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Catalytic asymmetric deprotonation of a phosphine borane: comparison of two-ligand and one-ligand catalysis

Steven J. Canipa [a], Peter O'Brien [a,*], Sven Taylor [b]

[a] *Department of Chemistry, University of York, Heslington, York YO10 5DD, UK*
[b] *F. Hoffmann-La Roche Ltd, CH-4070, Basel, Switzerland*

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ABSTRACT

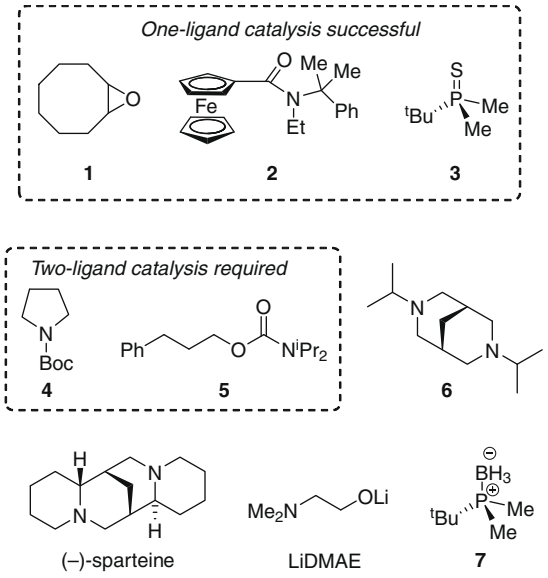
The catalytic asymmetric deprotonation of *tert*-butyldimethylphosphine borane using *s*-BuLi or *n*-BuLi and sub-stoichiometric amounts of (−)-sparteine under one-ligand and two-ligand manifolds has been investigated. Using *s*-BuLi, slightly higher enantioselectivity was obtained using two-ligand catalysis (use of sub-stoichiometric (−)-sparteine in the presence of a stoichiometric amount of a second achiral ligand) compared to one-ligand catalysis (use of sub-stoichiometric (−)-sparteine only). With *n*-BuLi, two-ligand catalysis using LiDMAE (DMAE = dimethylaminoethanol) as the stoichiometric ligand was the only method for obtaining good yield and enantioselectivity. In this case, one-ligand catalysis failed as the (−)-sparteine was not turned over.

1. Introduction

The chiral base obtained by combining *s*-BuLi or *n*-BuLi and (−)-sparteine is particularly effective for the asymmetric deprotonation of *O*-alkyl carbamates,[1] *N*-Boc heterocycles,[2] medium-ring epoxides,[3] ferrocene amides[4] and phosphine boranes and sulfides.[5] One limitation of the use of such chiral bases in synthesis is their reliance on a stoichiometric amount of chiral ligand. With this in mind, our group became interested in developing catalytic variants of existing asymmetric deprotonation reactions in which a sub-stoichiometric amount of (−)-sparteine is used. It is well established that complexing a diamine to an organolithium reagent increases its reactivity. From this, it follows that as long as there is little racemic (background) deprotonation by the uncomplexed organolithium reagent then it should be possible to carry out catalytic asymmetric deprotonation with high enantioselectivity. Indeed, Hodgson demonstrated this in the asymmetric lithiation-rearrangement of cyclooctene oxide **1**[3] whilst we have also reported successful examples with ferrocene amide **2**[6] and phosphine sulfide **3**[7] (Scheme 1). We refer to these examples as *one-ligand catalysis*.

In contrast, the attempted one-ligand catalytic asymmetric deprotonation of *N*-Boc pyrrolidine **4** or *O*-alkyl carbamate **5** led to low yields and poor enantioselectivity.[8] Suspecting that the problems lay with the poor turn-over of the chiral ligand, we introduced a second ligand into the system. The best results with *N*-Boc pyrrolidine **4**[8–10] or *O*-alkyl carbamate **5**[8,11] were obtained using achiral bispidine **6** (whose *s*-BuLi complex is sufficiently sterically hindered to minimise the background deprotonation). Thus, *N*-Boc pyrrolidine **4** and *O*-alkyl carbamate **5** require what we refer to as *two-ligand catalysis* for successful catalytic asymmetric deprotonation (Scheme 1). More recently, we have obtained high enantioselectivity using lithiated dimethylaminoethanol (LiDMAE) in two-ligand catalysis with *N*-Boc pyrrolidine **4**.[12]

On inspection of our original disclosures on two-ligand and one-ligand catalysis, we reported the catalytic asymmetric



Scheme 1. One-ligand and two-ligand catalytic asymmetric deprotonation.

* Corresponding author. Tel.: +44 01904 532535; fax: +44 01904 432516.
E-mail address: paob1@york.ac.uk (P. O'Brien).

