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Filling the Gaps in the Challenging Asymmetric Hydroboration of 1,1-Disubstituted Alkenes with Simple Phosphite-Based Phosphinooxazoline Iridium Catalysts

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We have identified a readily accessible phosphinooxazoline-based phosphite-oxazoline catalytic system, (*S*)-4-isopropyl-2-{2-[(3,3′,5,5′-tetra-*tert*-butyl-1,1′-biphenyl-2,2′-diyl)phosphite]-phenyl}-2-oxazoline (**L1 a**), that can hydroborate a range of 1,1-disubstituted aryl olefins with high enantioselectivity (up to 94%), excellent yields and perfect regioselectivity. The new phosphite-oxazoline ligands efficiently hydroborate a broader range of olefins than previous phosphinooxazoline ligands. In particular, a wide range of α-*tert*-butylstyrenes can be hydroborated that bear aryl substituents with different electronic and steric properties, which complements previous results with N-heterocyclic copper catalysts, the only other system reported to date that has achieved these reactions.

Introduction

Many of today's pharmaceutical, fragrance and agrochemical compounds, and the chemicals used in functional materials are required as pure enantiomers.[1] As a result, the industrial production of enantiopure chiral compounds is gaining importance and synthetic procedures are constantly evolving towards high selectivity and productivity, atom economy, operational simplicity, cost efficiency, environmental friendliness and low energy consumption. In comparison to other synthetic approaches, asymmetric catalysis is a smart strategy. A small amount of catalyst can produce large quantities of the desired chiral compound with only a few reaction steps and synthetic operations, thus bringing down the overall production cost, and decreasing the amount of by-products.

Chiral organoboron compounds have received a great deal of attention lately.[2] They are valuable organic intermediates because the C–B bond can be readily transformed to chiral C–N, C–O and C–C bonds.[2c,3] The synthesis of these compounds by transition-metal catalyzed asymmetric hydroboration is attracting considerable interest. However, whereas the asymmetric hydroboration of monosubstituted olefins (i.e., styrenes) and internal 1,2-disubstituted olefins (i.e., norbornadiene) has been well studied, the hydroboration of 1,1-disubstituted olefins remains a challenge.[2,4] This is because the chiral transition metal catalyst has difficulty in controlling not only the specific boration at the desired terminal β position rather than at the more substituted α-position (most catalysts favour Markovnikov regioselectivity)[5] but also the face selectivity coordination (due to the presence of the two relatively similar substituents at the geminal position). To date, high regio- and enantioselectivities have been reported in only three publications, with limited substrate scope (Scheme 1).[6] In 2008 Soderquist and co-workers reported the hydroboration of 1,1-disubstituted alkenes by using stoichiometric quantities of chiral boranes with *ee* values between 28 and 92% (Scheme 1 a).[6a] The highest *ee* was observed only with 2,3,3-trimethylbut-1-ene.

Subsequently, two important breakthroughs in the asymmetric hydroboration of 1,1-disubstituted olefins were reported (Scheme 1 b). They both included metal-catalyzed hydroboration processes instead of expensive and sacrificial stoichiometric chiral auxiliaries. One of them, reported by Hoveyda and co-workers, showed the asymmetric hydroboration of 1,1-disubstituted aryl-alkyl olefins with chiral copper-based bidentate N-heterocyclic carbene catalysts.[6b] A range of α-methylstyrenes and some aryl olefins with alkyl substituents other than the typical methyl unit and exocyclic alkenes were hydroborated with high regioselectivities and enantioselectivities in the range 61–92% *ee*. Despite this important advance, high catalyst loading (7.5%), long reaction times (48 h), low temperature (from −15 °C to −50 °C) and the presence of an almost equimolar amount of base were required (Scheme 1 b). Mazet and Gérard also reported the hydroboration of a range of 1,1-disubstituted aryl-alkyl olefins with excellent yields and regioselectivities (with exclusive attack at the desired β position) in which the iridium catalyst was modified with the readily accessible (*S*)-4-*tert*-butyl-2-[2-(diphenylphosphino)phenyl]-2-oxazoline ligand (PHOX-*t*Bu, Scheme 1 b).[6c] Enantioselectivity (up to 92% *ee*), however, was only high in the hydroboration of α-methylstyrene **S1**. The introduction of substituents at the aryl ring or the increase in steric requirements at the alkyl substituent of the substrate decreased the enantioselectivity consider-

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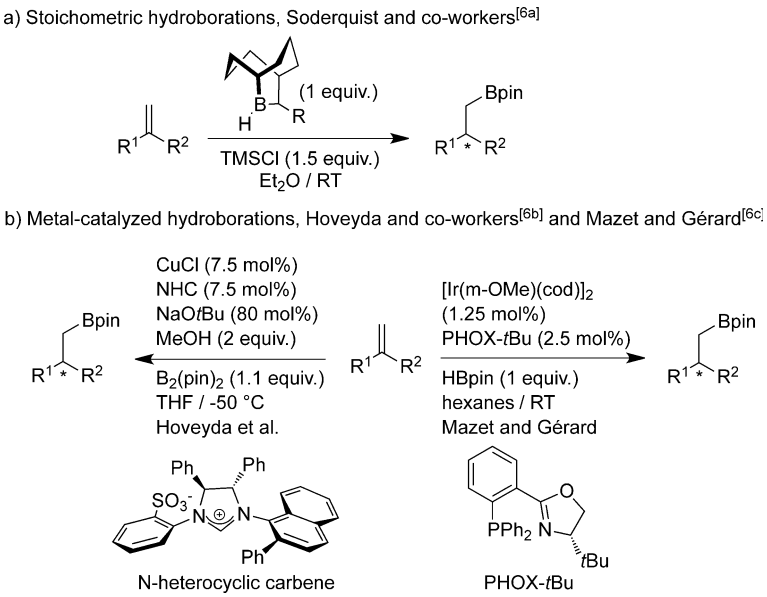


Scheme 1. State-of-the-art asymmetric hydroboration of challenging 1,1-disubstituted olefins. Bpin = Pinacolato.

ably. Although fewer substrates were hydroborated than with the copper carbene-based catalysts, the PHOX iridium catalysts allowed this transformation to take place under milder reaction conditions and with lower catalyst loading (Scheme 1 b), which would be advantageous for sustainable industrial process. Owing to the limited substrate scope of the three advances mentioned, new developments in this field are still needed.

In most asymmetric transformations involving olefins as prochiral reagents (e.g., epoxidation, hydrogenation), 1,1-disubstituted olefins are systematically challenging substrates,[7] mainly due to face selectivity issues (as in the hydroboration reaction). We recently demonstrated the highest reported enantioselectivities in the iridium-catalyzed hydrogenation of a very large range of simple 1,1-disubstituted olefins by introducing a biaryl phosphite moiety into the ligand.[7c–d,8] Inspired by the work of Mazet and Gérard[6c] and the similarities of the elementary steps involved in hydroboration and hydrogenation, we studied here whether the introduction of a biaryl phosphite moiety into the ligand was also beneficial for iridium-catalyzed hydroboration. To this end, we took the previously successful PHOX ligand family and replaced the phosphine group with biaryl phosphite moieties (ligands **L1**–**L4 a**–**c**, Figure 1). Herein, we present the application of the phosphite-oxazoline ligands

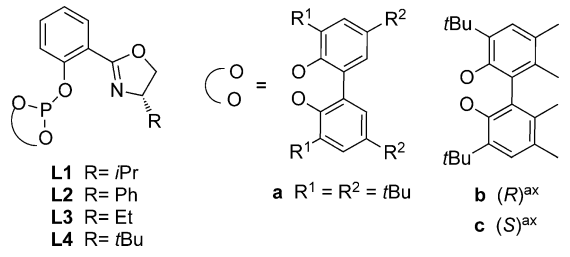
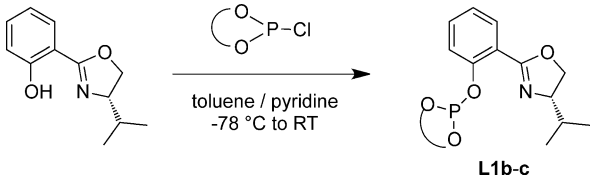


Figure 1. Phosphite-oxazoline PHOX-based ligands **L1**–**L4 a**–**c**.

