7.27). Carbon and phosphorus NMR spectra were recorded with broadband proton decoupling. Carbon NMR spectra were assigned using DEPT experiments. Infra-red spectra were recorded on an ATI Matteson Genesis FT-IR spectrometer. Optical rotations were recorded at room temperature (20 °C) on a Jasco DIP-370 polarimeter (using the sodium D line; 259 nm) and [α]D measurements are given in units of 10⁻¹ deg cm² g⁻¹. Melting points were measured on a Gallenkamp melting point apparatus. Chiral stationary phase HPLC was performed on an Agilent 1200 series instrument and a multiple wavelength, UV/Vis diode array detector. tert-Butyldimethyl phosphine borane 1 was prepared according to a literature procedure.¹
General Procedure A: Lithiation-substitution of \textit{tert}\-butyldimethylphosphine borane 1 using a stoichiometric amount of (–)-sparteine (1.2 eq.).

Alkyllithium (1.1 eq.) was added dropwise to a stirred solution of (–)-sparteine (1.2 eq.) in Et$_2$O (3 mL) at $-78$ °C under Ar. After stirring for 15 min at $-78$ °C, a solution of phosphine borane 1 (120 mg, 0.94 mmol) in Et$_2$O (2 mL) was added dropwise over 10 min via a syringe. The resulting solution was stirred at $-78$ °C for 3 h. Then, Me$_2$PhSiCl (1.1 eq.) was added via a syringe and the resulting solution allowed to warm to rt over 16 h. 1 M HCl$_{(aq)}$ (10 mL) and EtOAc (10 mL) were added and the layers separated. The aqueous layer was extracted with EtOAc (3 $\times$ 10 mL) and the combined organic layers were washed with 1 M HCl$_{(aq)}$ (10 mL), water (10 mL) and brine (10 mL), dried (MgSO$_4$) and evaporated under reduced pressure to give the crude product as a yellow oil.

General Procedure B: Lithiation-substitution of \textit{tert}\-butyldimethylphosphine borane 1 using a substoichiometric amount of (–)-sparteine (0.2 eq.).

Alkyllithium (1.1 eq.) was added dropwise to a stirred solution of (–)-sparteine (0.2 eq.) in Et$_2$O (10 mL) at $-78$ °C under Ar. After stirring for 15 min at $-78$ °C, a solution of phosphine borane 1 (120 mg, 0.94 mmol) in Et$_2$O (5 mL) was added dropwise over 10 min via a syringe. The resulting solution was stirred at $-78$ °C for 3 h. Then, Me$_2$PhSiCl (1.1 eq.) was added via a syringe and the resulting solution allowed to warm to rt over 16 h. 1 M HCl$_{(aq)}$ (10 mL) and EtOAc (10 mL) were added and the layers separated. The aqueous layer was extracted with EtOAc (3 $\times$ 10 mL) and the combined organic layers were washed with 1 M HCl$_{(aq)}$ (10 mL), water (10 mL) and brine (10 mL), dried (MgSO$_4$) and evaporated under reduced pressure to give the crude product as a yellow oil.

General Procedure C: Lithiation-substitution of \textit{tert}\-butyldimethylphosphine borane 1 using alkylolithium (1.1 eq.).

A solution of phosphine borane 1 (120 mg, 0.94 mmol) in Et$_2$O (2 mL) was added dropwise over 10 min via a syringe to a stirred solution of alkylolithium (1.1 eq.) in Et$_2$O (3 mL) at $-78$ °C under Ar. The resulting solution was stirred at $-78$ °C for 3 h. Then, Me$_2$PhSiCl (1.1 eq.) was added via a syringe and the resulting solution allowed to warm to rt over 16 h. 1 M
HCl\(_{\text{aq}}\) (10 mL) and EtOAc (10 mL) were added and the layers separated. The aqueous layer was extracted with EtOAc (3 × 10 mL) and the combined organic layers were washed with 1 M HCl\(_{\text{aq}}\) (10 mL), water (10 mL) and brine (10 mL), dried (MgSO\(_4\)) and evaporated under reduced pressure to give the crude product as a yellow oil.

**General Procedure D: Lithiation-substitution of tert-butyldimethylphosphine sulfide 4 using a stoichiometric amount of (−)-sparteine (1.2 eq.).**

Alklyllithium (1.1 eq.) was added dropwise to a stirred solution of (−)-sparteine (1.2 eq.) in Et\(_2\)O (3 mL) at −78 °C under Ar. After stirring for 15 min at −78 °C, a solution of phosphine sulfide 4 (100 mg, 0.67 mmol) in Et\(_2\)O (10 mL) was added dropwise over 10 min via a syringe. The resulting solution was stirred at −78 °C for 3 h. Then, Me\(_2\)PhSiCl (1.1 eq.) was added dropwise via a syringe and the resulting solution was allowed to warm to rt over 16 h. 1 M HCl\(_{\text{aq}}\) (6 mL) was added and the mixture stirred for 15 min to give a homogeneous biphasic solution. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with 1 M HCl\(_{\text{aq}}\) (5 mL), water (5 mL) and brine (5 mL), dried (MgSO\(_4\)) and evaporated under reduced pressure to give the crude product as a colourless oil.

