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Lithium Borohydride for Achiral and Stereospecific Reductive Boronation at Phosphorus: Lack of Electronic Effects on Stereoselective Formation of Alkoxyphosphonium Salts

Sulaiman S. Al Sulaimi,[a] Kamalraj V. Rajendran,[a] and Declan G. Gilheany*[a]

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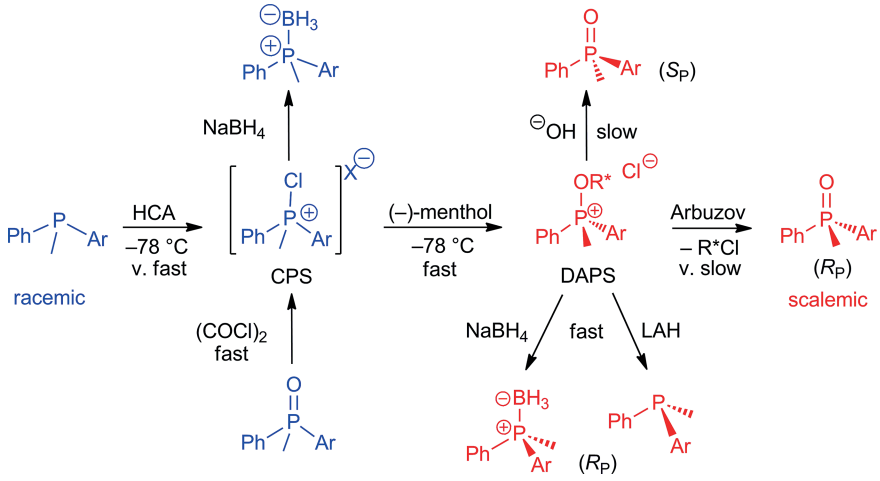
We report $LiBH_4$ as a preferred, simple and effective reagent for reductive boronation of achiral and racemic chlorophosphonium salts (CPS) and for diastereomeric alkoxyphosphonium salts (DAPS), both of which are, in turn, easily generated from either the corresponding phosphane or, more conveniently, the phosphane oxide. Further, we have shown that the DAPS reduction/boronation could be achieved with complete stereocontrol to give *scalemic* phosphane–borane directly in excellent yield and enantiomeric excess (*ee*). This new methodology was employed to investigate the effects of aryl substitution on the outcome of dynamic kinetic resolution of arylmethylphenylphosphanes and phosphane oxides via DAPS. It was found that substitution at the *ortho* position strongly affects the degree of stereoselection. However, surprisingly, we confirmed that there was no variation of stereoselectivity seen with the electronic effect of substituents on the *para* position.

Introduction

The use of scalemic *P*-stereogenic phosphane ligands in asymmetric catalysis is a well developed topic[1] and tremendous effort has been therefore focused on the synthesis of *P*-stereogenic compounds over the last few decades.[2,3] We have been working on this challenging topic for some time and, to date, have developed the only dynamic kinetic resolution approaches for both phosphanes and their oxides, as shown in Scheme 1.[4–7] The system is based on the reaction of a chlorophosphonium salt (CPS) with chiral non-racemic alcohol to generate a high yield of diastereomerically enriched alkoxyphosphonium salt (DAPS). The CPS can be generated under either Appel conditions from the phosphane[4a,4c] or by reaction of the oxide with oxalyl chloride.[4d,4e] We propose that the dynamic nature of the resolution arises through the extremely rapid interconversion of the enantiomers of the CPS.[5] The resultant DAPS can un-



Scheme 1. X = PCA or Cl; HCA = hexachloroacetone; PCA = pentachloroacetone; CPS = chlorophosphonium salt; DAPS = diastereomeric alkoxyphosphonium salt; blue: racemic; red: stereoenriched.

[a] Centre for Synthesis and Chemical Biology, School of Chemistry, University College Dublin,
Belfield, Dublin 4, Ireland
E-mail: declan.gilheany@ucd.ie

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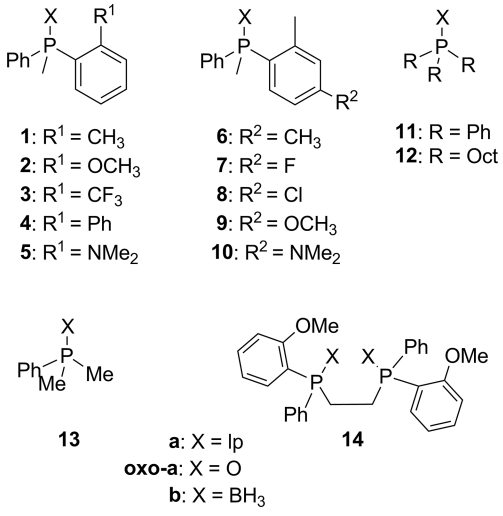
dergo slow Arbusov collapse in the normal manner or may be intercepted by metal hydride reduction to either the corresponding phosphane or its borane.[4d,6] Recently we showed that the other enantiomer of the oxide can be produced by hydrolysis of the DAPS, allowing access to both enantiomers from a single chirality source, effectively a type of dual resolution.[7]