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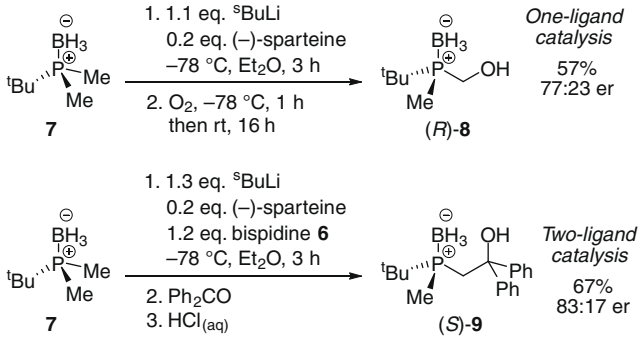
deprotonation of phosphine borane **7** using both approaches (Scheme 2).[13] For example, using one-ligand catalysis, lithiation–oxygenation of phosphine borane **7** with *s*-BuLi and 0.2 equiv (−)-sparteine gave hydroxy phosphine borane (*R*)-**8** in 57% yield with 77:23 er.[6] Slightly higher enantioselectivity was obtained in the two-ligand catalytic asymmetric deprotonation: lithiation of **7** using *s*-BuLi, 0.2 equiv (−)-sparteine and 1.2 equiv bispidine **6** and trapping with benzophenone-delivered hydroxy phosphine borane (*S*)-**9** in 67% yield and 83:17 er.[8]

The preliminary conclusion from the results in Scheme 2 is that two-ligand catalysis provides a slight improvement in enantioselectivity over one-ligand catalysis. However, since there are differences between these two examples (e.g., amount of *s*-BuLi used and different electrophile trapping procedures), we have now carried out a systematic comparison of the *s*-BuLi-mediated one-ligand and two-ligand catalytic asymmetric deprotonation of phosphine borane **7**. The study includes a wider range of achiral, regenerating ligands and examples with *n*-BuLi which behaves in a different fashion to *s*-BuLi. Herein, we report our results and provide some guidelines on the scope and limitations of the catalytic asymmetric deprotonation of phosphine boranes.



Scheme 2. Catalytic asymmetric deprotonation of phosphine borane **7**.

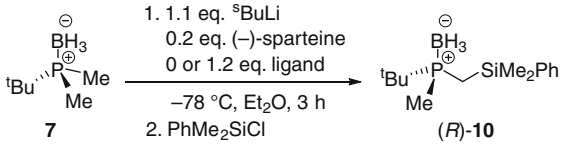
2. Results and discussion

For the purposes of comparing one-ligand and two-ligand catalysis, the lithiation reactions presented in Tables 1 and 2 utilise 1.1 equiv *s*-BuLi or *n*-BuLi and $PhMe_2SiCl$ for the electrophilic trap (thus generating silyl phosphine borane (*R*)-**10**). Using 1.1 equiv *s*-BuLi alone, lithiation–silylation gave adduct *rac*-**10** in 70% yield indicating a considerable background lithiation rate by *s*-BuLi in Et_2O at −78 °C. Carrying out the same reaction in the presence of stoichiometric (−)-sparteine (1.2 equiv) generated (*R*)-**10** in 74% yield and 92:8 er.[7] This is the benchmark result for the one-ligand and two-ligand catalysis study, the results of which are presented in Scheme 3 and Table 1.

Table 1
s-BuLi-mediated one-ligand and two-ligand catalytic asymmetric deprotonation of phosphine borane **7**→(*R*)-**10** (Scheme 3)

Entry	Ligand	Yield[a] (%)	er (*R*:*S*)[b]
1	—	76	74:26
2	Bispidine **6**	78	79:21
3	LiDMAE[c]	59	81:19
4	*N*-Me morpholine	67	65:35

[a] Yield after purification by flash column chromatography.
[b] Enantiomer ratio (er) determined by chiral HPLC.
[c] 1.2 equiv LiDMAE was formed in situ by deprotonation with an extra 1.2 equiv *s*-BuLi.

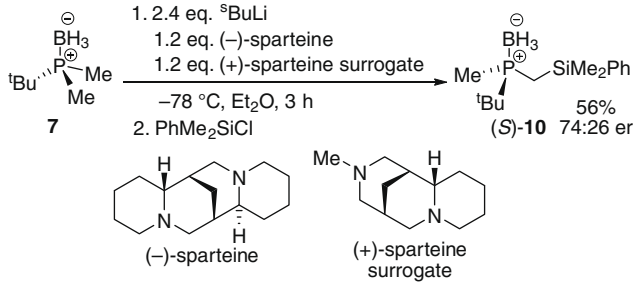


Scheme 3. *s*-BuLi-mediated one-ligand and two-ligand catalytic asymmetric deprotonation of phosphine borane **7**.

Using one-ligand catalysis (1.1 equiv *s*-BuLi and 0.2 equiv (−)-sparteine), adduct (*R*)-**10** was isolated in 76% yield and 74:26 er (Table 1, entry 1). This is in lower enantioselectivity than the stoichiometric reaction (92:8 er) and can be attributed to an appreciable degree of background (racemic) lithiation by *s*-BuLi. Slightly better results were obtained when 1.2 equiv bispidine **6** was added, under otherwise identical conditions: adduct (*R*)-**10** was formed in 78% yield with 79:21 er (Table 1, entry 2). This result clearly indicates the beneficial effect of adding bispidine **6** as the second ligand and is consistent with the trend shown in Scheme 2.

As part of this study, we also investigated two-ligand catalysis using LiDMAE and *N*-methyl morpholine as the second, regenerating ligands since both had given satisfactory results with *N*-Boc pyrrolidine **4**.[10,12] The use of LiDMAE (formed in situ by adding an extra 1.2 equiv *s*-BuLi to 1.2 equiv dimethylaminoethanol) gave adduct (*R*)-**10** in 59% yield and 81:19 er (Table 1, entry 3), similar enantioselectivity to that obtained with bispidine **6**. In contrast, poor enantioselectivity (65:35 er) was observed using *N*-methyl morpholine (Table 1, entry 4). Overall, the *s*-BuLi-mediated two-ligand catalytic asymmetric deprotonation of phosphine borane **7** proceeds with higher enantioselectivity using either bispidine **6** or LiDMAE (prepared in situ from commercially available DMAE) than the corresponding one-ligand catalysis.