L1–**L4 a**–**c** in the asymmetric iridium-catalyzed hydroboration of 1,1-disubstituted olefins. These ligands incorporate the advantages of biaryl phosphites such as higher resistance to oxidation than phosphines, facile synthesis from readily available chiral alcohols and a straightforward modular construction.[9] We investigated the catalytic performance by systematically varying the electronic and steric properties of the oxazoline substituents **L1**–**L4** and using different substituents and configurations in the biaryl phosphite group (**a**–**c**).



Scheme 2. Synthetic route for the synthesis of new phosphite-oxazoline PHOX-based ligands **L1 b** and **L1 c**.

Results and Discussion

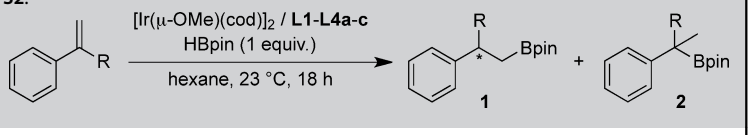
Ligand synthesis

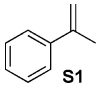
The new phosphite-oxazoline PHOX-based ligands **L1 b** and **L1 c** can be synthesized easily by following the procedure previously described for ligands **L1**–**L4 a**[10] (Scheme 2). They were prepared in one step by coupling the oxazoline-alcohol (*S*)-2-(4-isopropyl-4,5-dihydrooxazol-2-yl)phenol with one equivalent of the in situ-formed phosphorochloridite (**b**–**c**) under basic conditions (Scheme 2). All ligands were isolated in good yields as white solids after purification on neutral alumina. Advantageously, they were stable in air and very stable to hydrolysis, so further manipulation and storage was performed in air. The high-resolution electrospray ionization (ESI) mass spectra were in agreement with the assigned structures. **L1 b** and **L1 c** were also characterized by $^{31}P\{^{1}H\}$, ^{1}H and $^{13}C\{^{1}H\}$ NMR spectroscopy. The spectral assignments, made by using ^{1}H–^{1}H and ^{13}C–^{1}H correlation measurements, were as expected for these C_1-symmetric ligands.

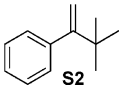
Initial screening experiments of phosphite-oxazoline PHOX-based ligands

As previously mentioned, the effectiveness of the catalyst in transferring the chiral information to the hydroborated product

Table 1. Asymmetric hydroboration of α-methylstyrene **S1** and α-*tert*-butylstyrene **S2**.[a]







Entry	L	Conv.[b] [%] (**1a**/**2a**)	*ee*[c] [%]	Conv.[b] [%] (**1b**/**2b**)	*ee*[c] [%]
1	**L1a**	100 (>99:1)	44 (*S*)	100 (>99:1)	88 (*S*)
2	**L1b**	50 (>99:1)	7 (*S*)	46 (>99:1)	43 (*S*)
3	**L1c**	60 (>99:1)	41 (*S*)	59 (>99:1)	79 (*S*)
4	**L2a**	100 (>99:1)	42 (*S*)	100 (>99:1)	86 (*S*)
5	**L3a**	100 (>99:1)	17 (*S*)	100 (>99:1)	43 (*S*)
6	**L4a**	96 (>99:1)	43 (*S*)	84 (>99:1)	88 (*S*)
7	PHOX-*t*Bu	100 (>99:1)	92 (*S*)[6c]	0	–

[a] All reactions performed in duplicate with 1 mmol of substrate, 1.25 mol% of [Ir(μ-OMe)(cod)]$_2$, 2.5 mol% of ligand and 2 mL of hexane. [b] Determined by using ^{1}H NMR, in all cases regioselectivities were >99%. [c] Determined by using HPLC after conversion to the corresponding alcohols.

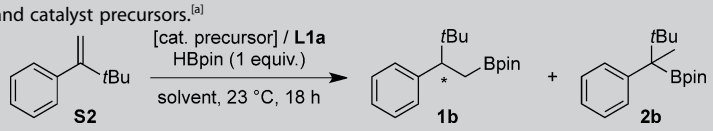
that ligands with an *S* biaryl phosphite group provided better enantioselectivities than ligands with an *R* biaryl phosphite group (Table 1, entry 2 vs 3). This is an advantage because it means that the inexpensive 3,3′,5,5′-tetra-*tert*-butyl-[1,1′-biphenyl]-2,2′-diyl phosphite moiety (**a**) can be used. For the oxazoline substituent, the enantioselectivities are highest with bulky isopropyl and *tert*-butyl groups (ligands **L1a** and **L4a**, Table 1, entries 1 and 6) but the activities are best if the steric demand on the oxazoline substituents is decreased. The trade-off between activities and enantioselectivities is therefore best with ligand **L1a** (Table 1, entry 1). This result contrasts with the one described by Mazet and Gérard, which required the presence of a *tert*-butyl oxazoline substituent to achieve high enantioselectivity, and it has an economic advantage because **L1a** is derived from L-valinol, which is around eight times cheaper than the L-*tert*-leucinol required for the synthesis of the PHOX-*t*Bu ligand.

depends mainly on its ability to sterically differentiate between the two geminal substituents of the olefin. To assess the potential of the phosphite-oxazoline PHOX-based ligands **L1**–**L4a**–**c** in the hydroboration of substrates with different steric requirements, we initially evaluated them in the asymmetric iridium-catalyzed hydroboration of model substrate **S1**[2,6] and the hydroboration of more demanding **S2** (Table 1).

For purposes of comparison, we first tested **L1**–**L4a**–**c** under the same optimal reaction conditions found in the previous study of Mazet and Gérard with related PHOX iridium catalytic systems.[6c] Reactions were performed at room temperature, with 2.5 mol% of in situ-generated catalyst ([Ir(μ-OMe)(cod)]$_2$/L) and hexane as solvent.[6c] The results are collected in Table 1. All of the ligands favoured the attack at the β position and the desired primary (pinacolato)boron adduct **1** was achieved with perfect regiocontrol (**1**/**2** ratio >99). Although enantioselectivities were moderate for α-methylstyrene **S1**, an unprecedentedly high enantioselectivity was achieved for the more challenging α-*tert*-butylstyrene **S2** (*ee* values up to 88%). Notably, the hydroboration of **S2** by using the related PHOX-*t*Bu ligand provided no conversion under the same reaction conditions (Table 1, entry 7). These important results indicate that both PHOX-based ligand families are complementary, thus, we can hydroborate both substrate types by the correct combination of substrate and ligand type (phosphine/oxazoline or phosphite/oxazoline).

