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Probing the Importance of the Hemilabile Site of Bis(phosphine) Monoxide Ligands in the Copper-Catalyzed Addition of Diethylzinc to *N*-Phosphinoylimines: Discovery of New Effective Chiral Ligands

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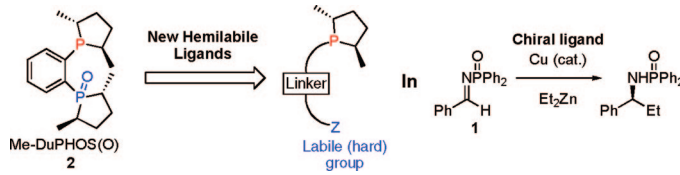

The hemilabile ligand Me-DuPHOS(O) **2** has proven to be a successful ligand for the copper-catalyzed addition of diethylzinc to *N*-phosphinoylimines. The corresponding α-chiral amines were obtained in high yields (80−98%) and enantiomeric ratios (19.0:1 to 99.0:1 er). Furthermore, this Cu•**2** catalytic system has been shown to be effective in the addition of diethylzinc to nitroalkenes and in the reduction of *β*,*β*-disubstituted vinyl phenyl sulfones. This paper describes a general structure/selectivity study in which the three ligand subunits (chiral phospholane−linker−labile coordinating group (Z)) are systematically modified and tested in the copper-catalyzed addition of diethylzinc to the *N*-phosphinoylimine **1** derived from benzaldehyde. This study led to the discovery of a new class of effective chiral ligands that combine a chiral phospholane unit and an achiral phosphine oxide.

Introduction

The discovery of Wilkinson's catalyst, $RhCl(PPh_3)_3$, for the hydrogenation of olefins was fundamental to the field of homogeneous catalysis.[1] With the increasing demand for optically pure compounds, many researchers focused on the development of chiral versions of the triphenylphosphine ligand employed in this system. The first examples of asymmetric hydrogenation reactions were reported in 1968 by Knowles[2a] and Horner[2b] who developed P-chirogenic monophosphines. Unfortunately, this class of ligands led to low enantiomeric ratios. Moreover, the difficult synthesis of these compounds contributed to the development of ligands where the chirality was held by the substituents on the phosphorus atom. Thus, Kagan[3] developed an easily accessible chiral diphosphine, DIOP, which gave excellent results for the hydrogenation of *N*-acetylphenylalanine and opened the path to the chiral diphosphines' era. As a result, BINAP and DuPHOS were discovered by Noyori[4] and Burk[5] in the 1980s and 1990s, respectively. These ligands and their derivatives are among the most widely studied and used in asymmetric catalysis to date.[6,7]

Another class of phosphine-based ligands known as hemilabile ligands emerged in the 1970s.[8] These are hybrid ligands of the general formula P,Z where the two groups, P (phosphorus) and Z, exhibit different donor properties toward the metal center (eq 1).

When complexed to a transition metal, the phosphorus center provides a soft donor site that binds strongly to the metal, but the hard site (Z) acts as a labile group that binds weakly to the metal. This results in an equilibrium creating a free coordination site around the metal (eq 1). There are a number of labile groups reported in the literature, and in general, oxygen-based substituents, such as ethers, esters, and phosphine oxides, are the most

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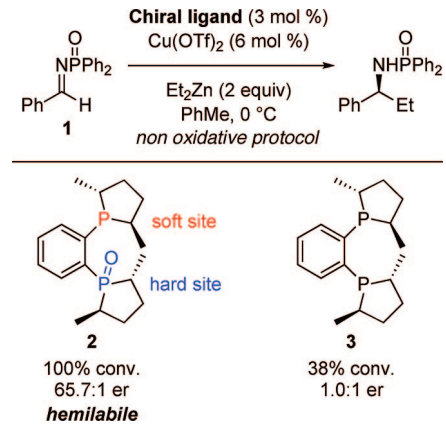
labile.[8a,b] Some hybrid ligands containing nitrogen, sulfur, or C═C functionalities also exhibit hemilabile properties.[9]

Hemilabile hybrid ligands display different behavior in catalysis compared to bidentate phosphine ligands, and they have been successfully used in several applications including the hydroformylation of olefins,[10] the carbonylation of methanol,[11] the oligomerization of ethylene,[12] and in Diels−Alder cycloaddition reactions.[13]

Recently, we developed a Cu(I)-catalyzed enantioselective addition of diorganozinc reagents to *N*-phosphinoylimines derived from both aromatic[14] and aliphatic[15] aldehydes that proceeded in high yields (80−98%) and enantiomeric ratios (19.0:1 to 99.0:1 er). At first, Me-DuPHOS **3** appeared to be an excellent ligand for this transformation.[16] However, a further investigation on the mechanism of the reaction led to the discovery that the hemilabile Me-DuPHOS(O) **2** was the active ligand leading to product with high enantiocontrol and high reaction rate. This ligand was formed in situ by the monoxidation of **3** with copper(I) or copper(II) triflate.[17] Employing the preformed monoxide ligand **2** was shown to give vastly superior results than diphosphine **3** when that latter was used under nonoxidizing conditions (Chart 1).[18]