As Kann[14] and ourselves have noted,[6–8] it is possible to access either enantiomer of phosphine boranes such as **8**, **9** and **10** using (−)-sparteine or (+)-sparteine surrogate.[15] In one-ligand and two-ligand catalysis with *s*-BuLi, we have previously noted that that higher enantioselectivity was obtained using the (+)-sparteine surrogate compared to (−)-sparteine under the same conditions.[6,8] This was rationalised by higher reactivity of the *s*-BuLi/(+)-sparteine surrogate complex, as noted in the deprotonations of *N*-Boc pyrrolidine **4**[9] and *O*-alkyl carbamate **5**.[11] To confirm this, a competition experiment was carried out (Scheme 4).



Scheme 4. Competition experiment between *s*-BuLi/(−)-sparteine and *s*-BuLi/(+)-sparteine surrogate.

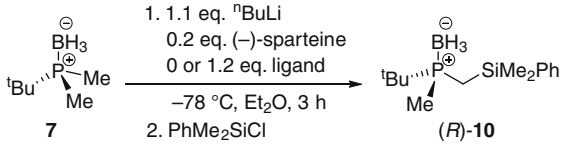
Thus, 2.4 equiv *s*-BuLi was combined with 1.2 equiv of each of (−)-sparteine and the (+)-sparteine surrogate in Et_2O at −78 °C. Phosphine borane **7** was then added to this mixture and, after 3 h, the lithiated intermediates were trapped with $PhMe_2SiCl$. This generated a 56% yield of (*S*)-**10** with 74:26 er. Since the major product is formed with the (+)-sparteine surrogate sense of induction, we conclude that the *s*-BuLi/(+)-sparteine surrogate complex is indeed more reactive in the deprotonation of phosphine borane **7** than *s*-BuLi/(−)-sparteine.

Next, we turned our attention to the use of *n*-BuLi. Using *n*-BuLi in Et_2O at −78 °C, we have been unable to lithiate phosphine borane **7** (despite numerous attempts and the use of different electrophiles). This reflects the lower basicity of *n*-BuLi compared to *s*-BuLi and is significant for catalysis since there should be no background racemic lithiation using *n*-BuLi. Under stoichiometric conditions (1.1 equiv *s*-BuLi and 1.2 equiv (−)-sparteine), lithiation occurred satisfactorily and, after trapping with $PhMe_2SiCl$, adduct (*R*)-**10** was obtained in 76% yield and 89:11 er.[7] For comparison with this stoichiometric result, one-ligand catalysis and two-ligand catalysis (with four regenerating ligands) were explored (Scheme 5 and Table 2).

Table 2
n-BuLi-mediated one-ligand and two-ligand catalytic asymmetric deprotonation of phosphine borane **7**→(*R*)-**10** (Scheme 5)

Entry	Ligand	Yield[a] (%)	er (*R*:*S*)[b]
1	—	21	84:16
2	Bispidine **6**	52	59:41
3	LiDMAE[c]	48	82:18
4	*N*-Me morpholine	22	87:13
5	PMDETA[d]	83	51:49

[a] Yield after purification by flash column chromatography.
[b] Enantiomer ratio (er) determined by chiral HPLC.
[c] 1.2 equiv LiDMAE was formed in situ by deprotonation with an extra 1.2 equiv *s*-BuLi.
[d] PMDETA = pentamethyldiethylenetriamine.

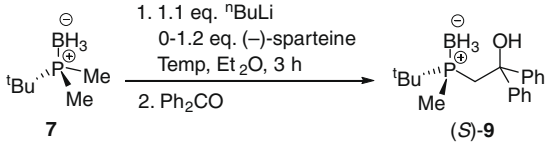


Scheme 5. *n*-BuLi-mediated one-ligand and two-ligand catalytic asymmetric deprotonation of phosphine borane **7**.

Under one-ligand catalytic conditions (1.1 equiv *n*-BuLi and 0.2 equiv (−)-sparteine), we isolated adduct (*R*)-**10** of 84:16 er but in only 21% yield (Table 2, entry 1). The low yield and high enantioselectivity indicate that the (−)-sparteine chiral ligand is not being turned over in a catalytic fashion. This is different to that observed with *s*-BuLi indicating that ligand turn-over depends on the organolithium reagent employed. Since two-ligand catalysis is a way of recycling the chiral diamine, we wondered whether a two-ligand catalytic system could be developed for the *n*-BuLi-mediated lithiations.