As far as the effect of the ligand parameters on activities and enantioselectivities is concerned, we found that bulky *tert*-butyl groups are needed at the *ortho* and *para* positions of the biaryl phosphite moiety to achieve the highest activities and enantioselectivities (Table 1, entry 1 vs 2 and 3). We also found

Table 2. Asymmetric hydroboration of α-*tert*-butylstyrene **S2**: effect of the solvent and catalyst precursors.[a]

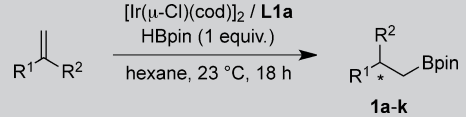


Entry	Solvent	[Cat. precursor]	Conv.[b] [%] (**1b**/**2b**)	*ee*[c] [%]
1	hexane	[Ir(μ-OMe)(cod)]$_2$	100 (>99:1)	88 (*S*)
2	THF	[Ir(μ-OMe)(cod)]$_2$	88 (>99:1)	76 (*S*)
3	CH_2Cl_2	[Ir(μ-OMe)(cod)]$_2$	100 (>99:1)	80 (*S*)
4	toluene	[Ir(μ-OMe)(cod)]$_2$	96 (>99:1)	83 (*S*)
5	hexane	[Ir(μ-Cl)(cod)]$_2$	100 (>99:1)[d]	92 (*S*)
6	hexane	[Ir(cod)**L1a**]BAr_F[e]	61 (>99:1)	66 (*S*)

[a] All reactions performed in duplicate with 1 mmol of substrate, 1.25 mol% of iridium catalyst precursor, 2.5 mol% of ligand and 2 mL solvent. [b] Determined by using ^{1}H NMR. [c] Determined by using HPLC after conversion to the corresponding alcohol. [d] 91% isolated yield. [e] $BAr_F = [B\{3,5\text{-}(CF_3)_2C_6H_3\}_4]^-$.

We next optimized the reaction conditions by evaluating a variety of solvents and catalyst precursors with ligand **L1a**, which had provided the best results (Table 2). Although in all cases regioselectivity towards the desired β adduct **1** remained excellent, activity and enantioselectivity were highly dependent on the solvent and the nature of the catalyst precursor. The combination of hexane and [Ir(μ-Cl)(cod)]$_2$ (cod = 1,5-cyclooctadiene) as catalyst precursor was found to be optimal (Table 2, entry 5). Under these new reaction conditions we were therefore able to increase the enantioselectivity to 92% while maintaining the excellent yield and regioselectivity of the desired β compound **1**. To the best of our knowledge, iridium–**L1a** is the first catalytic system that can hydroborate **S2** with perfect regioselectivity, excellent yield and high enantioselectivity.

Table 3. Asymmetric hydroboration of 1,1-disubstituted olefins: scope and limitations.[a]



1a-k

Entry	Substrate	R^1	R^2	**1/2**	Yield[b] [%]	*ee*[c] [%]
1	**S1**	C_6H_5	Me	>99:1	93	50 (*S*)
2	**S2**	C_6H_5	*t*Bu	>99:1	91	92 (S)
3	**S3**	C_6H_5	Et	>99:1	90	55 (S)
4	**S4**	C_6H_5	*i*Bu	>99:1	88	56 (S)
5	**S5**	C_6H_5	*i*Pr	>99:1	89	58 (S)
6	**S6**	4-Me-C_6H_4	*t*Bu	>99:1	92	94 (S)
7	**S7**	4-OMe-C_6H_4	*t*Bu	>99:1	91	93 (S)
8	**S8**	4-CF_3-C_6H_4	*t*Bu	>99:1	94	90 (S)
9	**S9**	2-naphthyl	*t*Bu	>99:1	89	87 (S)
10	**S10**	3-Me-C_6H_4	*t*Bu	>99:1	90	92 (*S*)
11	**S11**	4-OMe-C_6H_4	CF_3	>99:1	88	18 (*S*)
12[d]	**S11**	4-OMe-C_6H_4	CF_3	–	0	n.d.

[a] All reactions performed in duplicate with 1 mmol of substrate, 1.25 mol% of $[Ir(\mu\text{-Cl})(cod)]_2$, 2.5 mol% of **L1a** and 2 mL hexane. [b] Determined by using ^{1}H NMR. [c] Determined by using HPLC or GC after conversion to the corresponding alcohol. [d] Reaction performed by using PHOX-*t*Bu iridium catalyst; hydrogenated product isolated in 45% yield and 0% *ee*.

Asymmetric hydroboration of other 1,1-disubstituted olefins: scope and limitations

The unprecedented results obtained up to this point with the iridium–**L1a** catalyst in the hydroboration of **S2** encouraged us to test iridium–**L1a** in the hydroboration of other 1,1-disubstituted olefins (Table 3).

First, we studied the hydroboration of several phenyl and alkyl olefins bearing alkyl substituents with different steric demands (**S3**–**S5**, Table 3, entries 3–5). Excellent regioselectivities of the desired β adduct **1** were achieved. Enantioselectivities were moderate regardless of the steric demands of the alkyl substituent (entries 3–5). However, enantioselectivities were not as low as those observed with related PHOX iridium catalysts with increased steric hindrance on the alkyl substituents (i.e., *ee* values decreased from 92 to 31% on replacing Me by Et substituent).[6c]

We next studied several α-*tert*-butylstyrenes that had aryl substituents with different electronic and steric properties (**S6**–**S10**, Table 3, entries 6–10). Advantageously, iridium–**L1a** is very tolerant to variations in the substituents of the aryl ring and can hydroborate a wide range of α-*tert*-butylstyrenes with comparably high enantioselectivities (up to 94%) and yields and perfect regioselectivity. Accordingly, our results with several *para*-substituted α-*tert*-butylstyrenes (**S6**–**S8**) indicated that the enantioselectivity was relatively insensitive to the electronic effects in the aryl ring (*ee* values of 90–94%, entries 2, 6–8). Enantioselectivities were, however, highest in the hydroboration of electron-rich olefins **S6** and **S7** (entries 6–7). Enantioselectivities were also excellent in the hydroboration of *meta*-substituted olefins (**S9**–**S10**, entries 9–10). Again, these results contrasted with the ones described by Mazet and Gérard with related PHOX iridium catalysts for which the introduction of any type of substituent at the aryl ring of the substrate had a negative effect on enantioselectivity.[6c]

We then looked into the hydroboration of aryl and trifluoromethyl olefins. Owing to the unique properties of the fluorine, the efficient hydroboration of these substrates opened up an appealing route for obtaining organic intermediates for the preparation of drugs, agrochemicals and materials. To the best of our knowledge, only Hoveyda and co-workers have attempted the hydroboration of this substrate class with their N-heterocyclic carbene copper catalysts, although they obtained undesired difluoroallylboronates.[6b] Here, we have tested the new iridium–**L1a** and related PHOX iridium catalysts in the hydroboration of the model 1-methoxy-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene **S11** substrate (Table 3, entries 11 and 12). Although PHOX-*t*Bu iridium was found to be inadequate because it provided exclusively the hydrogenated product in racemic form, the iridium–**L1a** catalyst gave the desired hydroborated product with perfect regioselectivity and good yield, albeit with low enantiocontrol. This result opens up new possibilities for further research and it demonstrates once again that the behaviour is not that observed with PHOX iridium catalysts.

Conclusion

We have identified a readily accessible phosphinooxazoline (PHOX)-based phosphite-oxazoline iridium catalytic system (iridium–**L1a**) that can hydroborate a range of 1,1-disubstituted aryl olefins with high enantioselectivity (up to 94%), excellent yields and perfect regioselectivity. The new phosphite-oxazoline PHOX-based ligands could efficiently hydroborate a broader range of olefins than previous PHOX ligands. Particularly, we could hydroborate a wide range of α-*tert*-butylstyrenes, with aryl substituents that had different electronic and steric properties, thus complementing the results of N-heterocyclic carbene copper catalysts, the only other system reported to date that has attempted these reactions. In addition, the introduction of a biaryl phosphite moiety allowed, for the first time, the highly regioselective hydroboration of aryl and trifluoromethyl olefins. Another advantage over previous PHOX ligands was that the new ligands were stable to air and therefore easier to handle, manipulate and store. This contribution opens up the path for the synthesis of new iridium phosphite-based catalysts for the challenging hydroboration of 1,1-disubstituted olefins. Further studies on the design of new phosphite-based iridium catalysts to further broaden the scope of this hydroboration reaction are currently underway.