Early on in our attempts to study the mechanism and other decisive features accountable for the selectivity, we examined the effect of aryl substituents on the oxidation of arylmethylphenylphosphanes **1a**–**9a** (Scheme 2) under the asymmetric Appel conditions and found that there was apparently little electronic effect on the selectivity.[4a,4c] However, at the time, we could only assay the effect by measuring the % *ee* of the product phosphane oxides,[4c] making any conclusions about the source of selectivity tentative at best.



Scheme 2. Achiral and racemic phosphanes, oxides and boranes studied.

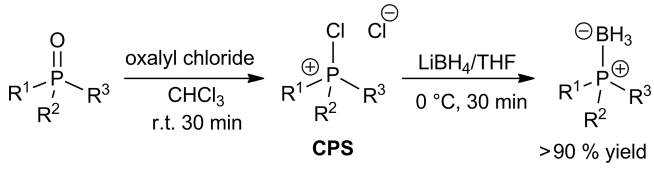
More recently, we found that the % *ee* values observed in the oxide or borane products do not truly reflect the selectivity of the reaction. Thus, both the Arbusov collapse and the hydride reduction of the intermediate diastereomeric alkoxyphosphonium salts (DAPS) are subject to a selectivity-eroding process.[4c,4d] We were able to determine this because we devised a way to determine the true selectivity of the reaction by measuring the % *de* of the intermediate DAPS by ^{31}P-NMR spectroscopy.[4d,8]

With a method in hand to determine the true selectivity, we were anxious to apply it to the case of the aryl(methyl)-phenylphosphanes in hopes to gain a better understanding of the selectivity process. We now report these studies, which were also greatly facilitated by our concurrent development of an improved method for the interception of the DAPS using $LiBH_4$ to produce scalemic phosphane–borane directly with high yield and stereospecificity.

Results and Discussion

Improved Achiral Reduction of Phosphane Oxides via CPS

Reduction of phosphane oxides has been a problem for more than four decades.[9] Recently in our laboratory, we discovered a convenient method to convert phosphane oxide to phosphane–borane directly using oxalyl chloride followed by $NaBH_4$. Reaction of the oxide with oxalyl chloride results in its deoxygenation with release of CO and CO_2 leaving behind solely the derived chlorophosphonium chloride (CPS), confirmed by ^{31}P-NMR of the reaction mixture. Subsequent in situ treatment of the CPS with sodium borohydride in diglyme resulted in clean conversion to phosphane–borane, all reactions at room temperature.[6a,10] Although this method is a superior way for converting phosphane oxides to phosphane–boranes, the use of $NaBH_4$ had certain limitations (vide infra), which we wished to overcome. After screening a number of hydride reagents ($NaCNBH_3$, Alpine borane, DIBAl-H, Red-Al) we found that $LiBH_4$ is a superior agent for this transformation (Scheme 3) and we digress to describe this for the achiral series.



Scheme 3. Reduction of phosphane oxide using oxalyl chloride and $LiBH_4$.

In the new protocol, phosphane oxide is treated with oxalyl chloride in chlorinated solvent at room temperature. After complete conversion to CPS (monitored by ^{31}P NMR), the solvent and any excess reagent are removed under vacuum and the residue redissolved for the next step. Treatment of the resulting solution at 0 °C with $LiBH_4$ in THF then results in rapid, clean and complete conversion of oxides to the corresponding phosphane–boranes.

However we faced a problem during the work up of the reaction: the product became contaminated with varying amounts of oxide. This may arise by deboronation and subsequent air oxidation. Extensive development was carried out to develop the best work up conditions to avoid this problem (Table 1). It was found that (a) changing the redissolution solvent to toluene, and (b) quenching the reaction by adding the reaction mixture to a HCl solution at 0 °C dropwise enabled the easy isolation of the phosphane–borane product with excellent yield. This methodology was then applied to a representative variety of alkyl and aryl achiral and racemic phosphane oxides, **oxo-1a** and **oxo-11a** to **oxo-14a**, on both milligram and gram scale. In each case, reaction with oxalyl chloride gave a single species in the ^{31}P NMR (δ_P = 63.3–107.0 ppm), and its reduction gave complete conversion (δ_P = 2.8–20.6 ppm) and excellent isolated yield (90–98%).