With bispidine **6** (Table 2, entry 2) and PMDETA (Table 2, entry 5), yields in excess of 20% were obtained, but the enantioselectivity was poor (59:41 er and 51:49 er, respectively). These results could be explained by a significant amount of background lithiation by *n*-BuLi/**6** and *n*-BuLi/PMDETA in Et_2O at −78 °C. This was confirmed for PMDETA: lithiation trapping using *n*-BuLi/PMDETA (Et_2O, −78 °C) gave adduct *rac*-**10** in 69% yield. Using *N*-methyl morpholine, there was no turn-over of (−)-sparteine and no background lithiation: adduct (*R*)-**10** was formed in 22% yield and 87:13 er (Table 2, entry 4). As with the *s*-BuLi results in Table 1, the highest yield and enantioselectivity with *n*-BuLi were obtained using LiDMAE in two-ligand catalysis. In this way, adduct (*R*)-**10** was isolated in 48% yield and with 82:18 er (Table 2, entry 3). This result indicates some turn-over of (−)-sparteine and the loss of er can be attributed to some background lithiation by *n*-BuLi/LiDMAE which was confirmed in a separate experiment. Lithiation trapping of phosphine borane **7** with *n*-BuLi/LiDMAE alone in Et_2O at −78 °C gave *rac*-**10** in 13% yield.

Given the rather disappointing results with the one-ligand and two-ligand catalytic asymmetric deprotonation of phosphine borane **7** using *n*-BuLi, we decided to investigate whether increasing the lithiation temperature might facilitate a turn-over of the (−)-sparteine under a one-ligand catalytic protocol. At higher temperatures, however, there may be reduced enantioselectivity and background lithiation may become an issue. Nevertheless, some interesting results were obtained from a temperature study on the *n*-BuLi/(−)-sparteine-mediated one-ligand catalytic deprotonation of phosphine borane **7**. In these examples, benzophenone was used as the electrophilic trap (Scheme 6 and Table 3).



Scheme 6. *n*-BuLi-mediated one-ligand catalytic asymmetric deprotonation of phosphine borane **7**.

Table 3
Temperature effect on the *n*-BuLi-mediated one-ligand catalytic asymmetric deprotonation of phosphine borane **7**→(*S*)-**9** (Scheme 6)

Entry	(−)-Sparteine (equiv)	Temperature (°C)	Yield[a] (%)	er (*R*:*S*)[b]
1	1.2	−78	56	88:12
2	0.2	−78	19	87:13
3	0	−78	0	—
4	0.2	−60	42	87:13
5	0	−60	0	—
6	0.2	−50	50	81:19
7	0	−50	11	—
8	1.2	−40	84	84:16
9	0.2	−40	69	78:22
10	0	−40	29	—

[a] Yield after purification by flash column chromatography.
[b] Enantiomer ratio (er) determined by chiral HPLC.

The stoichiometric lithiation trapping at −78 °C (1.1 equiv *s*-BuLi and 1.2 equiv (−)-sparteine) afforded a 56% yield of (*S*)-**9** with 88:12 er (Table 3, entry 1). Use of 0.2 equiv (−)-sparteine at −78 °C gave a 19% yield of (*S*)-**9** of 87:13 er (Table 3, entry 2), indicating no turn-over of (−)-sparteine and consistent with the result obtained using $PhMe_2SiCl$ (21% yield of (*R*)-**10** of 84:16 er; Table 2, entry 1). However, by raising the temperature to −60 °C, ligand turn-over was facilitated as the adduct (*S*)-**9** of high er was formed in >20% yield: 42% yield of (*S*)-**9** of 87:13 er (Table 3, entry 4). At −60 °C, there was no background lithiation (Table 3, entry 5) but an increasing amount of background lithiation was observed at higher temperatures: using *n*-BuLi alone gave an 11% yield of *rac*-**9** at −50 °C (Table 3, entry 7) and a 29% yield of *rac*-**9** at −40 °C (Table 3, entry 10). As a result, the catalytic reactions performed at −50 °C and −40 °C resulted in a drop in enantioselectivity (Table 3, entries 6 and 9). Stoichiometric lithiation-trapping was carried out at −40 °C and gave (*S*)-**9** in 84% yield with 84:16 er (Table 3, entry 8) indicating a lower enantioselectivity compared to that carried out at −78 °C (88:12 er; Table 3, entry 1). Overall, higher temperatures did allow (−)-sparteine to be turned over and, at −50 °C, (*S*)-**9** of 81:19 er was isolated in 50% yield using *n*-BuLi and 0.2 equiv (−)-sparteine (Table 3, entry 6).

3. Conclusion

In conclusion, we have provided definitive proof that two-ligand catalytic asymmetric deprotonation of phosphine borane **7** using *s*-BuLi gives higher enantioselectivity than the corresponding one-ligand catalysis. The best result with *s*-BuLi was obtained using LiDMAE as the second ligand (59% yield of (*R*)-**10** with 81:19 er) although bispidine **6** also worked well (78% yield of (*R*)-**10** with

79:21 er). With *n*-BuLi at −78 °C, one-ligand catalysis was unsuccessful as (−)-sparteine was not turned over and two-ligand catalysis only worked in the presence of LiDMAE: adduct (*R*)-**10** of 82:18 er was isolated in 48% yield. Alternatively, one-ligand catalysis with *n*-BuLi in the temperature range of −60 to −40 °C provided satisfactory results: at −50 °C, alcohol (*S*)-**9** of 81:19 er was formed in 50% yield. If a simple catalytic variant is to be employed for the deprotonation of phosphine boranes such as **7**, we advocate the use of *n*-BuLi in a one-ligand system at −50 °C or use of *s*-BuLi in a two-ligand system with bispidine **6** or LiDMAE (formed from commercially available DMAE). We believe that these catalytic protocols are useful for the synthesis of chiral phosphine ligands since a number of such ligands have been prepared via asymmetric deprotonation using a stoichiometric amount of (−)-sparteine.[16]

4. Experimental

4.1. General

Water used is distilled water. Et_2O was freshly distilled from benzophenone ketyl. Brine is a saturated aqueous solution. (−)-Sparteine, bispidine **6**, DMAE and PMDETA were distilled from CaH_2 before use. Petrol refers to the fraction of petroleum ether with a boiling range of 40–60 °C. All reactions were carried out under O_2-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 F_{254} alumina-backed silica plates. Proton (400 MHz) and carbon (100.6 MHz) NMR spectra were recorded on a Jeol ECX-400 instrument with internal deuterium lock. Chemical shifts are quoted as parts per million and referenced to $CHCl_3$ (7.27). Carbon NMR spectra were recorded with broadband proton decoupling and 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 $[\alpha]_D$ measurements are given in units of 10^{-1} deg cm^2 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.