Experimental Section

General

All reactions were performed by using standard Schlenk techniques under an argon atmosphere. Solvents were purified and dried by standard procedures. Phosphorochloridites were prepared easily in one step from the corresponding binaphthols.[11] Intermediate compound (*S*)-2-(4-isopropyl-4,5-dihydrooxazol-2-yl)phenol,[12] ligands **L1**–**L4a**[10] and substrates **S2**,[13] **S3**,[14] **S4**,[15] **S5**[13]

and **S11**[7c] were prepared as previously reported. Substrates **S6**–**S10** were prepared by using the Wittig olefination procedure (for details, see the Supporting Information). ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded by using a 400 MHz spectrometer. Chemical shifts are relative to those of $SiMe_4$ (^{1}H and ^{13}C) as internal standard or H_3PO_4 (^{31}P) as external standard. ^{1}H, ^{13}C and ^{31}P assignments were made on the basis of ^{1}H–^{1}H gCOSY and ^{1}H–^{13}C gHSQC NMR analyses.

Preparation of phosphite-oxazoline ligands L1–L4 a–c

General procedure: The corresponding phosphorochloridite (1.1 mmol) produced in situ was dissolved in toluene (5 mL) and pyridine (0.36 mL, 4.6 mmol) was added. Hydroxyl-oxazoline intermediate (1 mmol) was azeotropically dried with toluene (3×1 mL) and then dissolved in toluene (5 mL), to which pyridine (0.36 mL, 4.6 mmol) had been added. The hydroxyl-oxazoline solution was transferred slowly at −78 °C to the solution of phosphorochloridite. The reaction mixture was allowed to warm to RT and stirred overnight. The pyridine salts were then removed by filtration. Evaporation of the solvent gave a white foam, which was purified by flash chromatography (Al_2O_3, toluene/NEt_3 = 100:1) to produce the corresponding ligand.

(*S*)-4-isopropyl-2-{2-[(*R*)-3,3′-di-*tert*-butyl-5,5′,6,6′-tetra-methyl-1,1′-biphenyl-2,2′-diyl)phosphite]phenyl}-2-oxazoline (L1 b): Yield: 423 mg (72%); ^{31}P NMR (C_6D_6): δ = 132.6 ppm (s); ^{1}H NMR (C_6D_6): δ = 0.62 (d, 6H, $^3J_{H-H}$ = 6.4 Hz, CH_3, *i*Pr), 1.27 (s, 9H, CH_3, *t*Bu), 1.37 (s, 9H, CH_3, *t*Bu), 1.39 (m, 1H, CH, *i*Pr), 1.61 (s, 3H, CH_3), 1.68 (s, 3H, CH_3), 1.93 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 3.03 (dd, 1H, $^2J_{H-H}$ = 11.6 Hz, $^3J_{H-H}$ = 5.2 Hz, CH_2–O), 3.12 (dd, 1H, $^2J_{H-H}$ = 11.2 Hz, $^3J_{H-H}$ = 5.2 Hz, CH_2–O), 4.22 (m, 1H, CH–N), 6.7–7.5 (m, 6H, CH=), 8.59 ppm (d, 1H, $^3J_{H-H}$ = 6.4 Hz, CH=); ^{13}C NMR (C_6D_6): δ = 16.2 (CH_3, *i*Pr), 16.4 (CH_3, *i*Pr), 17.8 (CH_3), 19.1 (CH_3), 19.9 (CH_3), 20.0 (CH_3), 28.6 (CH, *i*Pr), 31.0 (d, CH_3, *t*Bu, J_{C-P} = 5.3 Hz), 31.3 (CH_3, *t*Bu), 34.4 (C, *t*Bu), 34.8 (C, *t*Bu), 45.3 (CH_2-O), 55.4 (CH-N), 118.4–150.9 (C_{Ar}), 163.4 ppm (C=N); HRMS (ESI): *m/z*: calcd for $C_{36}H_{46}NO_4P + Na^+$: 610.3062 [*M*–Na]$^+$, found 610.3067.

(*S*)-4-isopropyl-2-{2-[(*S*)-3,3′-di-*tert*-butyl-5,5′,6,6′-tetra-methyl-1,1′-biphenyl-2,2′-diyl)phosphite]phenyl}-2-oxazoline (L1 c): Yield: 376 mg (64%); ^{31}P NMR (C_6D_6): δ = 133.9 ppm (s); ^{1}H NMR (C_6D_6): δ = 0.55 (d, 3H, $^3J_{H-H}$ = 6.4 Hz, CH_3, *i*Pr), 0.63 (d, 3H, $^3J_{H-H}$ = 6.8 Hz, CH_3, *i*Pr), 1.35 (s, 9H, CH_3, *t*Bu), 1.39 (s, 9H; CH_3, *t*Bu), 1.42 (m, 1H, CH, *i*Pr), 1.65 (s, 3H, CH_3), 1.79 (s, 3H, CH_3), 1.97 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 3.35 (m, 2H, CH_2–O), 4.28 (m, 1H, CH–N), 6.7–7.7 (m, 6H, CH=), 8.60 ppm (d, 1H, $^3J_{H-H}$ = 8.0 Hz, $^4J_{H-H}$ = 2.0 Hz, CH=); ^{13}C NMR (C_6D_6): δ = 16.2 (CH_3, *i*Pr), 16.6 (CH_3, *i*Pr), 18.1 (CH_3), 19.1 (CH_3), 20.0 (CH_3), 21.4 (CH_3), 28.6 (CH, *i*Pr), 31.2 (d, CH_3, *t*Bu, J_{C-P} = 4.6 Hz), 31.4 (CH_3, *t*Bu), 34.4 (C, *t*Bu), 34.7 (C, *t*Bu), 45.6 (CH_2–O), 55.5 (CH–N), 119.3–150.4 (C_{Ar}), 163.4 ppm (C=N); HRMS (ESI): *m/z*: calcd for $C_{36}H_{46}NO_4P + Na^+$: 610.3062 [*M*–Na]$^+$, found 610.3068.

Asymmetric hydroboration of 1,1-disubstituted substrates

General procedure: The corresponding ligand (2.5×10^{-2} mmol) and [Ir(μ-Cl)(cod)]$_2$ (8.4 mg, 2.5×10^{-5} mmol) were dissolved in hexane (2 mL) and stirred for 10 min at RT. Then, the slightly turbid solution was cooled to 0 °C and the desired 1,1-disubstituted olefin (1.0 mmol) slowly added. After 5 min, pinacolborane (150 μL, 1.0 mmol) was added dropwise. The ice bath was then removed and the reaction stirred at RT. After 18 h, the volatiles were evaporated and the crude mixture purified by column chromatography (SiO_2, Et_2O/cyclohexane = (9:1) to give the hydroborated product as a colourless oil.

ee Values were determined after oxidation of the pinacolborane derivatives to the corresponding alcohols. Pinacolborane derivative (0.25 mmol) was dissolved in Et_2O (2 mL) and cooled to 0 °C. NaOH (3 N, 2.0 mL) and H_2O_2 (30%, 1.5 mL) were then added. The resulting solution was stirred at RT for 2 h. Then, the solution was extracted twice with Et_2O (2 mL) and dried over $MgSO_4$. The crude product was purified by column chromatography (SiO_2, Et_2O/cyclohexane = 4:1) to yield the desired chiral primary alcohol.