Table 1. Results of different workup protocols for achiral reduction.

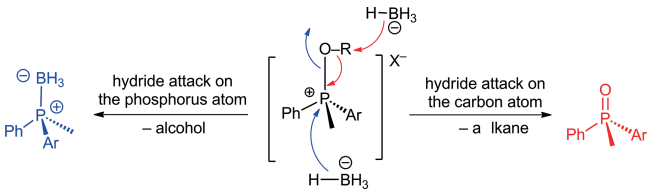
Conditions	% of **1a**[e]	% of **oxo-1a**[e]	% of **1b**[e]
IPA/H_2O[a]	3.0	7.0	90.0
DCM/HCl[b]	4.6	10.7	84.7
DCM/HCl[c]	2.0	2.0	96.0
Toluene/HCl[d]	0	0	100

[a] 2-propanol/water mixture added via syringe to the reaction mixture in DCM. [b] Hydrochloric acid solution added via syringe to the reaction mixture in DCM. [c] Reaction mixture in DCM added via syringe to hydrochloric acid solution. [d] Reaction mixture in toluene added via syringe to hydrochloric acid solution at 0 °C. [e] The amount of phosphane (**1a**), oxide (**oxo-1a**) and borane (**1b**) (as judged by ^{31}P NMR).

$LiBH_4$ has greater utility over $NaBH_4$ in this process for the following reasons: (1) unlike $NaBH_4$ (0.5 M diglyme), $LiBH_4$ can be used as a 2 M solution in THF which makes the isolation of the product phosphane–borane easier; (2) $LiBH_4$/THF is 4 times cheaper than $NaBH_4$/diglyme and (3) there is a significant advantage in the reduction of alkoxy-phosphonium salts (*see next section*).

Stereospecific Reduction of Diastereomerically Enriched Alkoxyphosphonium Salts (DAPS) Obtained from CPS

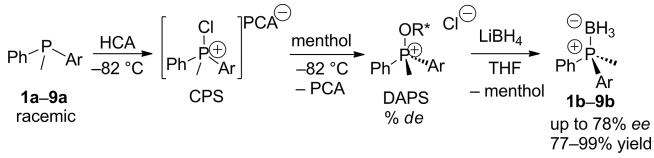
In our previous work, we had also shown that sodium borohydride could be used for stereospecific reduction of both enantimerically pure phosphane oxides[6a] and diastereomeric alkoxyphosphonium salts (DAPS, Scheme 1).[4d,6b] However a notable side reaction in the latter process was hydride attack on carbon to give phosphane oxide and alkane (Scheme 4),[11] which reduced the yield of the phosphane–borane. We were therefore delighted to find (see below) that lithium borohydride favoured attack at phosphorus to a much greater degree than its sodium counterpart. Together with the other advantages of $LiBH_4$ mentioned above, this makes it very much the superior reagent.



Scheme 4. Side reaction to produce phosphane oxide during hydride reduction/boronation of alkoxy phosphonium salt (minimised with $LiBH_4$).

With a more satisfactory reduction methodology in hand, we proceeded to apply it to a study of the effect of substitution in our dynamic resolution of arylmethylphenylphosphanes and the corresponding phosphane oxides. We had two linked objectives:
(a) To study the effect on selectivity of *ortho* and *para*-substitution in reactions with aryl(methyl)phenylphosphanes and oxides by measuring the % *de* of the DAPS leading, hopefully, to some insight into the mechanism of selectivity;
(b) To examine the utility of $LiBH_4$ for stereospecific reduction of the DAPS to synthesize scalemic phosphane–boranes, providing hopefully a better alternative to the selectivity-eroding Arbusov step.

As indicated in Scheme 1, we have two routes to CPS: derived from either the phosphane or the corresponding oxide. In the case of the phosphane, our protocol for the generation and reaction of the CPS calls for addition of the phosphane to the mixture of menthol and HCA at –82 °C in toluene.[12] In the ^{31}P-NMR spectrum of the mixture,[13] two transient peaks are seen at approx. δ = 63–69 ppm, corresponding to the DAPS, allowing measurement of the % *de*. The DAPS were then reduced in the same pot by adding $LiBH_4$ in THF at –82 °C to give the corresponding scalemic phosphane–boranes, Scheme 5. The reductions were performed at low temperature as a precaution to ensure that Arbusov collapse was minimised.



Scheme 5. Generation of DAPS from phosphanes and their subsequent reduction using $LiBH_4$ to give phosphane–borane directly.