**General Procedure E: Lithiation-substitution of tert-butyldimethylphosphine sulfide 4 using a substoichiometric amount of (−)-sparteine (0.05-0.2 eq.).**

Alklyllithium (1.1 eq.) was added dropwise to a stirred solution of (−)-sparteine (0.05-0.2 eq.) in Et\(_2\)O (10 mL) at −78 °C under Ar. After stirring for 15 min at −78 °C, a solution of phosphine sulfide 4 (300 mg, 2.00 mmol) in Et\(_2\)O (20 mL) was added dropwise over 10 min via a syringe. The resulting solution was stirred at −78 °C for 3 h. Then, Me\(_2\)PhSiCl (1.1 eq.) was added dropwise via a syringe and the resulting solution was allowed to warm to rt over 16 h. 1 M HCl\(_{\text{aq}}\) (18 mL) was added and the mixture stirred for 15 min to give a homogeneous biphasic solution. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with 1 M HCl\(_{\text{aq}}\) (15 mL), water (15 mL) and brine (15 mL), dried (MgSO\(_4\)) and evaporated under reduced pressure to give the crude product as a colourless oil.
General Procedure F: Lithiation-substitution of tert-butylidimethylphosphine sulfide 4 using alkyllithium (1.1 eq.).

Alklyllithium (1.1 eq.) was added dropwise over 10 min via a syringe to a stirred solution of phosphine sulfide 4 (100 mg, 0.67 mmol) in Et₂O (15 mL) at −78 °C under Ar. The resulting solution was stirred at −78 °C for 3 h. Then, Me₂PhSiCl (1.1 eq.) was added dropwise via a syringe and the resulting solution was allowed to warm to rt over 16 h. 1 M HCl(aq) (6 mL) was added and the mixture stirred for 15 min to give a homogeneous biphasic solution. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with 1 M HCl(aq) (5 mL), water (5 mL) and brine (5 mL), dried (MgSO₄) and evaporated under reduced pressure to give the crude product as a colourless oil.
**tert-Butyldimethylphosphine sulfide 4**

A solution of methylmagnesium bromide (55 mL of a 3 M solution in Et₂O, 164.0 mmol, 2.6 eq.) in THF (55 mL) was added to a stirred solution of tert-butyldichlorophosphine (10.0 g, 63.0 mmol, 1.0 eq.) in THF (100 mL) at −10 °C under Ar. The resulting heterogeneous mixture was stirred at rt for 5 h. Sulfur (2.6 g, 82.0 mmol, 1.3 eq.) was added and the mixture was heated at 80 °C for 5 min. After cooling to rt, the mixture was poured onto ice/water (120 mL) and conc. HCl (aq) (30 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed with 1 M HCl (aq) (30 mL), water (30 mL) and brine (30 mL), dried (MgSO₄) and evaporated under reduced pressure to give the crude product as a yellow solid. Purification by recrystallisation from hexane (50 mL) gave phosphine sulfide 4 (5.88 g, 62%) as a white solid, mp 206-207 °C (lit., 2 203 °C); Rᵣ(4:1 petrol-EtOAc) 0.1; IR (NaCl) 3020, 2975, 1215, 940, 910, 755 (P=S), 670, 630 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ: 1.64 (d, J = 12.5 Hz, 6H, PMe), 1.22 (d, J = 16.5 Hz, 9H, PCMe₃); ¹³C NMR (100.6 MHz, CDCl₃) δ: 32.5 (d, J = 52.5 Hz, PCMe₃), 24.3 (PCMe₃), 16.3 (d, J = 51.5 Hz, PMe); ³¹P{¹H} NMR (109 MHz, CDCl₃) δ: 54.2; (EI) m/z 150 (M⁺, 45), 94 (100), 79 (25), 57 (35), 41 (40); HRMS (EI) m/z calcd for C₆H₁₅PS M⁺ 150.0632, found 150.0629. Spectroscopic data consistent with that reported in the literature.²
(R)-tert-Butylmethylphosphineborane(methyl)dimethylphenylsilane (R)-5

(1.2 eq. (−)-sparteine, Table 1, entry 1)

Using general procedure A, (−)-sparteine (213 mg, 0.91 mmol) and s-BuLi (0.63 mL of a 1.32 M solution in cyclohexane, 0.83 mmol) in Et₂O (2 mL), phosphine borane 1 (100 mg, 0.76 mmol) in Et₂O (3 mL) and Me₂PhSiCl (0.14 mL, 0.83 mmol) gave the crude product as a yellow oil. Purification by flash chromatography with 98:2 petrol-Et₂O as eluent gave adduct (R)-5 (149 mg, 74%, 92:8 er) as a colourless oil which slowly crystallised to a white solid, mp 40-42 °C; [α]D +8.1 (c 1.00 in CHCl₃); Rf(4:1 petrol-EtOAc) 0.3; IR (NaCl) 2960, 2375, 1426, 1114, 1060, 904, 822, 738, 704 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ: 7.59-7.54 (m, 2H, Ph), 7.40-7.38 (m, 3H, Ph), 1.12 (d, J = 13.5 Hz, 9H, CMe₃), 1.06-0.97 (m, 2H, PCH₂), 1.00 (d, J = 10.0 Hz, 3H, PMe), 0.56 (s, 3H, SiMe), 0.52 (q, J = 93.0 Hz, 3H, BH₃), 0.50 (s, 3H, SiMe); ¹³C NMR (100.6 MHz, CDCl₃) δ: 138.4 (d, J = 4.5 Hz, ipso-Ph), 133.5 (Ph), 129.4 (Ph), 128.0 (Ph), 28.3 (d, J = 33.0 Hz, CMe₂), 24.5 (d, J = 2.5 Hz, CMe₂), 7.6 (d, J = 21.5 Hz, PCH₂), 7.2 (d, J = 35.5 Hz, PMe), –0.4 (d, J = 2.5 Hz, SiMe), –1.5 (SiMe); MS (ESI, NH₃) m/z 265 [(M – H)]; HRMS (ESI) m/z calcd for C₁₄H₂₈BP₅Si (M – H)⁺ 265.1713, found 265.1706; HPLC: Daicel Chiracel OD, 1:99 v/v iPrOH-hexane, 0.1 mL min⁻¹, 254 nm, 52.7 min [(R)-5], 56.3 min [(S)-5].