4.2. General procedure A: two-ligand catalytic asymmetric deprotonation of phosphine borane 7

s-BuLi (1.2 M solution in cyclohexane, 1.1 or 2.3 equiv) or *n*-BuLi (2.4 M solution in hexane, 1.1 or 2.3 equiv) was added dropwise to a stirred solution of (−)-sparteine (0.2 equiv) and a second ligand (1.2 equiv) in Et_2O (10 mL) at −78 °C under Ar. After stirring for 15 min at −78 °C, a solution of phosphine borane **7** (290 mg, 2.20 mmol) in Et_2O (5 mL) was added dropwise over 10 min via a cannula. The resulting solution was stirred at −78 °C for 3 h. Then, $Me_2PhSiCl$ (1.1 equiv or 2.3 equiv) was added via a syringe and the resulting solution was allowed to warm to rt over 16 h. Next, 1 M $HCl_{(aq)}$ (10 mL) and then EtOAc (10 mL) were added. The two layers were separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). 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.

4.3. General procedure B: stoichiometric asymmetric deprotonation of phosphine borane 7 using *n*-BuLi/(−)-sparteine

n-BuLi (2.4 M solution in hexane, 1.1 equiv) was added dropwise to a stirred solution of (−)-sparteine (1.2 equiv) in Et_2O (3 mL) at −78 or −40 °C under Ar. After stirring for 15 min at −78 or −40 °C, a solution of phosphine borane **7** (80 mg, 0.61 mmol) in Et_2O (3 mL) was added dropwise over 10 min via a cannula. The resulting solution was stirred at −78 or −40 °C for 3 h. Then, a solution of benzophenone (1.1 equiv) in Et_2O (3 mL) was added via a syringe and the resulting solution was allowed to warm to rt over 16 h. 1 M $HCl_{(aq)}$ (5 mL) and then EtOAc (5 mL) were added. The two 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 ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a white solid.

4.4. General procedure C: one-ligand catalytic asymmetric deprotonation of phosphine borane 7 using *n*-BuLi/(−)-sparteine

n-BuLi (2.4 M solution in hexane, 1.1 equiv) was added dropwise to a stirred solution of (−)-sparteine (0.2 equiv) in Et_2O (10 mL) at −78, −60, −50 or −40 °C under Ar. After stirring for 15 min at −78, −60, −50 or −40 °C, a solution of phosphine borane **7** (290 mg, 2.20 mmol) in Et_2O (5 mL) was added dropwise over 10 min via a cannula. The resulting solution was stirred at −78, −60, −50 or −40 °C for 3 h. Then, a solution of benzophenone (1.1 equiv) in Et_2O (5 mL) was added via a syringe and the resulting solution was allowed to warm to rt over 16 h. Next, 1 M $HCl_{(aq)}$ (10 mL) and then EtOAc (10 mL) were added. The two layers were separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). 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.

4.5. General procedure D: background lithiation of phosphine borane 7 using *n*-BuLi

At first, *n*-BuLi (2.4 M solution in hexane, 1.1 eq) was added dropwise to a stirred solution of phosphine borane **7** (80 mg, 0.61 mmol) in Et_2O (3 mL) at −78, −60, −50 or −40 °C under Ar. The resulting solution was stirred at −78, −60, −50 or −40 °C for 3 h. Then, a solution of benzophenone (1.1 equiv) in Et_2O (3 mL) was added via a syringe and the resulting solution was allowed to warm to rt over 16 h. Next, 1 M $HCl_{(aq)}$ (5 mL) and then EtOAc (5 mL) were added. The two 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 ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a white solid.

4.6. (*R*)-*tert*-Butylmethylphosphineborane(methyl)-dimethylphenylsilane (*R*)-10

Table 1, *entry 2*: Using general procedure A, (−)-sparteine (97 mg, 0.41 mmol), bispidine **6** (522 mg, 2.48 mmol) and *s*-BuLi (1.91 mL of a 1.19 M solution in cyclohexane, 2.28 mmol) in Et_2O (10 mL), phosphine borane **7** (273 mg, 2.07 mmol) in Et_2O (5 mL) and $Me_2PhSiCl$ (0.38 mL, 2.28 mmol) gave the crude product. Purification by flash chromatography on silica with petrol–Et_2O (98:2) as eluent gave adduct (*R*)-**10** (432 mg, 78%, 79:21 er by chiral HPLC) as a colourless oil which slowly crystallised to a white solid, mp 40–42 °C; $[\alpha]_D$ = +6.3 (*c* 1.10, $CHCl_3$), R_F (4:1 petrol–EtOAc) 0.3; IR (NaCl) 2960, 2375, 1426, 1265, 1114, 1060, 904, 887, 822, 738, 704 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59–7.54 (m, 2H, *o*-Ph), 7.40–7.38 (m, 3H, Ph), 1.12 (d, J_{PH} = 13.5 Hz, 9H, $PCMe_3$), 1.06–0.97 (m, 2H, PCH_2), 1.00 (d, J_{PH} = 10.0 Hz, 3H, PMe), 0.56 (s, 3H, SiMe), 0.50 (s, 3H, SiMe); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 138.4