The results for a variety of substituted phosphanes (**1a**–**9a**, checked with both isomers of menthol) are shown in Table 2. A gram scale synthesis of phosphane–borane **1b** was also undertaken to demonstrate the efficiency of this method. The results confirm that substitution at the *ortho* position in aryl(methyl)phenylphosphanes strongly affects the degree of stereoselection, with **1a** giving the best selectivity compared to all the phosphanes studied. In contrast for example, **2a** showed much lower stereoselection, and requires the use of a different chiral alcohol to get acceptable selectivity.[14] The study also confirmed that there was no variation of stereoselectivity on changing between EDG or EWG groups (see **6a**–**9a**) on the *para* position of the aryl ring of the aryl(methyl)phenylphosphanes: both lead to poorer selectivity. This is surprising because it might be expected that there would be a substantial change in the charge density on phosphorus during nucleophilic attack by alcohol, in turn prompting expectation of an electronic effect on the process.

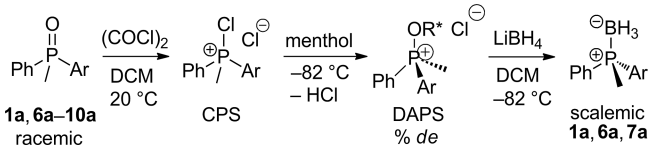
These results were also checked by using CPS derived from the easier-to-handle racemic phosphane oxide.[4d,4e] In this protocol the phosphane oxide was treated with oxalyl chloride to generate the intermediate CPS, which was then treated with chiral non-racemic menthol at –82 °C to form unequal amounts of DAPS[13] which was again treated with $LiBH_4$, in the same pot, at –82 °C to produce scalemic phosphane–boranes (Scheme 6). This is known to show a similar but slightly improved selectivity due to the change of counterion and the absence of pentachloroacetone by-product.[4e] The results of this cross comparison are also given in Table 2 (**oxo-1a** and **oxo-6a**–**oxo-10a**) and again the unusual (non)selectivity pattern was found with EWG and

Table 2. Generation and stereospecific reduction of DAPS to scalemic phosphane.

Phosphane[a]/ Phosphane oxide[b]	R^1 *ortho*	R^2 *para*	DAPS *de* [%][c]	Phosphane–borane *ee* [%][d]
1a	Me	H	82	78 (*R*)
2a	OMe	H	51	47 (*R*)
3a	CF_3	H	72	71 (*R*)
4a	Ph	H	75	74 (*R*)
5a	NMe_2	H	72	65
6a	Me	Me	80	78 (*R*)
7a	Me	F	78	75 (*R*)
8a	Me	Cl	79	78
9a	Me	OMe	80	78
oxo-1a	Me	H	88	84 (*R*)
oxo-6a	Me	Me	83	78 (*R*)
oxo-7a	Me	F	82	78 (*R*)
oxo-8a	Me	Cl	84	n.d.
oxo-9a	Me	OMe	84	n.d.
oxo-10a	Me	NMe_2	80	n.d.

[a] Reaction conditions: phosphane (0.3 mmol), (–)-menthol (0.4 mmol), HCA (0.3 mmol), $LiBH_4$ (1.5 mmol), all at –82 °C, crude ^{31}P NMR yields of borane 77–99%. [b] Reaction conditions: phosphane oxide (0.3 mmol), oxalyl chloride (0.9 mmol), (–)-menthol (0.5 mmol), $LiBH_4$ (1.5 mmol), all at –82 °C, crude ^{31}P NMR yields of borane: 88–99%. [c] *de* values of the DAPS with ^{31}P chemical shifts ca. 63–69 ppm using both (–)-menthol or (+)-menthol as chiral auxiliary (see the Supporting Information). [d] Determined by CSP HPLC, absolute configuration determined by comparison to literature where noted; n.d.: not determined.

EDG groups both giving lower selectivity. A gram scale synthesis of phosphane–borane **1a** using this protocol was again also undertaken for comparison.



Scheme 6. Generation of DAPS from phosphane oxides and their subsequent reduction using $LiBH_4$ to give phosphane–borane directly.

Table 2 also shows that there is a high degree of stereospecificity[15] in the $LiBH_4$ reduction process, making it notably better than $NaBH_4$[4d,6b] for this application. There is still a small amount of erosion of the stereoselection in nearly every case studied. We speculate that this is due to a difference in the rates of reaction of the major and minor diastereomers in the now minor but still competing reaction at carbon, see Scheme 4.

Conclusions

Lithium borohydride is an excellent reagent for achiral and racemic reduction/boronation of phosphane oxide via chlorophosphonium salt (CPS) to the borane-protected phosphane. The reagent has greater utility in the process than the sodium analogue.