4,4,5,5-Tetramethyl-2-(2-phenylpropyl)-1,3,2-dioxaborolane (1 a): ^{1}H NMR ($CDCl_3$): δ = 1.08 (s, 12H, CH_3, Bpin), 1.09 (m, 2H, CH_2), 1.20 (d, $^3J_{H-H}$ = 8 Hz, 3H, CH_3), 2.95 (m, 1H, CH), 7.0–7.2 ppm (m, 5H, CH=); ^{13}C NMR ($CDCl_3$): δ = 24.6 (CH_3, Bpin), 24.7 (CH_3, Bpin), 24.9 (CH_3), 35.8 (CH), 82.9 (C, Bpin), 125.7 (CH=), 126.6 (CH=), 128.1 (CH=), 149.2 ppm (C); HRMS elemental analysis calcd (%) for $C_{15}H_{23}BO_2$ [M^+]: 246.1791, found: 246.1794.

ee Values were determined after oxidation to phenylpropan-1-ol: ^{1}H NMR ($CDCl_3$): δ = 1.23 (d, $^3J_{H-H}$ = 8 Hz, 3H, CH_3), 2.95 (m, 1H, CH), 3.71 (m, 2H, CH_2), 7.2–7.4 ppm (m, 5H, CH=);^{13}C NMR ($CDCl_3$): δ = 17.5 (CH_3), 42.4 (CH), 68.7 (CH_2), 126.7 (CH=), 127.4 (CH=), 128.6 (CH=), 143.6 ppm (C); HRMS elemental analysis calcd (%) for $C_9H_{12}O$ [M^+]: 136.0888, found: 136.0885; *ee* (HPLC, Chiracel IA column, hexane/2-propanol = 99:1, 0.5 mL min^{-1}, λ = 254 nm): t_R = 38.9 (*R*), 41.7 min (*S*).

2-(3,3-Dimethyl-2-phenylbutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1 b): ^{1}H NMR ($CDCl_3$): δ = 0.83 (s, 9H, CH_3, *t*Bu), 0.91 (s, 6H, CH_3, Bpin), 0.96 (s, 6H, CH_3, Bpin), 1.18 (m, 2H, CH_2), 2.67 (m, 1H, CH), 7.05–7.20 ppm (m, 5H, CH=); ^{13}C NMR ($CDCl_3$): δ = 24.2 (CH_3, Bpin), 24.5 (CH_3, Bpin), 27.7 (CH_3, *t*Bu), 34.0 (C, *t*Bu), 51.6 (CH), 82.7 (C, Bpin), 125.6 (CH=), 127.1 (CH=), 129.7 (CH=), 144.3 ppm (C); HRMS elemental analysis calcd (%) for $C_{18}H_{29}BO2$ [M^+]: 288.2261, found: 288.2259.

ee Values were determined after oxidation to 3,3-dimethyl-2-phenylbutan-1-ol: ^{1}H NMR ($CDCl_3$): δ = 0.87 (s, 9H, CH_3, *t*Bu), 2.65 (m, 1H, CH), 4.01 (m, 2H, CH_2), 7.05–7.35 ppm (m, 5H, CH=); ^{13}C NMR ($CDCl_3$): δ = 28.4 (CH_3, *t*Bu), 33.1 (C, *t*Bu), 58.9 (CH), 62.6 (CH_2), 125.6 (CH=), 126.8 (CH=), 127.1 (CH=), 128.2 (CH=), 140.2 ppm (C); HRMS elemental analysis calcd (%) for $C_{12}H_{18}O$ [M^+]: 178.1358, found: 178.1357; *ee* (HPLC, Chiracel IA column, hexane/2-propanol = 98:2, 0.5 mL min^{-1}, λ = 220 nm): t_R = 23.0 (*S*), 25.2 min (*R*).

4,4,5,5-Tetramethyl-2-(2-phenylbutyl)-1,3,2-dioxaborolane (1 c): ^{1}H NMR ($CDCl_3$): δ = 0.73 (t, $^3J_{H-H}$ = 8.0 Hz, 3H, CH_3), 1.08 (s, 12H, CH_3, Bpin), 1.12 (m, 2H, CH_2), 1.59 (m, 2H, CH_2), 2.65 (m, 1H, CH), 7.0–7.2 ppm (m, 5H, CH=); ^{13}C NMR ($CDCl_3$): δ = 12.2 (CH_3), 24.6 (CH_3, Bpin), 24.7 (CH_3, Bpin), 35.8 (CH), 43.3 (CH_2), 82.9 (C, Bpin), 125.7 (CH=), 127.4 (CH=), 128.0 (CH=), 147.2 ppm (C); HRMS elemental analysis calcd (%) for $C_{16}H_{25}BO_2$ [M^+]: 260.1948, found: 260.1947.

ee Values were determined after oxidation to 2-phenylbutan-1-ol: ^{1}H NMR ($CDCl_3$): δ = 0.85 (t, $^3J_{H-H}$ = 8.0 Hz, 3H, CH_3), 1.5–1.8 (m, 2H, CH_2), 2.65 (m, 1H; CH), 3.75 (m, 2H, CH_2), 7.20–7.35 ppm (m, 5H, CH=); ^{13}C NMR ($CDCl_3$): δ = 12.5 (CH_3), 25.7 (CH_2), 50.5 (CH), 67.3 (CH_2), 126.7 (CH=), 128.1 (CH=), 128.6 (CH=), 142.2 ppm (C); HRMS elemental analysis calcd (%) for $C_{10}H_{14}O$ [M^+]: 150.1045, found: 150.1043; *ee* (GC, CP-Chirasil-Dex CB column, 90 kPa H_2, 110 °C isotherm): t_R = 8.8 (*S*), 9.2 min (*R*).

4,4,5,5-Tetramethyl-2-(4-methyl-2-phenylpentyl)-1,3,2-dioxaborolane (1 d): ^{1}H NMR ($CDCl_3$): δ = 0.81 (d, $^3J_{H-H}$ = 6.0 Hz, 3H, CH_3,

*i*Bu), 0.85 (d, $^3J_{H-H}$ = 8.0 Hz, 3H, CH_3, *i*Bu), 1.02 (s, 12H, CH_3, Bpin), 1.2–1.6 (m, 5H), 2.95 (m, 1H, CH), 7.1–7.3 ppm (m, 5H, CH=); ^{13}C NMR ($CDCl_3$): δ = 22.0 (CH_3, *i*Bu), 23.4 (CH_3, *i*Bu), 24.6 (CH_3, Bpin), 24.7 (CH_3, Bpin), 29.6 (CH_2, *i*Bu), 39.2 (CH, *i*Bu), 49.0 (CH), 82.8 (C, Bpin), 125.6 (CH=), 127.4 (CH=), 128.0 (CH=), 147.6 ppm (C); HRMS elemental analysis calcd (%) for $C_{18}H_{29}BO_2$ [M^+]: 288.2261, found: 288.2262.

ee Values were determined after oxidation to 4-methyl-2-phenylpentan-1-ol: ^{1}H NMR ($CDCl_3$): δ = 0.79 (m, 6H, CH_3, *i*Bu), 1.2–1.6 (m, 5H), 2.85 (m, 1H, CH), 3.62 (m, 2H, CH_2), 7.1–7.3 ppm (m, 5H, CH=); ^{13}C NMR ($CDCl_3$): δ = 21.8 (CH_3, *i*Bu), 23.5 (CH_3, *i*Bu), 25.3 (CH_2, *i*Bu), 41.1 (CH, *i*Bu), 46.4 (CH), 68.0 (CH_2), 126.7 (CH=), 128.1 (CH=), 128.6 (CH=), 142.4 ppm (C); HRMS elemental analysis calcd (%) for $C_{12}H_{18}O$ [M^+]: 178.1358, found: 178.1356; *ee* (HPLC using Chiracel IA column, hexane/2-propanol = 98:2, 0.5 mL min^{-1}, λ = 220 nm): t_R = 22.5 (*S*), 24.3 min (*R*).