CHART 1. Hemilabile versus Bidentate Ligand



Me-DuPHOS(O) also proved to be a very effective ligand in the addition of dialkylzinc reagents to nitroalkenes[19] and in the enantioselective reduction of β,β-disubstituted vinyl phenyl sulfones.[20]

Due to the success of **2** as a ligand for copper, we planned to develop new hemilabile ligands based on the same general structure consisting of a chiral phospholane, a linker group, and a labile coordinating group (Z) to further study the origin of the effectiveness of the Cu•**2** system. The ultimate aim was to generate chiral ligands with improved properties that can be employed in additional catalytic reactions. We also intended to simplify the structure of **2** in order to make the synthesis of the new ligands shorter and more easily tunable.

This paper will focus on the synthesis of these new hemilabile ligands and their effect in the copper-catalyzed addition of diethylzinc to **1**.

Results and Discussion

Often, in a given reaction, the progression of the catalytic species with phosphine-based ligands can be monitored by ^{31}P NMR. In our case, the presence of paramagnetic Cu(0) and Cu(II) species and the rapid equilibration and disproportionation between various complexes made this type of analysis difficult to exploit. As a result, we tried to isolate some of the putative reaction intermediates for X-ray analysis. Unfortunately, all of our attempts failed due to the instability of the Cu(I) species. Thus, to gain insight about the origin of the effectiveness of **2**, we designed several related hemilabile ligands. At the beginning of this study, we had already shown that the soft and hard sites should be kept in close proximity to each other to achieve good enantioinduction. Indeed, the use of phospholanes **4** and **5** led to high yields, but the product was isolated as a racemic mixture (Scheme 1).[14]

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(18) Côté, A.; Boezio, A. A.; Charette, A. B. *Angew. Chem., Int. Ed.* **2004**, *43*, 6525. In order to validate this hypothesis, we set out two protocols. The first one, the oxidative protocol, consisted of mixing the ligand and the copper salt for 1 h followed by the addition of diethylzinc. The second one, the nonoxidative protocol, was based on the formation of the EtCu(I) species ($Cu(OTf)_2 + Et_2Zn$, −40 °C, 20 min) prior to the addition of the ligand. Hence, in the latter, the monoxidation of the diphosphine was slowed down.

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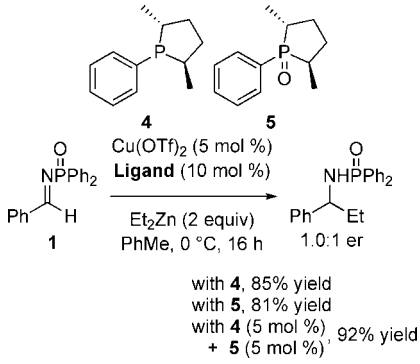
SCHEME 1. Use of a 1:1 Mixture of Ligands 4 and 5



Therefore, we designed ligands to vary the three main structural characteristics of **2**: the P−P linker, the projection of chirality from the phospholane unit, and the hard site (Z) (Figure 1).

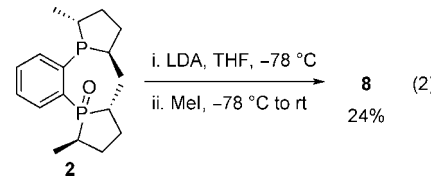
The P−P linker would be studied with ligand **6** by replacing the phenyl ring with a benzothiophene ring. The ligands **7**−**10** would offer information on the requirement of chirality on both sites (soft and hard) to achieve high enantioselectivities. Finally, it is known from the literature that the modification of the hard site can have a huge impact on the activity of the catalyst.[21,23] Thus, we planned to synthesize ligands **11**−**19** where the lability of the hard site was modulated.

Synthesis of Ligands 6 and 7. An attractive route to access diphosphine monoxides[24] such as ligands **6** and **7** was the monoxidation of the corresponding diphosphines. There were two methods reported in the literature to achieve this transformation. The Abatjoglou−Kapicak process is based on the selective formation of a monophosphonium salt (Ph_2P-$(CH_2)_n$-$P^+BnPh_2Br^-$) which is then hydrolyzed to the desired diphosphine monoxide (Ph_2P-$(CH_2)_n$-$P(O)Ph_2$).[25] The second method was developed by Grushin and is based on the palladium-catalyzed monoxidation of various diphosphines of the type Ph_2P-X-PPh_2.[26] These two methods gave generally good yields (53−87%) but were limited to diphenylphosphino diphosphines.[27] There were no reported methods for the monoxidation of dialkylaryl diphosphines.[28] Thus, we developed a two-step process for the synthesis of **2** starting from **3** (Scheme 2).[29] The first step involved monoprotection of **3** as the borane adduct using BH_3•DMS followed by oxidation with H_2O_2 to generate compound **20**. Deprotection with DABCO afforded **2** in excellent yields (93%).