Lithium borohydride is also an excellent reagent for the high-yield stereospecific reduction/boronation of diastereomeric alkoxyphosphonium salts (DAPS), which are generated from the CPS by reaction with chiral non-racemic alcohol. The CPS for this purpose can be generated either from the oxide or the phosphane itself, with similar results.

The methodologies were tested on a series of *ortho*- and *para*-substituted aryl(methyl)phenylphosphanes and their oxides. During the study, the selectivity in the reaction of the alcohol with the CPS was assayed by measuring the % *de* of the derived DAPS. The results from these experiments show that the substitution at the *ortho* position strongly affects the degree of stereoselection but the selectivity was almost the same on varying the electronic nature of the *para* substitution. The latter result implies that there is no net transfer of charge at phosphorus in the stereoselecting step. The implications of this for the mechanism will be explored in future work.

Experimental Section

General Experimental: All reactions were carried out under a nitrogen atmosphere in Schlenk-type reaction vessels. Dry degassed solvents were stored in Young-type flasks over molecular sieves (4 Å). Air and moisture sensitive liquids and solutions were transferred via syringe. The water content in all solutions as monitored by titration on an Aquamax KF instrument was less than 5 ppm v/v. Special precautions were taken to minimise water content of the solutions (see below under Stock Solutions).

Reagents and solvents were purchased from commercial suppliers and used as supplied unless otherwise stated. THF, DCM, toluene and diethyl ether were degassed and dried by passing through a Grubbs type Pure Solv-400–3-MD solvent purification system supplied by Innovative Technology Inc. Oxygen-free nitrogen was obtained from BOC gases and was passed through a column filled with dry molecular sieves (4 Å).

Thin-layer chromatography (TLC) was performed on Merck precoated Kieselgel $60F_{254}$ aluminium plates with realization by UV irradiation. Flash column chromatography was performed on Davisil particle size 0.040–0.063 mm. NMR spectra were recorded at 25 °C on Varian VNMRS 300, 400 and 600 spectrometers. Assignments were based on standard ^1H-^1H and ^1H-^{13}C two-dimensional techniques and, when required, NOE measurements. Peak integrations were determined by using a MestreNova software package. All NMR samples of potentially air-sensitive compounds were made up under a nitrogen atmosphere in dry degassed $CDCl_3$.

High-performance liquid chromatography was performed on an Agilent Technologies 1200 series instrument equipped with a 6 column switching device. HPLC grade solvents were purchased from Aldrich and Lennox Supplies Ireland and used as supplied. All samples were filtered through an Acrodisc CR 13 mm syringe filter with 0.2 μm PTFE prior to injection.

Phosphanes **1a**,[4c] **2a**,[4a] **3a**–**9a**,[4c] and oxides **oxo-1a**,[4c] **oxo-6a**–**oxo-9a**,[4c] **oxo-13a**[16] and **oxo-14a**[4c] were synthesised by the literature reported procedures, except the case of **oxo-10a**.

Oxo-10a: ^1H NMR ($CDCl_3$, 600 MHz): δ = 7.65 (dd, J = 12, J = 7 Hz, 2 H), 7.51 (dd, J = 13, J = 8 Hz, 1 H), 7.46 (t, J = 8 Hz, 1 H), 7.40 (t, J = 8 Hz, 2 H), 6.54 (d, J = 9 Hz, 1 H), 6.48 (s, 1 H), 2.99 (s, 6 H), 2.29 (s, 3 H), 1.96 (d, J = 13 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 151 MHz): δ = 152.7 (d, J = 2 Hz), 143.3 (d, J = 9 Hz), 136.0 (d, J = 100 Hz), 133.2 (d, J = 13 Hz), 131.1 (d, J = 3 Hz),

130.5 (d, J = 10 Hz), 128.5 (d, J = 12 Hz), 116.8 (d, J = 113 Hz), 114.6 (d, J = 11 Hz), 108.4 (d, J = 13 Hz), 40.0, 22.0 (d, J = 5.0 Hz), 17.5 (d, J = 75 Hz) ppm. ^{31}P NMR ($CDCl_3$, 243 MHz): δ = 31.4 ppm. HRMS (ES) m/z: Calculated for $[MH]^+$ $C_{16}H_{21}NOP$ 274.1361, found 274.1362.

The product boranes are mostly also known and fully characterised in the literature, including in many cases absolute configurations: **1b**,[6b,17] **2b**,[6b,18] **3b**,[6b,19] **4b**,[6b,20] **5b**,[21] **6b**,[6b] **7b**,[6b] except for the cases of **8b** and **9b**.