(S)-tert-Butylmethylphosphinothioyl(methyl)dimethylphenylsilane (S)-6

(1.2 eq. (−)-sparteine, Table 1, entry 2)

Using general procedure D, (−)-sparteine (204 mg, 0.87 mmol) and s-BuLi (0.60 mL of a 1.32 M solution in cyclohexane, 0.80 mmol) in Et₂O (2 mL), phosphine sulfide 4 (109 mg, 0.73 mmol) in Et₂O (7 mL) and Me₂PhSiCl (135 mg, 0.80 mmol) gave the crude product as a
colourless oil. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave adduct (S)-6 (153 mg, 74%, 84:16 er) as a colourless oil, \( R_t(4:1 \text{ petrol-EtOAc}) 0.4; [\alpha]_D \ +30.1 \ (c 1.15 \text{ in CHCl}_3); \) IR (NaCl) 3070, 2960, 1460, 1425, 1365, 1295, 1250, 1110, 885, 820, 735, 710, 640 cm\(^{-1}\); \( ^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta: 7.59:7.56 \ (m, 2H, \text{Ph}), 7.38:7.36 \ (m, 3H, \text{Ph}), 1.49:1.38 \ (m, 1H, \text{PC}H\_A\_H\_B), 1.37 \ (s, 3H, \text{PMe}), 0.63 \ (s, 3H, \text{SiMe}), 0.53 \ (s, 3H, \text{SiMe}); \)
\( ^1\)C NMR (100.6 MHz, CDCl\(_3\)) \( \delta: 138.7 \ (d, J = 4.5 \text{ Hz, ipso-Ph}), 134.0 \ (\text{Ph}), 129.8 \ (\text{Ph}), 128.3 \ (\text{Ph}), 34.6 \ (d, J = 50.5 \text{ Hz, CMe}_3), 24.5 \ (d, J = 12.0 \text{ Hz, CMe}_3), 16.6 \ (d, J = 51.5 \text{ Hz, PMe}), 15.7 \ (d, J = 39.0 \text{ Hz, PCH}_2), 0.2 \ (d, J = 3.5 \text{ Hz, SiMe}), 1.3 \ (\text{SiMe}); \)
\( ^{31}\)P{\( ^1\)H} NMR (109 MHz, CDCl\(_3\)) \( \delta: 56.8; \) MS (EI) \( m/z \) 284 (M\(^+\), 20), 269 [(M – Me)\(^+\), 15], 227 [(M – CMe\(_3\))\(^+\), 30], 207 [(M – Ph)\(^+\), 10], 150 [(M – SiMe\(_2\)Ph)\(^+\), 100], 135 [(M – CH\(_2\)SiMe\(_2\)Ph)\(^+\), 60]; HRMS (EI) \( m/z \) calcd for C\(_{14}\)H\(_{25}\)PSSi M\(^+\) 284.1184, found 284.1186; HPLC: Daicel Chiracel OD, 99:1 v/v hexane-iPrOH, 0.4 mL min\(^{-1}\), 230 nm, 16.8 min [(S)-6], 19.5 min [(R)-6].

\( (R)-\text{tert-Butylmethylphosphineborane(methyl)dimethylphenylsilane (R)-5} \)

\( (0.2 \text{ eq. (–)-sparteine, Table 1, entry 3}) \)

Using general procedure B, (–)-sparteine (70 mg, 0.30 mmol) and \( s\)-BuLi (1.24 mL of a 1.32 \text{ M solution in cyclohexane, 1.64 mmol}) in Et\(_2\)O (10 mL), phosphine borane 1 (197 mg, 1.49 mmol) in Et\(_2\)O (5 mL) and Me\(_2\)PhSiCl (0.28 mL, 1.64 mmol) gave the crude product as a yellow oil. Purification by flash chromatography with 98:2 petrol-Et\(_2\)O as eluent gave adduct (R)-5 (302 mg, 76%, 74:26 er) as a colourless oil which slowly crystallised to a white solid, \( [\alpha]_D \ +4.6 \ (c 1.05 \text{ in CHCl}_3). \)

\( (S)-\text{tert-Butylmethylphosphinothiolyl(methyl)dimethylphenylsilane (S)-6} \)

\( (0.2 \text{ eq. (–)-sparteine, Table 1, entry 4}) \)

Using general procedure E, (–)-sparteine (95 mg, 0.41 mmol, 0.2 eq.) and \( s\)-BuLi (1.72 mL of a 1.32 \text{ M solution in cyclohexane, 2.28 mmol}) in Et\(_2\)O (2 mL), phosphine sulfide 4 (310 mg, 2.07 mmol) in Et\(_2\)O (14 mL) and Me\(_2\)PhSiCl (388 mg, 2.28 mmol) gave the crude product as a colourless oil. Purification by flash chromatography with 19:1 petrol-EtOAc as
eluent gave adduct (S)-6 (439 mg, 75%, 60:40 er) as a colourless oil, \([\alpha]_D +9.4\) (c 1.10 in CHCl₃).