(d, J_{PC} = 4.5 Hz, *ipso*-Ph), 133.5 (Ph), 129.4 (Ph), 128.0 (Ph), 28.3 (d, J_{PC} = 33.0 Hz, P*C*Me$_3$), 24.5 (d, J_{PC} = 2.5 Hz, PMe), 7.6 (d, J_{PC} = 21.5 Hz, PCH$_2$), 7.2 (d, J_{PC} = 7.0 Hz, PC*Me*$_3$), −0.4 (d, J_{PC} = 2.5 Hz, SiMe), −1.5 (SiMe); MS (ESI) *m*/*z* 289 [(M+Na)$^+$]; HRMS (ESI) *m*/*z* calcd for $C_{14}H_{28}BPSi$ (M+Na)$^+$ 289.1683, found 289.1683 (0.1 ppm error). HPLC: Daicel Chiracel OD, 1:99 v/v *i*PrOH-hexane, 0.1 mL min^{-1}, 254 nm, 52.7 min [(*R*)-**10**], 56.3 min [(*S*)-**10**].

Table 1, *entry 3*: Using general procedure A, (−)-sparteine (91 mg, 0.39 mmol), dimethylaminoethanol (208 mg, 2.33 mmol) and *s*-BuLi (3.75 mL of a 1.19 M solution in cyclohexane, 4.46 mmol) in Et$_2$O (10 mL), phosphine borane **7** (256 mg, 1.94 mmol) in Et$_2$O (5 mL) and Me$_2$PhSiCl (0.75 mL, 4.46 mmol) gave the crude product. Purification by flash chromatography on silica with petrol–Et$_2$O (98:2) as eluent gave adduct (*R*)-**10** (304 mg, 59%, 81:19 er by chiral HPLC) as a colourless oil which slowly crystallised to a white solid, $[\alpha]_D$ = +6.3 (*c* 1.00, CHCl$_3$).

Table 1, *entry 4*: Using general procedure A, (−)-sparteine (102 mg, 0.44 mmol), *N*-methyl morpholine (264 mg, 2.61 mmol) and *s*-BuLi (2.01 mL of a 1.19 M solution in cyclohexane, 2.39 mmol) in Et$_2$O (10 mL), phosphine borane **7** (287 mg, 2.18 mmol) in Et$_2$O (5 mL) and Me$_2$PhSiCl (0.40 mL, 2.39 mmol) gave the crude product. Purification by flash chromatography on silica with petrol–Et$_2$O (98:2) as eluent gave adduct (*R*)-**10** (390 mg, 67%, 65:35 er by chiral HPLC) as a colourless oil which slowly crystallised to a white solid, $[\alpha]_D$ = +3.2 (*c* 1.10, CHCl$_3$).

Scheme 4, *competition experiment*: *s*-BuLi (0.98 mL of a 1.29 M solution in cyclohexane, 1.26 mmol) was added dropwise to a stirred solution of (−)-sparteine (148 mg, 0.63 mmol) and (+)-sparteine surrogate (123 mg, 0.63 mmol) in Et$_2$O (2 mL) at −78 °C under Ar. After stirring for 15 min at −78 °C, a solution of phosphine borane **7** (70 mg, 0.53 mmol) in Et$_2$O (3 mL) was added dropwise over 10 min via a cannula. The resulting solution was stirred at −78 °C for 3 h. Then, Me$_2$PhSiCl (0.21 mL, 1.27 mmol) was added via a syringe and the resulting solution was allowed to warm to rt over 16 h. 1 M HCl$_{(aq)}$ (5 mL) and then EtOAc (5 mL) were added. The two 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 (MgSO$_4$) and evaporated under reduced pressure to give the crude product as a yellow oil. Purification by flash chromatography on silica with petrol–Et$_2$O (98:2) as eluent gave adduct (*S*)-**10** (79 mg, 56%, 74:26 er by chiral HPLC) as a colourless oil which slowly crystallised to a white solid, $[\alpha]_D$ = −4.7 (*c* 1.05, CHCl$_3$).

Table 2, *entry 2*: Using general procedure A, (−)-sparteine (116 mg, 0.50 mmol), bispidine **6** (622 mg, 2.96 mmol) and *n*-BuLi (1.13 mL of a 2.40 M solution in cyclohexane, 2.72 mmol) in Et$_2$O (10 mL), phosphine borane **7** (326 mg, 2.47 mmol) in Et$_2$O (5 mL) and Me$_2$PhSiCl (0.46 mL, 2.72 mmol) gave the crude product. Purification by flash chromatography on silica with petrol–Et$_2$O (98:2) as eluent gave adduct (*R*)-**10** (344 mg, 52%, 59:41 er by chiral HPLC) as a colourless oil which slowly crystallised to a white solid, $[\alpha]_D$ = +2.1 (*c* 1.05, CHCl$_3$).