This strategy was then applied to (*R*)-butiphane[30] developed by Solvias and to the P-chirogenic diphosphine **21** developed by Hoge[31] (Scheme 3).

Ligands **6** and **7** were obtained in good yields (51 and 71%, respectively). In the case of (*R*)-butiphane, the lower yield was due to the competition between phosphorus and sulfur toward borane protection. The structure of ligand **6** was confirmed by X-ray analysis.[32]

Synthesis of Ligand 8. Ligand **8** was synthesized in one step from **2** by deprotonation with LDA at low temperature and alkylation with MeI to afford **8** in 24% yield (eq 2).



The low yield can be explained by the steric hindrance around the reactive site. The structure of ligand **8** was confirmed by X-ray analysis.[32,33]

Synthesis of Ligands 9 and 10. Our retrosynthesis for these two ligands is depicted in Scheme 4. We hoped to obtain both ligands **9** and **10** by the monoxidation of diphosphine **22**.

Our synthesis of diphosphine **22** used a mixture of cyclic sulfates, **24** and **25**, according to Burk's procedure for the synthesis of **3**.[34] Unfortunately, after the S_N2 reaction, an inseparable mixture of the three possible diphosphines (**3**, **22**, and **26**) was obtained in favor of the two C_2-symmetric ligands, **3** and **26** (Scheme 5). This mixture was then treated under the monoxidation conditions described in Scheme 2. At that stage, the mixture of compounds was separable. Deprotection of the borane adduct **28** with DABCO provided ligand **9** in sufficient quantities for the current study. However, we were not able to isolate synthetically useful amount of **29**.

In order to access useful quantities of ligand **10**, a new route was designed based on the formation of the phosphine oxide moiety prior to the introduction of the chiral phospholane unit (Scheme 6).

This route started with the synthesis of phosphonate **30** by a palladium-catalyzed coupling reaction between 1-bromo-2-iodobenzene and diethylphosphite.[35] Reduction of **30** provided primary phosphine **31** in 29% yield. This was reacted with cyclic

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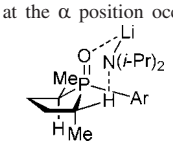
(30) (*R*)-Butiphane was kindly provided by Solvias AG.
(31) Hoge, G. *J. Am. Chem. Soc.* **2004**, *126*, 9920.
(32) See Supporting Information for crystal structure of compounds **6** and **8**.
(33) The deprotonation at the α position occurs *syn* to the P═O moiety.



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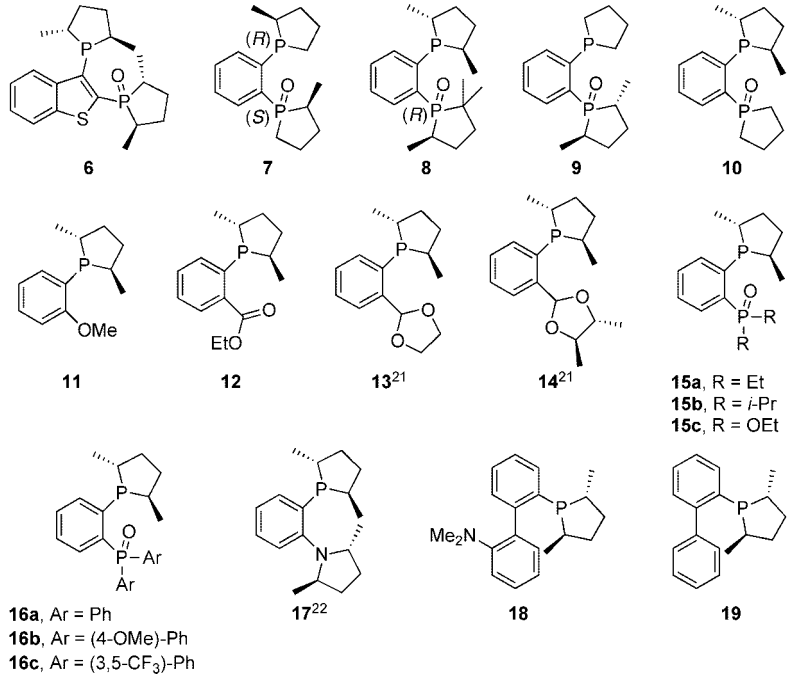
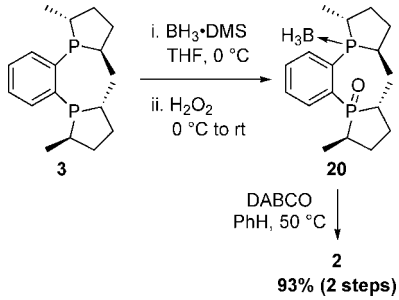
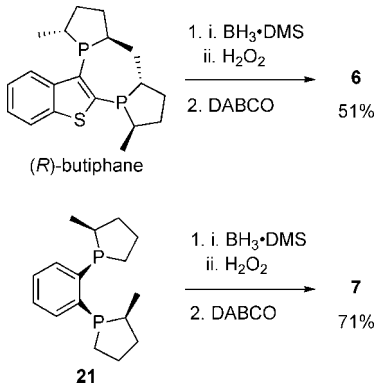


FIGURE 1. Hemilabile ligands designed for the study of the addition of diethylzinc to **1**.