4,4,5,5-Tetramethyl-2-(3-methyl-2-phenylbutyl)-1,3,2-dioxaborolane (1 e): ^{1}H NMR ($CDCl_3$): δ = 0.65 (d, $^3J_{H-H}$ = 8.0 Hz, 3H, CH_3, *i*Pr), 0.87 (d, $^3J_{H-H}$ = 8.0 Hz, 3H, CH_3, *i*Pr), 1.02 (s, 12H, CH_3, Bpin), 1.04 (s, 12H, CH_3, Bpin), 1.0–1.2 (m, 2H, CH_2), 1.68 (m, 1H, CH, *i*Pr), 2.55 (m, 1H, CH), 7.0–7.2 ppm (m, 5H, CH=);^{13}C NMR ($CDCl_3$): δ = 20.4 (CH_3, *i*Pr), 20.6 (CH_3, *i*Pr), 24.4 (CH_3, Bpin), 24.6 (CH_3, Bpin), 35.3 (CH, *i*Pr), 48.3 (CH), 82.7 (C, Bpin), 125.6 (CH=), 127.7 (CH=), 128.3 (CH=), 146.1 ppm (C); HRMS elemental analysis calcd (%) for $C_{17}H_{27}BO_2$ [M^+]: 274.2104, found: 274.2102.

ee Values were determined after oxidation to 3-methyl-2-phenylbutan-1-ol: ^{1}H NMR ($CDCl_3$): δ = 0.75 (d, $^3J_{H-H}$ = 8.0 Hz, 3H, CH_3, *i*Pr), 1.02 (d, $^3J_{H-H}$ = 8.0 Hz, 3H, CH_3, *i*Pr), 1.93 (m, 1H, CH, *i*Pr), 2.55 (m, 1H, CH), 3.8–4.0 (m, 2H, CH_2), 7.2–7.4 ppm (m, 5H, CH=); ^{13}C NMR ($CDCl_3$): δ = 21.0 (CH_3, *i*Pr), 21.1 (CH_3, *i*Pr), 30.1 (CH, *i*Pr), 55.8 (CH), 65.2 (CH_2), 126.7 (CH=), 128.5 (CH=), 128.7 (CH=), 141.6 ppm (C); HRMS elemental analysis calcd (%) for $C_{11}H_{16}O$ [M^+]: 164.1201, found: 164.1202; *ee* (HPLC, Chiracel IA column, hexane/2-propanol = 98:2, 0.5 mL min^{-1}, λ = 210 nm): t_R = 25.2 (*S*), 26.5 min (*R*).

2-(3,3-Dimethyl-2-(p-tolyl)butyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1 f): ^{1}H NMR ($CDCl_3$): δ = 0.85 (s, 9H, CH_3, *t*Bu), 0.94 (s, 6H, CH_3, Bpin), 0.97 (s, 6H, CH_3, Bpin), 1.21 (m, 2H, CH_2), 2.27 (s, 3H, CH_3), 2.67 (m, 1H, CH), 6.9–7.1 ppm (m, 4H, CH=); ^{13}C NMR ($CDCl_3$): δ = 20.9 (CH_3), 24.2 (CH_3, Bpin), 24.5 (CH_3, Bpin), 27.7 (CH_3, *t*Bu), 34.0 (C, *t*Bu), 51.2 (CH), 82.7 (C, Bpin), 127.7 (CH=), 129.5 (CH=), 134.9 (C), 141.2 ppm (C); HRMS elemental analysis calcd (%) for $C_{19}H_{31}BO_2$ [M^+]: 302.2417, found: 302.2415.

ee Values were determined after oxidation to 3,3-dimethyl-2-(p-tolyl)butan-1-ol: ^{1}H NMR ($CDCl_3$): δ = 0.88 (s, 9H, CH_3, *t*Bu), 2.33 (s, 3H, CH_3), 2.64 (m, 1H, CH), 4.0 (m, 2H, CH_2), 7.1–7.2 ppm (m, 4H, CH=); ^{13}C NMR ($CDCl_3$): δ = 21.0 (CH_3), 28.4 (CH_3, *t*Bu), 33.0 (C, *t*Bu), 58.9 (CH), 62.5 (CH_2), 128.9 (CH=), 129.6 (CH=), 136.3 (C), 136.7 ppm (C); HRMS elemental analysis calcd (%) for $C_{13}H_{20}O$ [M^+]: 192.1514, found: 192.1511; *ee* (GC using Chiradex B-DM column, 77 kPa H_2, 110 °C isotherm): t_R = 26.5 (*S*), 27.5 min (*R*).

2-(2-(4-Methoxyphenyl)-3,3-dimethylbutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1 g): ^{1}H NMR ($CDCl_3$): δ = 0.83 (s, 9H, CH_3, *t*Bu), 0.90 (s, 6H, CH_3, Bpin), 0.97 (s, 6H, CH_3, Bpin), 1.22 (m, 2H, CH_2), 2.65 (m, 1H, CH), 3.76 (s, 3H, OCH_3), 6.75 (d, 2H, $^3J_{H-H}$ = 8.0 Hz, CH=), 7.07 ppm (d, 2H, $^3J_{H-H}$ = 8.0 Hz, CH=); ^{13}C NMR ($CDCl_3$): δ = 24.2 (CH_3, Bpin), 24.6 (CH_3, Bpin), 27.6 (CH_3, *t*Bu), 34.1 (C, *t*Bu), 50.7 (CH), 55.2 (OCH_3), 82.7 (C, Bpin), 112.5 (CH=), 130.4 (CH=), 136.6 (C), 157.7 ppm (C); HRMS elemental analysis calcd (%) for $C_{19}H_{31}BO_3$ [M^+]: 318.2366, found: 318.2365.

ee Values were determined after oxidation to 2-(4-methoxyphenyl)-3,3-dimethylbutan-1-ol: ^{1}H NMR ($CDCl_3$): δ = 0.87 (s, 9H, CH_3, *t*Bu), 2.63 (m, 1H, CH), 3.82 (s, 3H, CH_3O), 3.97 (m, 2H, CH_2), 6.87 (d, 2H, $^3J_{H-H}$ = 8.4 Hz, CH=), 7.14 ppm (d, 2H, $^3J_{H-H}$ = 8.4 Hz, CH=); ^{13}C NMR ($CDCl_3$): δ = 28.3 (CH_3, *t*Bu), 33.1 (C, *t*Bu), 55.2 (OCH_3), 58.1 (CH), 62.5 (CH_2), 113.6 (CH=), 130.6 (CH=), 131.6 (C), 158.4 ppm (C); HRMS elemental analysis calcd (%) for $C_{13}H_{20}O_2$ [M^+]: 208.1463, found: 208.1460; *ee* (GC, CP-Chirasil-Dex CB column, 90 kPa H_2, 110 °C for 40 min, 5 °C min^{-1} until 150 °C, 20 °C min^{-1} until 170 °C): t_R = 49.6 (*S*), 49.9 min (*R*).

2-(3,3-Dimethyl-2-(4-(trifluoromethyl)phenyl)butyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1 h): ^{1}H NMR ($CDCl_3$): δ = 0.86 (s, 6H, CH_3, Bpin), 0.88 (s, 6H, CH_3, Bpin), 0.95 (s, 9H, CH_3, *t*Bu), 1.27 (m, 2H, CH_2) 2.77 (m, 1H, CH), 7.28 (d, 2H, $^3J_{H-H}$ = 8.0 Hz, CH=), 7.47 ppm (d, 2H, $^3J_{H-H}$ = 8.0 Hz, CH=); ^{13}C NMR ($CDCl_3$): δ = 24.1 (CH_3, Bpin), 24.5 (CH_3, Bpin), 27.6 (CH_3, *t*Bu), 29.7 (C, *t*Bu), 51.6 (CH), 82.9 (C, Bpin), 124.1 (CH=), 132.2 (CH=), 128.9 (C), 152.3 ppm (C); HRMS elemental analysis calcd (%) for $C_{19}H_{28}BF_3O_2$ [M^+]: 356.2134, found: 356.2133.

ee Values were determined after oxidation to 3,3-dimethyl-2-(4-(trifluoromethyl)phenyl)butan-1-ol: ^{1}H NMR ($CDCl_3$): δ = 0.87 (s, 9H, CH_3, *t*Bu), 2.76 (m, 1H, CH), 4.06 (m, 2H, CH_2), 7.34 (d, 2H, $^3J_{H-H}$ = 7.6 Hz, CH=), 7.59 ppm (d, 2H, $^3J_{H-H}$ = 7.6 Hz, CH=); ^{13}C NMR ($CDCl_3$): δ = 28.3 (CH_3, *t*Bu), 32.1 (C, *t*Bu), 58.8 (CH), 62.5 (CH_2), 125.0 (CH=), 130.6 (CH=), 145.8 (C), 160.0 ppm (C); HRMS elemental analysis calcd (%) for $C_{13}H_{17}BF_3O$ [M^+]: 246.1231, found: 246.1229; *ee* (HPLC, Chiracel IA column, hexane/2-propanol = 98:2, 0.5 mL min^{-1}, λ = 220 nm): t_R = 32.7 (*S*), 38.4 min (*R*).