8b: ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 7.62 (m, 1 H), 7.57 (m, 2 H), 7.48 (m, 1 H), 7.43 (m, 2 H), 7.31 (d, J = 9 Hz, 1 H), 7.21 (s, 1 H), 2.17 (s, 3 H), 1.87 (d, J = 10 Hz, 3 H), 1.26–0.80 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 151 MHz): δ = 144.4 (d, J = 9 Hz), 138.0 (d, J = 3 Hz), 133.9 (d, J = 11 Hz), 131.9 (d, J = 9 Hz), 131.6 (d, J = 10 Hz), 131.3 (d, J = 3 Hz), 130.7 (d, J = 55 Hz), 129.1 (d, J = 10 Hz), 126.9 (d, J = 55 Hz), 126.4 (d, J = 11 Hz), 21.7 (d, J = 5.0 Hz), 13.0 (d, J = 41 Hz) ppm. ^{11}B NMR ($CDCl_3$, 160 MHz): δ = –36.7 ppm. ^{31}P NMR ($CDCl_3$, 243 MHz): δ = 10.6 ppm. HRMS (ES) m/z: Calculated for $[M]^+$ $C_{14}H_{17}BClP^+$ 260849, found 260852.

9b: ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 7.67 (m, 1 H), 7.56 (m, 2 H), 7.44 (m, 1 H), 7.40 (m, 2 H), 6.75 (m, 1 H), 6.84 (m, 1 H), 3.82 (s, 3 H), 2.16 (s, 3 H), 1.85 (d, J = 10 Hz, 3 H), 1.26–0.81 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 151 MHz): δ = 162.3, 144.4 (d, J = 9 Hz), 134.8 (d, J = 12 Hz), 131.4 (d, J = 10 Hz), 130.8 (d, J = 2 Hz), 130.8 (d, J = 2 Hz), 128.9 (d, J = 10 Hz), 117.8 (d, J = 9 Hz), 11.3 (d, J = 11 Hz), 55.4, 22.0 (d, J = 5.0 Hz), 13.1 (d, J = 42 Hz) ppm. ^{11}B NMR ($CDCl_3$, 160 MHz): δ = –36.3 ppm. ^{31}P NMR ($CDCl_3$, 243 MHz): δ = 8.9 ppm. HRMS (ES) m/z: Calculated for $[M]^+$ $C_{15}H_{20}BOP^+$ 258.1345, found 258.1348.

Achiral Reduction of Phosphane Oxides to Phosphane–Boranes Using $LiBH_4$

Exemplar: Methyl(phenyl)(*o*-tolyl)phosphane–Borane (1b): Oxalyl chloride (neat, 0.13 mL, 1.5 mmol, 1.5 equiv.) was added dropwise at room temperature to the solution of phosphane oxide (0.23 g, 1 mmol) in dry $CHCl_3$ (3 mL) in 25 mL dry Schlenk tube and the reaction was allowed to stir for 30 min under nitrogen. A sample (0.1 mL) of the mixture was added to $CDCl_3$ (0.6 mL) for ^{31}P-NMR to confirm full conversion of phosphane oxide to chlorophosphonium salt (δ_P = 70.1 ppm). Solvent and excess oxalyl chloride were then completely removed through a dedicated cold trap connected to Schlenk manifold until the syrupy residue formed a light off-white foam. Toluene (3.0 mL) was added to the reaction mixture to redissolve CPS and the mixture was cooled to 0 °C and $LiBH_4$ in THF (1.5 mL, 3.0 mmol, 3.0 equiv.) added dropwise via syringe. The reaction mixture was stirred under nitrogen at 0 °C for 1 h and quenched into HCl solution (1 M in deionised water). The aqueous layer was extracted with toluene (2 × 5 mL) and the combined organic layers were washed with deionised water (3 × 5 mL) and dried with anhydrous $MgSO_4$. The drying agent was removed by filtration, and the solvent was removed in vacuo. to give colourless oil, which was eluted through a silica plug with cyclohexane/ethyl acetate (50:50). Solvent removal in vacuo yielded the pure phosphane–borane. (0.22 g, 97%), ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.72–7.12 (m, 9 H, Ar), 2.19 (s, 3 H, $ArCH_3$), 1.87 (d, $^2J_{PH}$ = 9.9 Hz, 3 H, CH_3), 1.66–0.81 (br., 3 H, BH_3) ppm. ^{31}P NMR ($CDCl_3$, 121 MHz): δ = 10.3 (ref.[6a] 10.2) ppm.

Triphenylphosphane–Borane (11b): From triphenylphosphane oxide (1.0 g): (0.95 g, 95%) ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.73–7.52 (m, 15 H, Ar), 1.87–0.95 (br., 3 H, BH_3) ppm. ^{31}P NMR ($CDCl_3$, 121 MHz): δ = 20.6 (ref.[6a] 21.5) ppm.