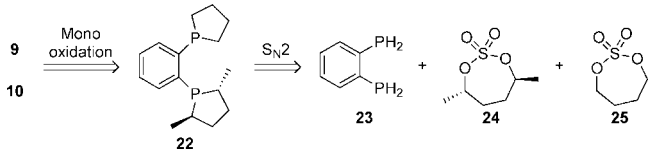
SCHEME 2. Synthesis of 2 by Monoxidation of 3



SCHEME 3. Monoxidation of (*R*)-Butiphane and 21



SCHEME 4. Retrosynthesis for Ligands 9 and 10



sulfate **25** under basic conditions to afford **32** in 74% overall yield after deprotection of the corresponding borane adduct. Then, a Li−Br exchange/trapping sequence followed by oxidation with H_2O_2 led to **33** in 71% yield containing the desired phosphine oxide unit. A borane protection/deprotection sequence was added to facilitate the purification of the polar compound **33**. Phosphonate **33** was then submitted to LAH reduction with careful control of the reaction temperature,[36] and the primary phosphine **34** was quickly converted to the borane adduct **29** using standard conditions. Finally, deprotection with DABCO afforded ligand **10** in 75% yield.

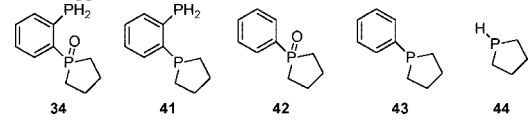
Synthesis of Ligands 11−19. Two different routes, A and B, were envisioned for the synthesis of the C_1-symmetric ligands **11**−**19** (Scheme 7).

Routes A and B differ in the order of introduction of the hard site (Z) and the chiral phospholane unit. Route A was followed for the synthesis of ligands **11**, **13**, **14**, **16a**, and **17**−**19**. In the case of ligands **12**, **15**, and **16b**,**c** where the functionality of the hard site (Z) (−CO_2Et, −P(O)R_2) would not be tolerated under the LAH conditions required for the introduction of the phospholane unit, route B was followed.

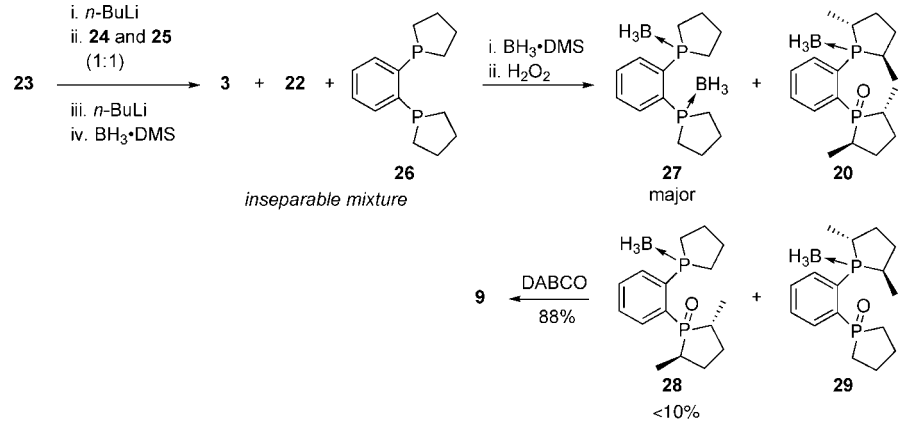
Results from Route A. As shown in Scheme 7, this route starts with the synthesis of the corresponding phosphonates **35** from commercially available reactants (Chart 2).

Typically, commercially available compounds were transformed into the desired aryl bromides **38** possessing the desired functionality (Z). Then, a sequence of Li−Br exchange followed by trapping with chlorodiethylphosphate afforded the desired phosphonates **35** in good yields (65−91%). For phosphonate **35g**, bearing a methoxy group, the procedure was slightly modified. Hence, phenol was treated with diethylphosphite to