Table 2, *entry 3*: Using general procedure A, (−)-sparteine (107 mg, 0.46 mmol), dimethylaminoethanol (244 mg, 2.74 mmol) and *n*-BuLi (2.19 mL of a 2.40 M solution in cyclohexane, 5.25 mmol) in Et$_2$O (10 mL), phosphine borane **7** (301 mg, 2.28 mmol) in Et$_2$O (5 mL) and Me$_2$PhSiCl (0.88 mL, 5.25 mmol) gave the crude product. Purification by flash chromatography on silica with petrol–Et$_2$O (98:2) as eluent gave adduct (*R*)-**10** (290 mg, 48%, 82:18 er by chiral HPLC) as a colourless oil which slowly crystallised to a white solid, $[\alpha]_D$ = +6.5 (*c* 1.05, CHCl$_3$).

Table 2, *entry 4*: Using general procedure A, (−)-sparteine (103 mg, 0.44 mmol), *N*-methyl morpholine (267 mg, 2.64 mmol) and *n*-BuLi (1.01 mL of a 2.40 M solution in cyclohexane, 2.42 mmol) in Et$_2$O (10 mL), phosphine borane **7** (290 mg, 2.20 mmol) in Et$_2$O (5 mL) and Me$_2$PhSiCl (0.41 mL, 2.42 mmol) gave the crude product. Purification by flash chromatography on silica with petrol–Et$_2$O (98:2) as eluent gave adduct (*R*)-**10** (131 mg, 22%, 87:13 er by chiral HPLC) as a colourless oil which slowly crystallised to a white solid, $[\alpha]_D$ = +4.8 (*c* 1.00, CHCl$_3$).

Table 2, *entry 5*: Using general procedure A, (−)-sparteine (91 mg, 0.39 mmol), PMDETA (404 mg, 2.33 mmol) and *n*-BuLi (0.89 mL of a 2.40 M solution in cyclohexane, 2.14 mmol) in Et$_2$O (10 mL), phosphine borane **7** (256 mg, 1.94 mmol) in Et$_2$O (5 mL) and Me$_2$PhSiCl (0.36 mL, 2.14 mmol) gave the crude product. Purification by flash chromatography on silica with petrol–Et$_2$O (98:2) as eluent gave adduct (*R*)-**10** (427 mg, 83%, 51:49 er by chiral HPLC) as a colourless oil which slowly crystallised to a white solid, $[\alpha]_D$ = +0.3 (*c* 1.05, CHCl$_3$).

4.7. (*S*)-*P*-(2,2-Diphenyl-2-hydroxyethyl)-*P*-methyl-*tert*-butylphosphine (*S*)-9

Table 3, *entry 1*: Using general procedure B, (−)-sparteine (171 mg, 0.73 mmol) and *n*-BuLi (0.32 mL of a 2.10 M solution in hexane, 0.67 mmol) in Et$_2$O (2 mL), phosphine borane **7** (80 mg, 0.61 mmol) in Et$_2$O (3 mL) and benzophenone (122 mg, 0.67 mmol) in Et$_2$O (3 mL) at −78 °C gave the crude product. Purification by flash chromatography on silica with petrol–EtOAc (19:1) as eluent gave adduct (*S*)-**9** (106 mg, 56%, 88:12 er by chiral HPLC) as a white solid, $[\alpha]_D$ = +20.4 (*c* 1.05, CHCl$_3$) {lit.,[14b] $[\alpha]_D$ = −14.7 (*c* 0.47, CHCl$_3$) for (*R*)-**9** of 96:4 er}; 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 (app t, J_{PH} = J_{HH} = 14.5 Hz, 1H, PCH_AH$_B$), 2.67 (dd, J_{HH} = 14.5 Hz, J_{PH} = 6.5 Hz, 1H, PCH$_A$$H_B$), 1.17 (d, J_{PH} = 13.5 Hz, 9H, CMe$_3$), 0.74 (d, J_{PH} = 10.0 Hz, 3H, PMe), 0.88–0.23 (m, 3H, BH$_3$); ^{13}C NMR (100.6 MHz, CDCl$_3$) δ: 147.7 (d, J_{PC} = 8.5 Hz, *ipso*-Ph), 145.3 (d, J_{PC} = 1.5 Hz, *ipso*-Ph), 128.3 (Ph), 128.2 (Ph), 127.2 (Ph), 125.3 (Ph), 34.2 (d, J_{PC} = 28.5 Hz, PCH$_2$), 28.0 (d, J_{PC} = 36.0 Hz, *C*Me$_3$), 24.7 (d, J_{PC} = 2.5 Hz, C*Me*$_3$), 6.5 (d, J_{PC} = 34.5 Hz, PMe) (some aromatic signals not resolved and one carbon overlaps with CDCl$_3$); HPLC: Daicel Chiracel OD, 1:19 v/v *i*PrOH–hexane, 0.5 mL min^{-1}, 254 nm, 11.1 min [(*R*)-**9**], 13.5 min [(*S*)-**9**]. Spectroscopic data were consistent with those reported in the literature.[14b]

Table 3, *entry 2*: Using general procedure C, (−)-sparteine (107 mg, 0.46 mmol) and *n*-BuLi (1.06 mL of a 2.37 M solution in hexane, 2.51 mmol) in Et$_2$O (10 mL), phosphine borane **7** (301 mg, 2.28 mmol) in Et$_2$O (5 mL) and benzophenone (457 mg, 2.51 mmol) in Et$_2$O (5 mL) at −78 °C gave the crude product. Purification by flash chromatography on silica with petrol–EtOAc (19:1) as eluent gave adduct (*S*)-**9** (139 mg, 19%, 87:13 er by chiral HPLC) as a white solid.