**rac-**tert-Butylmethylphosphineborane(methyl)dimethylphenylsilane rac-5

(no ligand, Table 1, entry 5)

Using general procedure C, s-BuLi (0.63 mL of a 1.32 M solution in cyclohexane, 0.83 mmol) in Et₂O (2 mL), phosphine borane 1 (100 mg, 0.76 mmol) in Et₂O (3 mL) and Me₂PhSiCl (0.14 mL, 0.83 mmol) gave the crude product as a yellow oil. Purification by flash chromatography with 98:2 petrol-Et₂O as eluent gave adduct rac-5 (141 mg, 70%) as a colourless oil which slowly crystallised to a white solid.

**rac-**tert-Butylmethylphosphinothioyl(methyl)dimethylphenylsilane rac-6

(no ligand, Table 1, entry 6)

Using general procedure F, s-BuLi (0.56 mL of a 1.32 M solution in cyclohexane, 0.73 mmol), phosphine sulfide 4 (100 mg, 0.67 mmol, 1.0 eq.) in Et₂O (7 mL) and Me₂PhSiCl (125 mg, 0.73 mmol) gave the crude product as a colourless oil. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave adduct rac-6 (156 mg, 83%) as a colourless oil.

(R)-**tert-**Butylmethylphosphineborane(methyl)dimethylphenylsilane (R)-5

(1.2 eq. (−)-sparteine, Table 1, entry 7)

Using general procedure A, (−)-sparteine (265 mg, 1.13 mmol) and n-BuLi (0.46 mL of a 2.25 M solution in hexanes, 1.04 mmol) in Et₂O (2 mL), phosphine borane 1 (124 mg, 0.94 mmol) in Et₂O (3 mL) and Me₂PhSiCl (0.17 mL, 1.04 mmol) gave the crude product as a yellow oil. Purification by flash chromatography with 98:2 petrol-Et₂O as eluent gave adduct (R)-5 (191 mg, 76%, 89:11 er) as a colourless oil which slowly crystallised to a white solid.
(S)-**tert-Butylmethylphosphinothioyl(methyl)dimethylphenylsilane (S)-6**

(1.2 eq. (−)-sparteine, Table 1, entry 8) and

Using general procedure D, (−)-sparteine (187 mg, 0.80 mmol, 1.2 eq.) and n-BuLi (0.33 mL of a 2.25 M solution in hexanes, 0.73 mmol, 1.1 eq.) in Et₂O (2 mL), phosphine sulfide 4 (100 mg, 0.67 mmol, 1.0 eq.) in Et₂O (7 mL) and Me₂PhSiCl (125 mg, 0.73 mmol) gave the crude product as a colourless oil. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave adduct (S)-6 (167 mg, 88%, 88:12 er) as a colourless oil.

**(R)-****tert-Butylmethylphosphineborane(methyl)dimethylphenylsilane (R)-5**

(0.2 eq. (−)-sparteine, Table 1, entry 9)

Using general procedure B, (−)-sparteine (117 mg, 0.50 mmol) and n-BuLi (1.14 mL of a 2.40 M solution in hexanes, 2.75 mmol) in Et₂O (10 mL), phosphine borane 1 (329 mg, 2.50 mmol) in Et₂O (5 mL) and Me₂PhSiCl (0.46 mL, 2.75 mmol) gave the crude product as a yellow oil. Purification by flash chromatography with 98:2 petrol-Et₂O as eluent gave adduct (R)-5 (138 mg, 21%, 84:16 er) as a colourless oil which slowly crystallised to a white solid.

(S)-**tert-Butylmethylphosphinothioyl(methyl)dimethylphenylsilane (S)-6**

(0.2 eq. (−)-sparteine, Table 1, entry 10) and (0.2 eq. (−)-sparteine, Table 2, entry 2)

Using general procedure E, (−)-sparteine (87 mg, 0.37 mmol, 0.2 eq.) and n-BuLi (0.91 mL of a 2.25 M solution in hexanes, 2.04 mmol, 1.1 eq.) in Et₂O (2 mL), phosphine sulfide 4 (278 mg, 1.86 mmol) in Et₂O (14 mL) and Me₂PhSiCl (349 mg, 2.04 mmol) gave the crude product as colourless oil. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave adduct (S)-6 (432 mg, 82%, 83:17 er) as a colourless oil, [α]₀^D +26.4 (c 0.95 in CHCl₃).
(S)-tert-Butylmethylphosphinothioyl(methyl)dimethylphenylsilane (S)-6

(no ligand, Table 1, entry 12) and (Table 2, entry 5)

Using general procedure F, \( n\)-BuLi (0.32 mL of a 2.25 M solution in hexanes, 0.73 mmol, 1.1 eq.), phosphine sulfide 4 (100 mg, 0.67 mmol, 1.0 eq.) in Et₂O (7 mL) and Me₂PhSiCl (125 mg, 0.73 mmol) gave the crude product as a colourless oil. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave adduct rac-6 (85 mg, 45%) as a colourless oil.

(S)-tert-Butylmethylphosphinothioyl(methyl)dimethylphenylsilane (S)-6

(1.2 eq. (−)-sparteine, Table 1, entry 14)

Using general procedure D, (−)-sparteine (180 mg, 0.77 mmol) and Me₃SiCH₂Li (0.70 mL of a 1 M solution in pentane, 0.70 mmol) in Et₂O (2 mL), phosphine sulfide 4 (96 mg, 0.64 mmol) in Et₂O (7 mL) and Me₂PhSiCl (120 mg, 0.70 mmol) gave the crude product as a colourless oil. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave adduct (S)-6 (167 mg, 92%, 88:12 er) as a colourless oil, \([\alpha]_D^{+} +32.1\) (c 1.05 in CHCl₃).