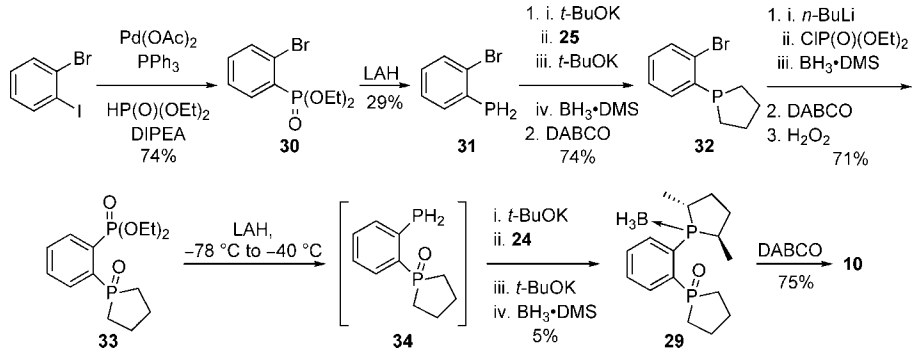
(36) The reduction gave rise to a mixture of the starting material **33**, the desired primary phosphine **34**, compounds **41** and **42**. If the temperature of the reaction mixture was allowed to rise above−40 °C, additional compounds (**43**, **44**) started to appear.



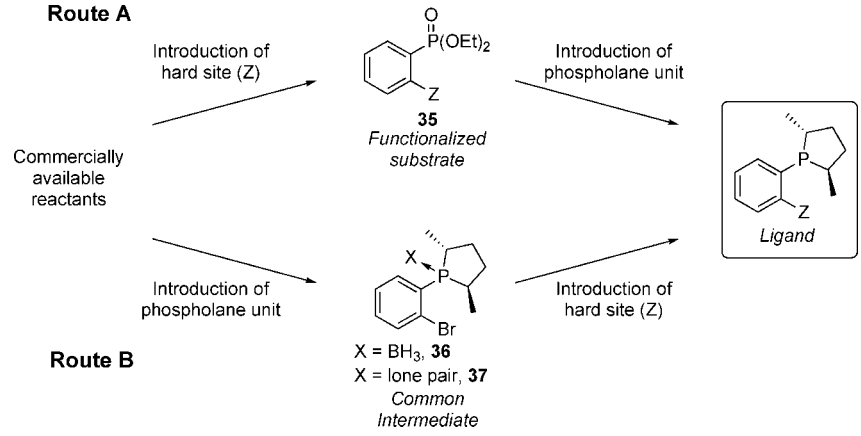
SCHEME 5. Synthesis of Ligand 9



SCHEME 6. Synthesis of Ligand 10



SCHEME 7. Two Routes for the Synthesis of the C_1-Symmetric Ligands 11−19



give the corresponding phosphate.[37] Then, *ortho*-lithiation with LDA followed by an intramolecular transfer of the phosphonate[38] and alkylation with methyl iodide afforded **35g** in 61% overall yield.

The next stage to access the final ligands typically involved three steps: (1) the reduction of the phosphonates **35** into their corresponding primary phosphines, which were used without further purification; (2) the introduction of the chiral phospholane unit; and (3) the deprotection of the borane adduct (Chart 3).

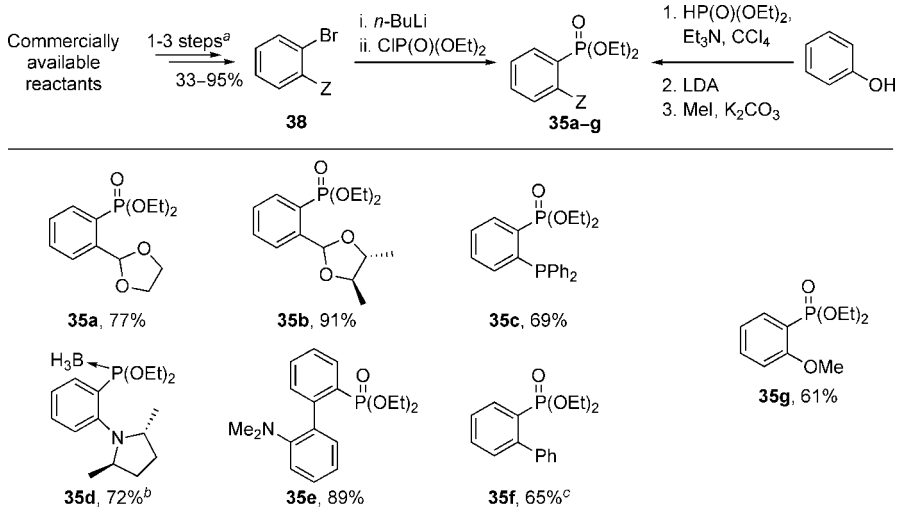
The borane adducts were generally obtained in moderate to good yields (24−66%) except for **13•BH$_3$** (8%) and **14•BH$_3$** (2%). Interestingly, the monoborane adduct **40**, precursor to the borane adduct **16a•BH$_3$**, was obtained according to the following procedure (Scheme 8).

After introducing the chiral phospholane unit and quenching with an excess of BH$_3$•DMS, the corresponding diborane adduct **39** was allowed to stir with silica gel in THF for 7 h. This led to the selective deprotection of the less nucleophilic phosphorus atom (−PPh$_2$). The monodeprotection was easily monitored by TLC analysis.