2-(3,3-Dimethyl-2-(naphthalen-2-yl)butyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1 i): ^{1}H NMR ($CDCl_3$): δ = 0.81 (s, 9H, CH_3, *t*Bu), 0.87 (s, 6H, CH_3, Bpin), 0.91 (s, 6H, CH_3, Bpin), 1.2–1.4 (m, 2H, CH_2), 2.89 (m, 1H, CH), 7.4–7.8 ppm (m, 7H, CH=); ^{13}C NMR ($CDCl_3$): δ = 24.1 (CH_3, Bpin), 24.5 (CH_3, Bpin), 27.8 (CH_3, *t*Bu), 34.4 (C, *t*Bu), 51.7 (CH), 82.7 (C, Bpin), 124.4 (CH=), 125.4 (CH=), 126.3 (CH=), 127.3 (CH=), 127.7 (CH=), 132.2 (C), 133.0 ppm (C); HRMS elemental analysis calcd (%) for $C_{22}H_{31}BO_2$ [M^+]: 338.2417, found: 338.2415.

ee Values were determined after oxidation to 3,3-dimethyl-2-(naphthalen-2-yl)butan-1-ol: ^{1}H NMR ($CDCl_3$): δ = 0.83 (s, 9H, *t*Bu), 2.79 (m, 1H, CH), 4.07 (m, 2H, CH_2), 7.30–7.77 ppm (m, 7H, CH=); ^{13}C NMR ($CDCl_3$): δ = 28.5 (CH_3, *t*Bu), 33.7 (C, *t*Bu), 59.1 (CH), 62.6 (CH_2), 125.5 (CH=), 126.1 (CH=), 127.5 (CH=), 127.6 (CH=), 127.7 (CH=), 132.5 (C), 133.2 (C), 137.7 ppm (C); HRMS elemental analysis calcd (%) for $C_{16}H_{20}O$ [M^+]: 228.1514, found: 228.1513; *ee* (HPLC, Chiracel IA column, hexane/2-propanol = 98:2, 0.5 mL min^{-1}, λ = 220 nm): t_R = 40.4 (*S*), 44.5 min (*R*).

2-(3,3-Dimethyl-2-(*m*-tolyl)butyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1 j): ^{1}H NMR ($CDCl_3$): δ = 0.93 (s, 9H, CH_3, *t*Bu), 0.95 (s, 6H, CH_3, Bpin), 0.96 (s, 6H, CH_3, Bpin), 1.23 (m, 2H, CH_2), 2.29 (s, 3H, CH_3), 2.68 (m, 1H, CH), 6.9–7.1 ppm (m, 5H, CH=); ^{13}C NMR ($CDCl_3$): δ = 21.4 (CH_3), 24.2 (CH_3, Bpin), 24.5 (CH_3, Bpin), 27.7 (CH_3, *t*Bu), 34.0 (C, *t*Bu), 51.5 (CH), 82.6 (C, Bpin), 126.2 (CH=), 127.0 (CH=), 136.3 (CH=), 138.0 (C), 144.3 ppm (C); HRMS elemental analysis calcd (%) for $C_{19}H_{31}BO_2$ [M^+]: 302.2417, found: 302.2414.

ee Values were determined after oxidation to 3,3-dimethyl-2-(*m*-tolyl)butan-1-ol: ^{1}H NMR ($CDCl_3$): δ = 0.89 (s, 9H, CH_3, *t*Bu), 2.35 (s, 3H, CH_3), 2.65 (m, 1H, CH), 4.01 (m, 2H, CH_2), 7.05–7.2 ppm (m, 5H, CH=); ^{13}C NMR ($CDCl_3$): δ = 21.6 (CH_3), 28.4 (CH_3, *t*Bu), 33.0 (C, *t*Bu), 58.9 (CH), 62.6 (CH_2), 126.8 (CH=), 128.05 (CH=), 137.7 ppm (C); HRMS calcd for $C_{13}H_{20}O$ [M^+]: 192.1514, found: 192.1512; *ee* (GC,

CP-Chirasil-Dex CB column, 90 kPa H_2, 110 °C isotherm): $t_R = 20.1$ (*S*), 21.9 min (*R*).

4,4,5,5-Tetramethyl-2-(3,3,3-trifluoro-2-(4-methoxyphenyl)propyl)-1,3,2-dioxaborolane (1 k): ^{1}H NMR ($CDCl_3$): $\delta = 1.03$ (s, 6H, CH_3, Bpin), 1.09 (s, 6H, CH_3, Bpin), 1.40 (m, 2H, CH_2), 3.54 (m, 1H, CH), 3.79 (s, 3H, CH_3O), 6.84 (d, 2H, $^3J_{H-H} = 8.4$ Hz, CH=), 7.23 ppm (d, 2H, $^3J_{H-H} = 8.4$ Hz, CH=); ^{13}C NMR ($CDCl_3$): $\delta = 24.3$ (CH_3, Bpin), 24.4 (CH_3, Bpin), 44.8 (q, CH, $^3J_{H-F} = 28.1$ Hz), 55.2 (CH_3O), 83.0 (C, Bpin), 113.6 (CH=), 128.5 (d, C, $J_{C-F} = 29.7$ Hz), 128.7 (C), 130.0 (CH=), 159.2 ppm (C); HRMS elemental analysis calcd (%) for $C_{16}H_{22}BF_3O_3$ [M^+]: 330.1614, found: 330.1612.

ee Values were determined after oxidation to 3,3,3-trifluoro-2-(4-methoxyphenyl)propan-1-ol: ^{1}H NMR ($CDCl_3$): $\delta = 3.45$ (m, 1H, CH), 3.8 (s, 3H, CH_3O), 3.98 (m, 1H, CH_2), 4.16 (m, 1H, CH_2), 6.92 (d, 2H, $^3J_{H-H} = 8.4$ Hz, CH=), 7.25 ppm (d, 2H, $^3J_{H-H} = 8.4$ Hz, CH=); ^{13}C NMR ($CDCl_3$): $\delta = 51.5$ (q, CH, $J_{C-F} = 25.4$ Hz), 55.2 (CH_3O), 61.2 (CH_2), 114.3 (CH=), 124.6 (d, C, $J_{C-F} = 30.2$ Hz), 130.2 (CH=), 159.7 ppm (C); HRMS elemental analysis calcd (%) for $C_{10}H_{11}F_3O$ [M^+]: 220.0711, found: 220.0712; *ee* (GC, CP-Chirasil-Dex CB column, 90 kPa H_2, 110 °C isotherm): $t_R = 28.2$ (*S*), 29.4 min (*R*).