(S)-tert-Butylmethylphosphinothioyl(methyl)dimethylphenylsilane (S)-6

(0.2 eq. (−)-sparteine, Table 1, entry 15)

Using general procedure E, (−)-sparteine (91 mg, 0.39 mmol) and Me₃SiCH₂Li (2.14 mL of a 1 M solution in pentane, 2.14 mmol) in Et₂O (2 mL), phosphine sulfide 4 (291 mg, 1.94 mmol) in Et₂O (14 mL) and Me₂PhSiCl (364 mg, 2.14 mmol) gave the crude product as a colourless oil. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave adduct (S)-6 (435 mg, 79%, 82:18 er) as a colourless oil, \([\alpha]_D^{+} +27.1\) (c 1.00 in CHCl₃).
(S)-tert-Butylmethylphosphinothioyl(methyl)dimethylphenylsilane (S)-6

(no ligand, Table 1, entry 16)

Using general procedure F, Me₂SiCH₂Li (0.73 mL of a 1 M solution in pentane, 0.73 mmol, 1.1 eq.) and phosphine sulfide 4 (100 mg, 0.67 mmol, 1.0 eq.) in Et₂O (7 mL) and Me₂PhSiCl (125 mg, 0.73 mmol) gave the crude product as a clear oil. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave adduct rac-6 (33 mg, 18%) as a colourless oil.

(S)-tert-Butylmethylphosphinothioyl(methyl)dimethylphenylsilane (S)-6

(0.1 eq. (−)-sparteine, Table 2, entry 3)

Using general procedure E, (−)-sparteine (80 mg, 0.34 mmol) and n-BuLi (1.56 mL of a 2.4 M solution in hexanes, 3.74 mmol) in Et₂O (2 mL), phosphine sulfide 4 (512 mg, 3.40 mmol) in Et₂O (25 mL) and Me₂PhSiCl (640 mg, 3.74 mmol, 1.1 eq.) gave the crude product as a colourless oil. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave adduct (S)-6 (714 mg, 74%, 84:16 er) as a colourless oil, [α]D +28.1 (c 1.10 in CHCl₃).

(S)-tert-Butylmethylphosphinothioyl(methyl)dimethylphenylsilane (S)-6

(0.05 eq. (−)-sparteine, Table 2, entry 4)

Using general procedure E, (−)-sparteine (48 mg, 0.20 mmol) and n-BuLi (1.8 mL of a 2.5 M solution in hexanes, 4.51 mmol) in Et₂O (2 mL), phosphine sulfide 4 (615 mg, 4.10 mmol, 1.0 eq.) in Et₂O (25 mL) and Me₂PhSiCl (771 mg, 4.51 mmol, 1.1 eq.) gave the crude product as a clear oil. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave adduct (S)-6 (1.021 g, 88%, 74:26 er) as a colourless oil, [α]D +22.6 (c 0.90 in CHCl₃).
**(S)-**<sub>tert</sub>-Butylmethylphosphinothioyl(methyl)dimethylphenylsilane (**S**) -6

(1.2 eq. (--)sparteine, toluene, Table 2, entry 6)

Using general procedure D, (--)-sparteine (197 mg, 0.84 mmol) and n-BuLi (0.32 mL of a 2.4 M solution in hexanes, 0.77 mmol) in toluene (2 mL) phosphine sulfide 4 (105 mg, 0.70 mmol) in toluene (7 mL) and Me<sub>2</sub>PhSiCl (132 mg, 0.77 mmol) gave the crude product as a colourless oil. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave adduct (**S**)-6 (180 mg, 90%, 89:11 er) as a colourless oil, \([\alpha]_D^{+}28.5 \text{ (c 1.00 in CHCl}_3\))

**(S)-**<sub>tert</sub>-Butylmethylphosphinothioyl(methyl)dimethylphenylsilane (**S**) -6

(0.2 eq. (--)sparteine, toluene, Table 2, entry 7)

Using general procedure E, (--)-sparteine (90 mg, 0.38 mmol, 0.2 eq.) and n-BuLi (0.88 mL of a 2.4 M solution in hexanes, 2.10 mmol) in toluene (2 mL), phosphine sulfide 4 (288 mg, 1.90 mmol) in toluene (14 mL) and Me<sub>2</sub>PhSiCl (359 mg, 2.1 mmol) gave the crude product as a colourless oil. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave adduct (**S**)-6 (479 mg, 89%, 83:17 er) as a colourless oil, \([\alpha]_D^{+}28.8 \text{ (c 1.10 in CHCl}_3\))

**(S)-**<sub>tert</sub>-Butylmethylphosphinothioyl(methyl)dimethylphenylsilane (**S**) -6

(0.05 eq. (--)sparteine, toluene, Table 2, entry 8)

Using general procedure E, (--)-sparteine (27 mg, 0.125 mmol) and n-BuLi (1.00 mL of a 2.5 M solution in hexanes, 2.50 mmol) in toluene (2 mL), phosphine sulfide 4 (346 mg, 2.31 mmol) in toluene (8 mL) and Me<sub>2</sub>PhSiCl (430 mg, 2.51 mmol) gave the crude product as a colourless oil. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave adduct (**S**)-6 (576 mg, 88%, 85:15 er) as a colourless oil.
(S)-**tert-**Butylmethylphosphinothioyl(methyl)dimethylphenylsilane (S)-6

(no ligand, toluene, Table 2, entry 9)

Using general procedure F, *n*-BuLi (0.30 mL of a 2.4 M solution in hexanes, 0.73 mmol) and phosphine sulfide 4 (100 mg, 0.67 mmol) in toluene (7 mL) and Me₂PhSiCl (124 mg, 0.73 mmol) gave the crude product as a colourless oil. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave adduct *rac*-6 (102 mg, 54%) as a colourless oil and recovered phosphine sulfide 4 (40 mg, 40%) as a white solid.