Trioctylphosphane–Borane (12b): From trioctylphosphane oxide (0.38 g): (0.37 g, 98%) ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.50–1.20 (m, 42 H) ppm, 0.83–0.79 (m, 9 H) ppm. ^{31}P NMR ($CDCl_3$, 121 MHz): δ_P = 14.4 (ref.[22] 15.6) ppm.

Dimethylphenylphosphane–Borane (13b): From dimethylphenylphosphane oxide (0.15 g): (0.14 g, 95%) ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.88–7.28 (m, 5 H, Ar), 1.69 (d, $^2J_{PH}$ = 10.5 Hz, 6 H, CH_3) 1.40–0.39 (br., 3 H, BH_3) ppm. ^{31}P NMR ($CDCl_3$, 121 MHz): δ_P = 2.8 ppm (ref.[23] 2.8 ppm).

1,2-Ethanediylbis[(o-anisylphenyl)phenylphosphane–Borane] (14b): From 1,2-ethanediylbis[(*o*-anisylphenyl)phenylphosphane oxide] (0.11 g): (0.10 g, 90%), ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.03–6.93 (m, 18 H, Ar), 3.75 (s, 6 H, OCH_3), 2.72 (m, 4 H, PCH_2), 1.67–0.99 (br., 6 H, BH_3) ppm. ^{31}P NMR ($CDCl_3$, 300 MHz): δ_P = 18.3 ppm (ref.[6a] 18.5 ppm).

Synthesis of Scalemic Phosphane–Boranes from Racemic Phosphanes

Stock Solutions of Menthol, Phosphane and HCA: Flask A: a flame-dried nitrogen-filled 250 mL Schlenk flask was charged with dry toluene (200 mL) (from Grubbs' system) and menthol (4.28 g, 27.4 mmol, 0.137 M, 1.2 equiv.). Flask B: a 250 mL Schlenk flask was kept in the oven (120 °C) for 1 h, then was flame-dried, put under vacuum and back-filled with nitrogen. Molecular sieves (4 Å) were added to the flask by funnel and the flask and sieves were flame-dried for approx. 2 min, put under vacuum and back-filled with nitrogen. This process was repeated three times and the flask kept under under nitrogen till cooled. The contents of Flask A were then transferred via syringe to a Flask B. The same procedures were applied for HCA (5.29 g, 22.8 mmol, 0.10 M, 1.0 equiv.) and phosphane (0.10 M, 1.0 equiv.). In each case the solutions were kept overnight and analysed by KF titration before use.

Exemplar Reaction with Methyl(phenyl)(*o*-tolyl)phosphane (1a) on Small Scale: A flame-dried and degassed Schlenk flask fitted with a stirring bar and septum was charged with phosphane stock solution (3.0 mL, 0.33 mmol, 0.10 M, 1.0 equiv.). The flask was then immersed in ethyl acetate/ liquid nitrogen bath and cooled to –82 °C and (–)-menthol stock solution (3.0 mL, 0.41 mmol, 0.137 M, 1.2 equiv.) was added dropwise via a syringe, followed by a HCA stock solution (3.0 mL, 0.33 mmol, 0.10 M, 1.0 equiv.) also dropwise through a syringe. When all the HCA had been added, the reaction was stirred at –82 °C for 30 min under nitrogen. Sampling of DAPS for ^{31}P-NMR was then performed (see ref.[12]). Then the solvent was completely removed from the reaction mixture in the flask under vacuum at 0 °C. The residue was dissolved in dry DCM (3 mL) and cooled to –82 °C. A solution of $LiBH_4$ in THF (0.75 mL, 1.5 mmol, 5 equiv.) was added dropwise through a syringe. The reaction mixture was stirred and warmed under nitrogen from to room temperature overnight. The reaction mixture was then cooled to 0 °C and quenched with HCl solution 1 M in deionized water. The aqueous layer was extracted with DCM (2 × 5 mL) and the combined organic layers were washed with deionised water (3 × 5 mL), dried with anhydrous $MgSO_4$. The drying agent was removed by filtration, and the solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel ethyl acetate/cyclohexane (6:94) yielding the phosphane–borane as a colourless oil (0.06 g, 80%). A sample (approx. 1.5 mg) was dissolved in the HPLC solvent mixture (1.5 mL) and analysed (CHIRALPAK® ASH column. 98:2; retention times 9.4, 10.6 min), heptane/EtOH, 1 mL/min: 78% *ee*. A further sample (20 mg) was dissolved in $CDCl_3$ (0.7 mL) and used for ^{1}H NMR and ^{31}P NMR studies.