Results from Route B. This route was designed for ligands bearing functionalities (Z), which are incompatible with the use of LAH (ligands **12**, **15**, and **16b**,**c**). As depicted in Scheme 7, the functionality (Z) will be introduced after the chiral phospholane unit by derivatization of a common intermediate (**36** or **37**).

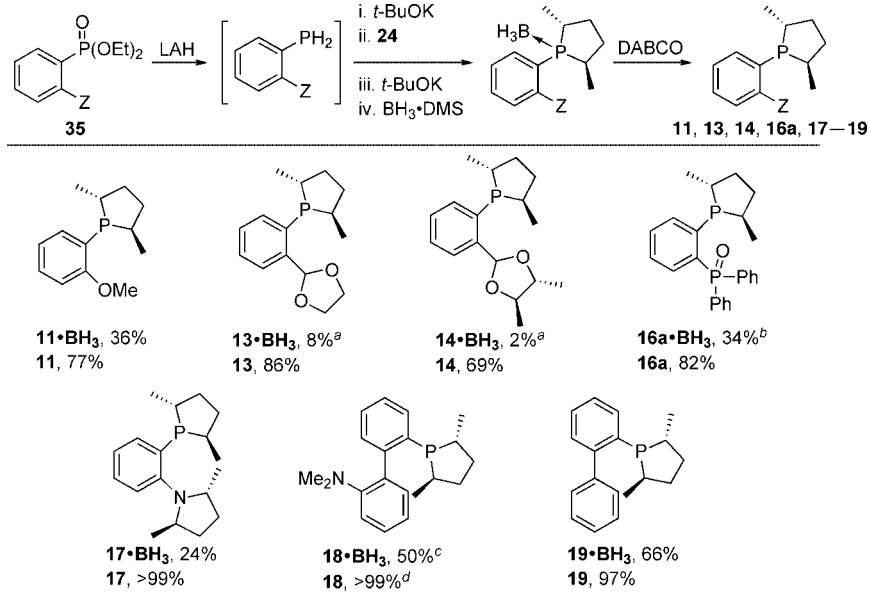
(37) Kenner, G. W.; Williams, N. R. *J. Chem. Soc.* **1955**, 522.
(38) Melvin, L. S. *Tetrahedron Lett.* **1981**, *22*, 3375.

CHART 2. Synthesis of Phosphonates 35



[a] See Supporting Information for detailed procedures. [b] $ClP(OEt)_2$ followed by BH_3•DMS was used as described by Moberg et al.[22b] [c] The iodo derivative of **38** was used instead.

CHART 3. Synthesis of the Final Ligands



[a] Reaction performed under nonoptimized conditions (see Supporting Information for details). [b] Oxidation with H_2O_2 was performed prior at the end of the sequence. [c] The product was isolated as a mixture of tropoisomers (1:1.3). [d] The product was isolated as a mixture of tropoisomers (1:2).

The synthesis of these intermediates was accomplished under the conditions previously described (Scheme 9).

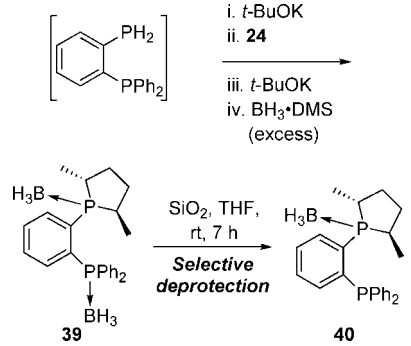
Then, intermediates **36** and **37** were functionalized using a Li−Br exchange followed by trapping with the appropriate electrophile. The reaction was then quenched either with H_2O_2 (from **36**) or with BH_3•DMS (from **37**). A final deprotection step led to the desired ligands in moderate to good yields (16−68%) (Chart 4).

Screening of Ligands and Discussion. All the ligands synthesized above (Figure 1) were tested in the copper-catalyzed addition of diethylzinc to **1**.

The effect of varying the linker group and the projection of chirality from the phospholane unit were first studied with ligands **6** and **7**−**10**, respectively, in the copper-catalyzed addition of diethylzinc to **1** (Table 1).

As can be seen from Table 1, the modification of the P−P linker (ligand **6**) led to results comparable to those of **2** with a slight decrease in enantioselectivities (entries 1 and 2, Table 1). Furthermore, the reaction seems sensitive to steric hindrance around the copper center since both conversions (65%) and enantioselectivities (4.0:1 er) were affected by the presence of the *gem*-dimethyl group in ligand **8** (entry 3, Table 1). The removal of one methyl group on both the soft and hard sites (ligand **7**) led to high conversions (99%), but a significant drop in enantioselectivities was observed (8.1:1 er) (entry 4, Table 1). Thus, at first sight, the results obtained with ligands **7** and **8** tend to indicate that the chirality is necessary on both sites to achieve high enantioselectivities. However, the results from ligands **9** and **10** were striking. Hence, the complete removal of chirality from the soft site (ligand **9**) gave high conversions (99%) but led to low enantioselectivities (1.3:1 er) (entry 5, Table 1). On the other hand, the absence of the two methyl substituents from the hard site (ligand **10**) led to higher conversions (95%) and identical enantioselectivities (49.0:1 er)

SCHEME 8. Selective Deprotection of Diborane Adduct 39



compared to **2** (entries 1 and 6, Table 1). These results demonstrated that only the chirality on the hard site is necessary for high levels of enantioinduction. Therefore, it could be anticipated that a careful choice of the hard site would lead to a successful ligand that could be more easily accessible.