![Chemical structure of (S)-6](image)

(S)-**tert-**Butylmethylphosphinesulfide-diphenylphosphinomethaneborane (S)-9

*n*-BuLi (0.88 mL of a 2.4 M solution in hexanes, 2.1 mmol) was added dropwise to a stirred solution of (−)-sparteine (25 mg, 0.11 mmol) in toluene (5 mL) at −78 °C under Ar. After stirring for 15 min at −78 °C, a solution of phosphine sulfide 4 (316 mg, 2.1 mmol) in toluene (21 mL) was added dropwise over 20 min *via* a syringe. The resulting mixture was stirred at −78 °C for 3 h. Then, chlorodiphenylphosphine (463 mg, 2.1 mmol) was added dropwise *via* a syringe and the resulting solution was allowed to warm to rt over 16 h. The solution was cooled to 0 °C and BH₃Me₂S (1.6 mL of a 2.0 M solution in THF, 3.15 mmol) was added dropwise *via* a syringe. After stirring at rt for 3 h, 1 M HCl(aq) (15 mL) was added slowly over 10 min (CAUTION – vigorous effervescence) and the resulting mixture was stirred for 15 min at rt to give a homogeneous biphasic solution. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with 1 M HCl(aq) (20 mL), water (20 mL) and brine (20 mL), dried (MgSO₄) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography with toluene then 90:10 toluene-EtOAc as eluent gave adduct (S)-9 (566 mg, 77%, 85:15 er) as a white crystalline solid, mp 176-177 °C; [α]D −26.3 (c 0.93 in CHCl₃); *R*ₚ(90:10 toluene-EtOAc) 0.5; IR (NaCl) 2960, 2380, 1464, 1437, 1365, 1159, 1104, 1057, 892, 793, 740, 694 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ: 7.86 (ddd, *J* = 11.5, 8.5, 1.0 Hz, 2H, Ph), 7.56 (ddd, *J* = 11.0, 8.0, 1.5 Hz, 2H, Ph), 7.48-7.29 (m, 6H, Ph), 2.92 (q, *J* = 14.5 Hz, 1H, PC₇H₅H₃), 1.56 (d, *J* = 12.5 Hz, 3H, PMe), 1.14 (d, *J* = 17.0 Hz, 3H, PhMe).
Hz, 9H, CMe3); $^3$C NMR (100.6 MHz, CDCl$_3$) δ: 133.5 (d, $J = 10.5$ Hz, Ph), 132.0 (d, $J = 2.5$ Hz, Ph), 131.5 (d, $J = 9.5$ Hz, Ph), 131.3 (d, $J = 2.5$ Hz, Ph), 131.1 (d, $J = 56.5$ Hz, ipso-Ph), 131.2, (d, $J = 56.5$ Hz, ipso-Ph), 128.9 (d, $J = 10.0$ Hz, Ph), 128.7 (d, $J = 10.5$ Hz, Ph), 128.9 (dd, $J = 51.0$, 3.0 Hz, PPh2), 24.1 (d, $J = 2.0$ Hz, PCMe3), 15.6 (d, $J = 55.0$ Hz, PMe); $^{31}$P{1H} NMR (161 MHz, CDCl$_3$) δ: 56.0 (PCMe$_3$), 15.3 (PPh$_2$); MS (ESI) m/z 349 [(M + H)$^+$, 95], 347 [(M − H)$^+$, 100]; HRMS (ESI) m/z calcd for C$_{18}$H$_{28}$BP$_2$S (M + H)$^+$ 349.1475, found 349.1467; HPLC: Daicel Chiracel AD, 99:1 v/v hexane-iPrOH, 1.0 mL min$^{-1}$, 28.0 min [(S)-9], 34.3 min [(R)-9].

(R)-tert-Butylmethylphosphinesulfide-diphenylphosphinomethaneborane (R)-9

n-BuLi (0.88 mL of a 2.4 M solution in hexanes, 2.1 mmol, 1.0 eq.) was added dropwise to a stirred solution of diamine 3 (25 mg, 0.11 mmol, 0.05 eq.) in toluene (5 mL) at −78 °C under Ar. After stirring at −78 °C for 15 min, a solution of phosphine sulfide 4 (316 mg, 2.1 mmol, 1.0 eq.) in toluene (21 mL) was added dropwise over 20 min via a syringe. The resulting mixture was stirred at −78 °C for 3 h. Then, chlorodiphenylphosphine (463 mg, 2.1 mmol, 1.0 eq.) was added dropwise via a syringe and the mixture was allowed to slowly warm to rt over 16 h. The solution was cooled to 0 °C and BH$_3$.Me$_2$S (1.7 mL of a 2.0 M solution in THF, 3.3 mmol) was added dropwise via a syringe. After stirring at rt for 3 h, 1 M HCl$_{aq}$ (15 mL) was added slowly over 10 min (CAUTION – vigorous effervescence) and the resulting mixture was stirred for 15 min at rt to give a homogeneous biphasic solution. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with 1 M HCl$_{aq}$ (20 mL), water (20 mL) and brine (20 mL), dried (MgSO$_4$) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography with toluene then 90:10 toluene-EtOAc as eluent gave adduct (R)-9 (658 mg, 86%, 78:22 er) as a white crystalline solid, [α]$_D$ +19.1 (c 1.05 in CHCl$_3$). A sample of the product (353 mg) was recrystallised from chloroform-petrol to give adduct rac-9 (184 mg, 52%, 50:50 er) as white needles. The filtrate was evaporated under reduced pressure to give adduct (R)-9 (169 mg, 48%, 99:1 er) as a white crystalline solid, mp 156-157 °C.
(S)-tert-Butylmethylphosphineborane-diphenylphosphinomethaneborane (S)-10