Similar procedures were followed to generate other scalemic phosphane–boranes **1b-9b** from the corresponding phosphanes **1a-9a** on

small scale (see Supporting Information for ^{31}P NMR and HPLC data).

The procedure with methyl(phenyl)(*o*-tolyl)phosphane **1a** was also repeated in a similar manner on a larger scale: phosphane stock solution (47.0 mL, 4.7 mmol, 0.10 M, 1.0 equiv.); (–)-menthol stock solution (47.0 mL, 6.4 mmol, 0.137 M, 1.2 equiv.) and HCA stock solution (47 mL, 4.7 mmol, 0.10 M, 1.0 equiv.) to yield 0.89 g (83%) of product (78% *ee*) after column chromatography.

Scalemic-methyl(phenyl)(*o*-tolyl)phosphane–Borane (1b): (0.89 g, 83%), ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.71–7.15 (m, 9 H, Ar), 2.17 (s, 3 H, $ArCH_3$), 1.83 (d, $^2J_{PH}$ = 9.9 Hz, 3 H, CH_3), 1.68–0.77 (br., 3 H, BH_3) ppm. ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 10.3 ppm. (ref.[6a] 10.2) ppm.

Synthesis of Scalemic Phosphane–Boranes from Racemic Phosphane Oxides

Exemplar: Reaction with Methyl(phenyl)(*o*-tolyl)phosphane Oxide (oxo-1a): Oxalyl chloride neat (0.10 mL, 1.2 mmol, 1.2 equiv.) was added dropwise at room temperature to a solution of phosphane oxide (0.25 g, 1.0 mmol, 1.2 equiv.) in 7.0 mL of dry DCM in 25 mL Young's tube and the reaction was allowed to stir for 2 h. A sample of 0.1 mL of the mixture was added to 0.60 mL of $CDCl_3$ for ^{31}P-NMR to confirm full conversion of phosphane oxide to CPS. DCM and excess oxalyl chloride were completely removed through a dedicated cold trap connected to Schlenk manifold until the syrupy residue forms light off-white foam. 4.0 mL of dry DCM was added to the reaction mixture to dissolve CPS again. The reaction mixture was cooled to –82 °C using ethyl acetate/N_2 mixture and (–)-menthol stock solution (11.7 mL, 1.6 mmol, 0.137 M, 1.6 equiv.) was added in dry toluene dropwise to the reaction mixture. The reaction was maintained at –82 °C for 3 h and then warmed to 0 °C and kept in an ice bath. Sampling of DAPS for ^{31}P-NMR was then performed (see ref.[13]).

Then the solvent was completely removed from the reaction mixture in the flask under vacuum at 0 °C. The residue was dissolved in dry DCM (3 mL) and was cooled to –82 °C. $LiBH_4$ in THF (0.75 mL, 1.5 mmol, 5 equiv.) was added dropwise through a syringe. The reaction mixture was stirred under nitrogen –82 °C to room temperature overnight. The reaction mixture was cooled to 0 °C and quenched with HCl solution 1 M in deionized water. The aqueous layer was extracted with DCM (2 × 5 mL) and the combined organic layers were washed with deionized water (3 × 5 mL), dried with anhydrous $MgSO_4$. The drying agent was removed by filtration, and the solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel ethyl acetate/cyclohexane (6:94) yielding the phosphane–borane as a colourless oil (0.2 g, 88%). HPLC and NMR analysis as above [CHIRALPAK® ASH column, (98:2), heptane/EtOH, 1.0 mL/min: 84% *ee*, R_t = 9.5, 11.7 min].

Similar procedures were followed to generate other scalemic phosphane–boranes **6b-7b** from the corresponding **oxo-6a**, **oxo-7a**, (see Supporting Information). The same procedure but excluding the hydride reduction was performed for **oxo-8a**–**oxo10a**.

Supporting Information (see footnote on the first page of this article): Examplar ^1H, ^{31}P spectra of phosphane, phosphane oxide, CPS and phosphane–boranes. ^{31}P-NMR spectra of all DAPS species and HPLC chromatograms for all product phosphane–boranes. Characterisation of phosphane oxide **10a** and boranes **8b/9b**.

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[12] The temperature of –82 °C was used for operational reasons in our laboratory. We have previously shown that reaction at –78 °C gives only very slightly lower selectivity (see ref.[4d]).

[13] Sampling DAPS: 0.5 mL of the reaction mixture was syringed into a separate Schlenk tube at 0 °C and the solvent was completely removed under vacuum at 0 °C. The residue was dissolved in dry $CDCl_3$ (0.7 mL) at 0 °C and transferred to a cold NMR tube. The % *de* was measured by ^{31}P NMR with 128 scans and 3 second relaxation delay at 25 °C.

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