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[1] a) *Comprehensive Asymmetric Catalysis* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto) Springer, Berlin, **1999**; b) *Catalytic Asymmetric Synthesis, 3rd ed.* (Ed.: I Ojima), John Wiley & Sons, Hoboken, **2010**; c) *Asymmetric Catalysis in Industrial Scale: Challenges, Approaches and Solutions, 2nd ed.* (Eds.: H. U. Blaser, H.-J. Federsel) Wiley-VCH, Weinheim, Germany, **2010**; d) *Asymmetric Catalysis in Organic Synthesis* (Ed.: R. Noyori) Wiley, New York, **1994**; e) C. A. Busacca, D. R. Fandrick, J. J. Song, C. H. Senanayakl, *Adv. Synth. Catal.* **2011**, *353*, 1825 – 1864.

[2] For reviews, see: a) K. Burgess, M. J. Ohlmeyer, *Chem. Rev.* **1991**, *91*, 1179 – 1191; b) T. Hayashi in *Comprehensive Asymmetric Catalysis, Vol. 1* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto) Springer, Berlin, **1999**, pp. 351 – 366; c) C. M. Crudden, D. Edwards, *Eur. J. Org. Chem.* **2003**, 4695 – 4712; d) A.-M. Carroll, T. P. O'Sullivan, P. J. Guiry, *Adv. Synth. Catal.* **2005**, *347*, 609 – 631; e) C. M. Crudden, B. W. Glasspoole, C. J. Lata, *Chem. Commun.* **2009**, 6704 – 6716; f) E. Fernández, P. J. Guiry, K. P. T. Connole, J. M. Brown, *J. Org. Chem.* **2014**, *79*, 5391 – 5400.

[3] See for example: a) D. S. Matteson, *Chem. Rev.* **1989**, *89*, 1535 – 1551; b) E. Hupe, I. Marek, P. Knochel, *Org. Lett.* **2002**, *4*, 2861 – 2863; c) D. Imao, B. W. Glasspoole, V. S. Laberge, C. M. Crudden, *J. Am. Chem. Soc.* **2009**, *131*, 5024 – 5025.

[4] S. P. Thomas, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2009**, *48*, 1896 – 1898; *Angew. Chem.* **2009**, *121*, 1928 – 1930.

[5] a) M. Sato, N. Miyaura, A. Suzuki, *Tetrahedron Lett.* **1990**, *31*, 231 – 234; b) K. Burgess, M. J. Ohlmeyer, *J. Org. Chem.* **1988**, *53*, 5178 – 5179; c) K. Burgess, W. A. van der Donk, M. J. Ohlmeyer, *Tetrahedron: Asymmetry* **1991**, *2*, 613 – 621; d) T. Hayashi, Y. Matsumoto, Y. Ito, *Tetrahedron: Asymmetry* **1991**, *2*, 601 – 612.

[6] a) A. Z. Gonzalez, J. G. Román, E. Gonzalez, J. Martinez, J. R. Medina, K. Matos, J. A. Soderquist, *J. Am. Chem. Soc.* **2008**, *130*, 9218 – 9219; b) R. Corberán, N. W. Mszar, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2011**, *50*, 7079 – 7082; *Angew. Chem.* **2011**, *123*, 7217 – 7220; c) C. Mazet, D. Gérard, *Chem. Commun.* **2011**, *47*, 298 – 300.

[7] See for example: a) B. Wang, O. A. Wong, M.-X. Zhao, Y. Shi, *J. Org. Chem.* **2008**, *73*, 9539 – 9543 (epoxidation); b) X. Wang, M. Zak, M. Maddess, P. O'Shea, R. Tillyer, E. J. J. Grabowski, P. J. Reider, *Tetrahedron Lett.* **2000**, *41*, 4865 – 4869 (dihydroxylation); c) J. Mazuela, J. J. Verendel, M. Coll, B. Schäffner, A. Börner, P. G. Andersson, O. Pàmies, M. Diéguez, *J. Am. Chem. Soc.* **2009**, *131*, 12344 – 12353 (hydrogenation); d) O. Pàmies, P. G. Andersson, M. Diéguez, *Chem. Eur. J.* **2010**, *16*, 14232 – 14240 (hydrogenation).

[8] a) M. Diéguez, J. Mazuela, O. Pàmies, J. J. Verendel, P. G. Andersson, *J. Am. Chem. Soc.* **2008**, *130*, 7208 – 7209; b) M. Diéguez, O. Pàmies, J. J. Verendel, P. G. Andersson, *Chem. Commun.* **2008**, 3888 – 3890; c) J. Mazuela, P.-O. Norrby, P. G. Andersson, O. Pàmies, M. Diéguez, *J. Am. Chem. Soc.* **2011**, *133*, 13634 – 13645; d) M. Coll, O. Pàmies, M. Diéguez, *Chem. Commun.* **2011**, *47*, 9215 – 9217; e) J. Mazuela, O. Pàmies, M. Diéguez, *Adv. Synth. Catal.* **2013**, *355*, 2569 – 2583; f) J. Mazuela, O. Pàmies, M. Diéguez, *ChemCatChem* **2013**, *5*, 2410 – 2417; g) M. Coll, O. Pàmies, M. Diéguez, *Adv. Synth. Catal.* **2013**, *355*, 143 – 160; h) J. Margalef, X. Caldentey, E. A. Karlsson, M. Coll, J. Mazuela, O. Pàmies, M. Diéguez, M. A. Pericàs, *Chem. Eur. J.* **2014**, *20*, 12201 – 12214.

[9] a) C. Claver, O. Pàmies, M. Diéguez in *Phosphorus Ligands in Asymmetric Catalysis* (Ed.: A. Börner), Wiley-VCH, Weinheim, **2008**, pp. 506 – 528; b) P. W. N. M. van Leeuwen, P. C. J. Kamer, C. Claver, O. Pàmies, M. Diéguez, *Chem. Rev.* **2011**, *111*, 2077 – 2118.

[10] O. Pàmies, M. Diéguez, C. Claver, *J. Am. Chem. Soc.* **2005**, *127*, 3646 – 3647.

[11] G. J. H. Buisman, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Tetrahedron: Asymmetry* **1993**, *4*, 1625 – 1634.

[12] M. Gómez-Simón, S. Jansat, G. Muller, D. Panyella, M. Font-Bardía, X. Solans, *J. Chem. Soc. Dalton Trans.* **1997**, 3755 – 3764.

[13] J. Barluenga, F. J. Fañanás, R. Sanz, C. Marcos, J. M. Ignacio, *Chem. Commun.* **2005**, 933 – 935.

[14] D. B. Reitz, P. Beak, R. F. Farney, L. S. Helmick, *J. Am. Chem. Soc.* **1978**, *100*, 5428 – 5436.

[15] E. Nakamura, S. Mori, M. Nakamura, K. Morokuma, *J. Am. Chem. Soc.* **1997**, *119*, 4887 – 4899.

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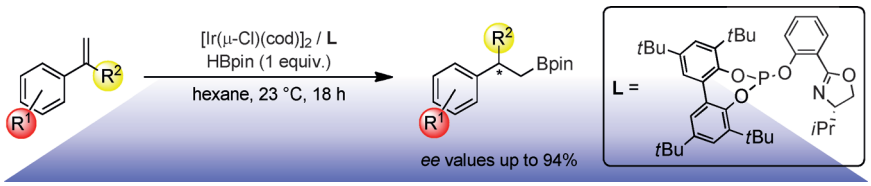
Filling the Gaps in the Challenging Asymmetric Hydroboration of 1,1-Disubstituted Alkenes with Simple Phosphite-Based Phosphinooxazoline Iridium Catalysts



Might of the phosphite: The highly regio- and enantioselective hydroboration of challenging 1,1-disubstituted olefins is achieved by using iridium catalysts modified with chiral phosphite-based phosphinooxazoline ligands. Use of the biaryl phosphite moiety in the ligand design is adventitious in terms of substrate versatility. The scope of the new phosphite-based catalysts is complementary to that exhibited by *tert*-butyl-substituted phosphinooxazoline iridium and N-heterocyclic carbene copper catalysts. Bpin = Pinacolato.