Si$_2$Cl$_6$ (1.73 mL of a 1.86 M solution in toluene, 3.22 mmol) was added dropwise to a stirred solution of phosphine sulfide (R)-9 (150 mg, 0.43 mmol, 78:22 er) in toluene (15 mL) at rt under Ar. The resulting solution was stirred and heated at 80 °C for 2 h. After cooling to rt, the solution was added dropwise via cannula to degassed 30% w/w NaOH$_{aq}$ (15 mL) under Ar at 0 °C. The resulting solution was stirred and heated at 50 °C until the aqueous layer became clear. The organic top layer was transferred via cannula to a flame-dried flask. The remaining aqueous layer was extracted with degassed toluene (10 mL) and the organic top layer was transferred via cannula to the same flame-dried flask. This process was repeated twice (2 × 10 mL of degassed toluene). The combined organic extracts were washed with degassed 30% w/w NaOH$_{aq}$ (10 mL) under Ar and the organic top layer was transferred via cannula to a flame-dried flask containing MgSO$_4$. The solution was then transferred via cannula to a flame-dried flask and BH$_3$.Me$_2$S (0.65 mL of a 2.0 M solution in THF, 1.3 mmol) was added dropwise via a syringe. The resulting solution was stirred at rt for 2 h. Then, 1 M HCl$_{aq}$ (15 mL) was added slowly over 10 min and the resulting mixture was stirred for 15 min at rt to give a homogeneous biphasic solution. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with 1 M HCl$_{aq}$ (20 mL), water (20 mL) and brine (20 mL), dried (MgSO$_4$) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography with 95:5 petrol:EtOAc then 85:15 petrol:EtOAc as eluent gave adduct (S)-10 (125 mg, 88%, 79:21 er) as a white crystalline solid, mp 167-169 °C; [α]$_D$ +13.5 (c 1.15 in CHCl$_3$); $R_f$(80:20 petrol-EtOAc) 0.4; IR (NaCl) 2959, 2383, 2343, 1464, 1437, 1368, 1165, 1105, 1062, 895, 809, 740, 694 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ: 7.91-7.85 (m, 2H, Ph), 7.65-7.41 (m, 8H, Ph), 2.74 (td, $J = 15.0$, 6.5 Hz, 1H, PC$_{H_A}$H$_B$), 2.35 (ddd, $J = 15.0$, 13.0, 10.0 Hz, 1H, PCH$_2$H$_3$), 1.31 (d, $J = 10.0$ Hz, 3H, PMe), 1.19 (d, $J = 14.0$ Hz, 9H, CMe$_3$), 1.07−−0.26 (m, 6H, PBH$_3$); $^{13}$C NMR (67.9 MHz, CDCl$_3$) δ: 133.2 (d, $J = 10.0$ Hz, Ph), 132.2 (d, $J = 2.5$ Hz, Ph), 131.3 (d, $J = 9.5$ Hz, Ph), 131.2 (d, $J = 2.5$ Hz, Ph), 129.0 (d, $J = 4.5$ Hz, Ph), 128.8 (d, $J = 5.0$ Hz, Ph), 126.7 (d, $J = 56.0$ Hz, ipso-Ph), 28.9 (dd, $J = 32.0$, 3.5 Hz, PCMe$_3$), 24.8 (d, $J = 2.5$ Hz, PCMe$_3$), 18.2 (t, $J = 25.5$ Hz, PCH$_2$), 6.0 (d, $J = 33.5$ Hz,
31P NMR (109.3 MHz, CDCl3) δ: 29.5 (d, J = 65.5 Hz, Ph2PBH3), 14.9 (d, J = 65.5 Hz, tBuPBH3); MS (ESI) m/z 353 [(M + Na)+, 100]; HRMS (ESI) m/z calcd for C18H30B2P2 (M + Na)+ 353.1907, found 353.1901; HPLC: Daicel Chiracel OD, 98:2 v/v hexane-iPrOH, 1.0 mL min−1, 9.1 min [(S)-10], 10.3 min [(R)-10].

**rac-tert-Butylmethylphosphineborane-diphenylphosphinomethaneborane rac-10**

s-BuLi (0.77 mL of a 1.3 M solution in cyclohexane, 1.0 mmol) was added dropwise to a stirred solution of phosphine borane 1 (132 mg, 1.0 mmol) in THF (14 mL) at 0 °C under Ar. The resulting mixture was stirred at 0 °C for 1 h. Then, chlorodiphenylphosphine (220 mg, 1.0 mmol) was added and the solution was stirred at 0 °C for 2 h. Then, BH3·Me2S (0.55 mL of a 2.0 M solution in THF, 1.1 mmol) was added dropwise. After stirring at rt for 3 h, 1 M HCl(aq) (15 mL) was added slowly over 10 min and the resulting mixture was stirred for 15 min at rt to give a homogeneous biphasic solution. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with 1 M HCl(aq) (20 mL), water (20 mL) and brine (20 mL), dried (MgSO4) and evaporated under reduced pressure to give the crude product as a white solid. Purification by flash chromatography with 95:5 petrol-EtOAc then 85:15 petrol-EtOAc as eluent gave adduct rac-10 (251 mg, 76%) as a white crystalline solid, mp 174-177 °C.