Table 3, *entry 3*: Using general procedure D, *n*-BuLi (0.27 mL of a 2.45 M solution in hexane, 0.67 mmol) in Et$_2$O (3 mL), phosphine borane **7** (80 mg, 0.61 mmol) in Et$_2$O (2 mL) and benzophenone (121 mg, 0.67 mmol) in Et$_2$O (3 mL) at −78 °C gave the crude product. No evidence of adduct *rac*-**9** was observed in the ^{1}H NMR spectrum of the crude product.

Table 3, *entry 4*: Using general procedure C, (−)-sparteine (109 mg, 0.47 mmol) and *n*-BuLi (1.08 mL of a 2.37 M solution in hexane, 2.56 mmol) in Et$_2$O (10 mL), phosphine borane **7** (307 mg, 2.33 mmol) in Et$_2$O (5 mL) and benzophenone (467 mg, 2.56 mmol) in Et$_2$O (5 mL) at −60 °C gave the crude product. Purification by flash chromatography on silica with petrol–EtOAc (19:1) as eluent gave adduct (*S*)-**9** (306 mg, 42%, 87:13 er by chiral HPLC) as a white solid, $[\alpha]_D$ = +18.7 (*c* 1.00, CHCl$_3$).

Table 3, *entry 5*: Using general procedure D, *n*-BuLi (0.44 mL of a 2.10 M solution in hexane, 0.92 mmol) in Et$_2$O (2 mL), phosphine borane **7** (110 mg, 0.83 mmol) in Et$_2$O (3 mL) and benzophenone (167 mg, 0.92 mmol) in Et$_2$O (3 mL) at −60 °C gave the crude product as a white solid. No evidence of adduct *rac*-**9** was observed in the ^{1}H NMR spectrum of the crude product.

Table 3, *entry 6*: Using general procedure C, (−)-sparteine (121 mg, 0.52 mmol) and *n*-BuLi (1.20 mL of a 2.37 M solution in hexane, 2.84 mmol) in Et_2O (10 mL), phosphine borane **7** (340 mg, 2.58 mmol) in Et_2O (5 mL) and benzophenone (517 mg, 2.84 mmol) in Et_2O (5 mL) at −50 °C gave the crude product. Purification by flash chromatography on silica with petrol–EtOAc (19:1) as eluent gave adduct (*S*)-**9** (402 mg, 50%, 81:19 er by chiral HPLC) as a white solid, $[\alpha]_D$ = +19.0 (*c* 1.10, $CHCl_3$).

Table 3, *entry 7*: Using general procedure D, *n*-BuLi (0.39 mL of a 2.14 M solution in hexane, 0.83 mmol) in Et_2O (2 mL), phosphine borane **7** (100 mg, 0.76 mmol) in Et_2O (3 mL) and benzophenone (152 mg, 0.83 mmol) in Et_2O (3 mL) at −50 °C gave the crude product. Purification by flash chromatography on silica with petrol–EtOAc (19:1) as eluent gave adduct *rac*-**9** (27 mg, 11%) as a white solid.

Table 3, *entry 8*: Using general procedure B, (−)-sparteine (188 mg, 0.80 mmol) and *n*-BuLi (0.34 mL of a 2.14 M solution in hexane, 0.73 mmol) in Et_2O (2 mL), phosphine borane **7** (88 mg, 0.67 mmol) in Et_2O (3 mL) and benzophenone (134 mg, 0.73 mmol) in Et_2O (3 mL) at −40 °C gave the crude product. Purification by flash chromatography on silica with petrol–EtOAc (19:1) as eluent gave adduct (*S*)-**9** (177 mg, 84%, 84:16 er by chiral HPLC) as a white solid, $[\alpha]_D$ = +13.8 (*c* 1.10, $CHCl_3$).

Table 3, *entry 9*: Using general procedure C, (−)-sparteine (83 mg, 0.36 mmol) and *n*-BuLi (0.93 mL of a 2.16 M solution in hexane, 2.00 mmol) in Et_2O (10 mL), phosphine borane **7** (240 mg, 1.82 mmol) in Et_2O (5 mL) and benzophenone (364 mg, 2.00 mmol) in Et_2O (5 mL) at −40 °C gave the crude product. Purification by flash chromatography on silica with petrol–EtOAc (19:1) as eluent gave adduct (*S*)-**9** (396 mg, 69%, 78:22 er by chiral HPLC) as a white solid, $[\alpha]_D$ = +8.5 (*c* 1.10, $CHCl_3$).

Table 3, *entry 10*: Using general procedure D, *n*-BuLi (0.35 mL of a 2.14 M solution in hexane, 0.74 mmol) in Et_2O (3 mL) phosphine borane **7** (89 mg, 0.68 mmol) in Et_2O (2 mL) and benzophenone (135 mg, 0.74 mmol) in Et_2O (3 mL) at −40 °C gave the crude product. Purification by flash chromatography on silica with petrol–EtOAc (19:1) as eluent gave adduct *rac*-**9** (61 mg, 29%) as a white solid.

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