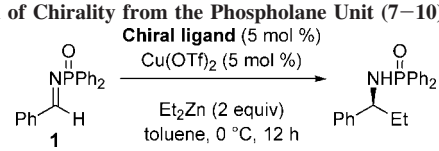
The effect of changing the degree of lability of the hard site was first studied with ligands **11**−**14** and **17**−**19** (Table 2).

The majority of the ligands screened in this category gave low conversions (<20%) and enantioselectivities (<1.3:1 er) (entries 2 and 4−7, Table 2). This again demonstrates the importance of the hard site for catalytic activity and that the degree of lability strongly influences the outcome of the reaction. Highly labile ether and acetal groups[39] (**11**, **13**, **14**) and more strongly binding, less labile nitrogen substituents[8b,40] (**17**, **18**) both gave poor conversions and enantioselectivities, suggesting that fine adjustments to the degree of lability can affect the results significantly. Ligand **19** led to high conversions (97%), but the *N*-phosphinoylamide was obtained as a racemic mixture (entry 8, Table 2). This result is similar to the one obtained from the monophospholanes **4** and **5** (eq 2). This indicates that the phenyl ring does not act as a labile moiety.[41] Ligand **12** gave good conversions (68%) along with low enantioselectivities (1.8:1 er) (entry 3, Table 2). This result is in agreement with the fact that the lability of ester groups is between that of ethers (most labile oxygen-based groups) and phosphine oxides (less labile oxygen-based groups). The phosphine oxide moiety seems to exhibit the right balance between electronic and steric properties that lead to high conversions and enantioselectivities. Therefore, we designed ligands **15** bearing alkyl and ethoxy substituents on the phosphine oxide and ligands **16** bearing aromatic groups with different electronic properties in order to study electronic effects. The results obtained with these ligands are listed in Table 3.

These results confirmed that the phosphine oxide was the optimal hard site. The aliphatic series (**15**) highlighted the sensitivity of the reaction toward steric hindrance. Indeed, ligand **15a** bearing a more flexible hard site (−P(O)Et_2) than ligand **10** (−P(O)-$(CH_2)_4$−) led to a slight decrease in conversions (75%) and enantioselectivities (19.0:1 er) (entry 2, Table 3). In addition, the presence of isopropyl groups (ligand **15b**) highly affected the reaction (10% conversions, entry 3, Table 3). In the case of ligand **15c**, the enantioselectivities were quite good (4.0:1 er) but the conversions were low (36%) (entry 4, Table 3), suggesting electronic effects are also important. In the aromatic series, ligand **16a** bearing two phenyl groups gave high conversions (91%) and enantioselectivities (13.3:1 er) (entry 5, Table 3). This indicates that alkyl groups (ligands **10** or **15a**) are not a prerequisite to form an efficient catalyst. The electronic properties of the aromatic groups were next examined. This revealed that the presence of electron-rich substituents such as methoxy groups (ligand **16b**, entry 6, Table 3) led to higher enantioselectivities (32.3:1 er) while maintaining good conversions (84%), whereas a significant drop in conversions (49%) and enantioselectivities (2.2:1 er) was observed with electron-poor substituents such as trifluoromethyl groups (ligand **16c**, entry 7, Table 3). A similar trend has also been reported with diphosphines and phosphite-type ligands in hydrogenation reactions.[42]

In the copper-catalyzed addition of diethylzinc to *N*-phosphinoylimines, we believe that the bond length and polarizability of the phosphine oxide moiety meets the specific requirements to align the substrate into the chiral pocket and to regenerate the catalytic active species. The following intermediate is

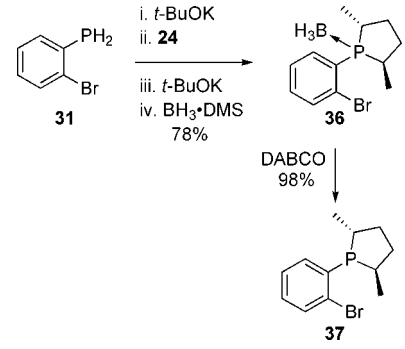
TABLE 1. Study of the Variation of the Linker Group (6) and the Projection of Chirality from the Phospholane Unit (7−10)



entry	chiral ligand	conversion (%)[a]	er (%)[b]
1	**2**	85	49.0:1
2	**6**	89	13.3:1
3	**8**	65	4.0:1
4	**7**	99	8.1:1[c]
5	**9**	99	1.3:1
6	**10**	95	49.0:1

[a] Conversions were determined by ^{1}H NMR with an internal standard. [b] Enantiomeric ratios were determined by chiral HPLC or SFC. [c] The (*R*) enantiomer was predominant.