**Experimental for the reactions referred to in the references.**

**rac-P-(2,2-Diphenyl-2-hydroxyethyl)-P-methyl-tert-butyl-phosphine borane**

(Reference 12, 1.1 eq. n-BuLi, –50 °C)

Using general procedure C, n-BuLi (0.39 mL of a 2.14 M solution in hexanes, 0.83 mmol) in Et2O (2 mL), phosphine borane 1 (100 mg, 0.76 mmol) in Et2O (3 mL) and benzophenone (152 mg, 0.83 mmol) in Et2O (3 mL) at –50 °C gave the crude product as a white solid.
Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave the title compound (27 mg, 11%) as a white solid, $R_f$ (4:1 petrol-EtOAc) 0.3; $^1$H NMR (400 MHz, CDCl$_3$) δ: 7.51-7.46 (m, 4H, Ph), 7.35-7.29 (m, 4H, Ph), 7.26-7.20 (m, 2H, Ph), 4.58 (s, 1H, OH), 2.88 (t, $J = 14.5$ Hz, 1H, PCH$_A$H$_B$), 2.67 (dd, $J = 14.5$ Hz, 6.5 Hz, 1H, PCH$_A$H$_B$), 1.17 (d, $J = 13.5$ Hz, 9H, CMe$_3$), 0.74 (d, $J = 10.0$ Hz, 3H, PMe), 0.88-0.23 (m, 3H, BH$_3$); $^{13}$C NMR (100.6 MHz, CDCl$_3$) δ: 147.7 (d, $J = 8.5$ Hz, ipso-Ph), 145.3 (d, $J = 1.5$ Hz, ipso-Ph), 128.3 (Ph), 128.2 (Ph), 127.2 (Ph), 125.3 (Ph), 34.2 (d, $J = 28.5$ Hz, PCH$_2$), 28.0 (d, $J = 36.0$ Hz, CMe$_3$), 24.7 (d, $J = 2.5$ Hz, CMe$_3$), 6.5 (d, $J = 34.5$ Hz, PMe) (some aromatic signals not resolved and one carbon overlaps with CDCl$_3$). Spectroscopic data consistent with that reported in the literature.$^3$

**rac-P-(2,2-Diphenyl-2-hydroxyethyl)-P-methyl-tert-butyl-phosphine borane**

(Reference 12, 1.1 eq. n-BuLi, $-42 \, ^\circ$C)

Using general procedure C, n-BuLi (0.35 mL of a 2.14 M solution in hexanes, 0.74 mmol) in Et$_2$O (2 mL) phosphine borane I (89 mg, 0.68 mmol) in Et$_2$O (3 mL) and benzophenone (135 mg, 0.74 mmol) in Et$_2$O (3 mL) at $-42 \, ^\circ$C gave the crude product as a white solid. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave the title compound (61 mg, 29%) as a white solid.

**rac-P-(2,2-Diphenyl-2-hydroxyethyl)-P-methyl-tert-butyl-phosphine borane**

(Reference 12, 1.1 eq. n-BuLi, 0 \, ^\circ$C)

Using general procedure C, n-BuLi (0.27 mL of a 2.45 M solution in hexanes, 0.67 mmol) in Et$_2$O (2 mL) phosphine borane I (80 mg, 0.61 mmol) in Et$_2$O (3 mL) and benzophenone (121 mg, 0.67 mmol) in Et$_2$O (3 mL) at 0 \, ^\circ$C gave the crude product as a white solid. Purification by flash chromatography with 19:1 petrol-EtOAc as eluent gave the title compound (97 mg, 51%) as a white solid.
(R)-tert-Butylmethylphosphineborane(methyl)dimethylphenylsilane (R)-5

(Reference 14, 0.2 eq. (–)-sparteine, –50 °C)

Using general procedure B, (–)-sparteine (94 mg, 0.41 mmol) and n-BuLi (0.92 mL of a 2.40 M solution in hexanes, 2.21 mmol) in Et₂O (10 mL), phosphine borane 1 (264 mg, 2.01 mmol) in Et₂O (5 mL) and Me₂PhSiCl (0.37 mL, 2.21 mmol) gave the crude product as a yellow oil. Purification by flash chromatography with 98:2 petrol-Et₂O as eluent gave adduct (R)-5 (262 mg, 49%, 80:20 er) as a colourless oil which slowly crystallised to a white solid.

(R)-tert-Butylmethylphosphineborane(methyl)dimethylphenylsilane (R)-5

(Reference 15, 1.2 eq. (–)-sparteine)

Using general procedure A, (–)-sparteine (213 mg, 0.91 mmol) and Me₃SiCH₂Li (0.83 mL of a 1.00 M solution in pentane, 0.83 mmol) in Et₂O (10 mL), phosphine borane 1 (100 mg, 0.76 mmol) in Et₂O (5 mL) and Me₂PhSiCl (0.14 mL, 0.83 mmol) at –20 °C gave the crude product as a yellow oil. Purification by flash chromatography with 98:2 petrol-Et₂O as eluent gave adduct (R)-5 (151 mg, 75%, 75:25 er) as colourless oil which slowly crystallised to a white solid, [α]D +0.6 (c 1.10 in CHCl₃).
References