SCHEME 9. Synthesis of the Common Intermediates 36 and 37



(39) (a) See ref 7. (b) Braunstein, P.; Chauvin, Y.; Nähring, J.; DeCian, A.; Fischer, J.; Tiripicchio, A.; Ugozzoli, F. *Organometallics* **1996**, *15*, 5551. (c) Mecking, S.; Keim, W. *Organometallics* **1996**, *15*, 2650.

(40) Ligands **17** and **18** could promote the addition of diethylzinc to **1** without the involvement of copper species.

(41) Coordination between copper and a phenyl ring has already been observed: Hubig, S. M.; Lindeman, S. V.; Kochi, J. K. *Coord. Chem. Rev.* **2000**, *200*−*202*, 831.

(42) (a) RajanBabu, T. V.; Radetich, B.; You, K. K.; Ayers, T. A.; Casalnuovo, A. L.; Calabrese, J. C. *J. Org. Chem.* **1999**, *64*, 3429. (b) Matsumura, K.; Shimizu, H.; Saito, T.; Kumobayashi, H. *Adv. Synth. Catal.* **2003**, *343*, 180. (c) Flanagan, S. P.; Guiry, P. J. *J. Organomet. Chem.* **2006**, *691*, 2125.

(43) EtZnOTf is generated during the formation of EtCu(I) from Et_2Zn and $Cu(OTf)_2$. For the reduction of Cu(II) to Cu(I) in the presence of Et_2Zn, see: (a) Alexakis, A. Asymmetric Conjugate Addition. In *Organocopper Reagents: A Practical Approach*; Taylor, R. J. K., Ed.; Oxford University Press: Oxford, 1994; pp 159−183. (b) *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinheim, Germany, 2002. For a beneficial effect of EtZnOTf, see: (c) Alexakis, A.; Vastra, J.; Mangeney, P. *Tetrahedron Lett.* **1997**, *38*, 7745. (d) Arnold, L. A.; Imbos, R.; Mandoli, A.; de Vries, A. H. M.; Naasz, R.; Feringa, B. L. *Tetrahedron* **2000**, *56*, 2865.

CHART 4. Functionalization of 36 and 37

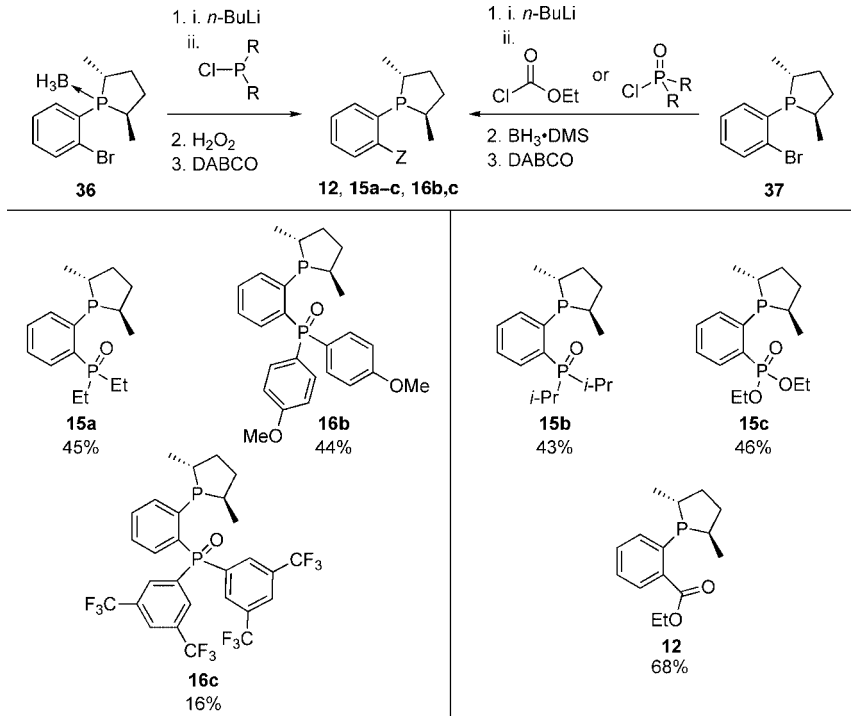
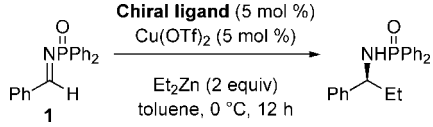


TABLE 2. Study of the Variation of the Lability of the Hard Site



entry	chiral ligand	conversion (%)[a]	er (%)[b]
1	**2**	85	49.0:1
2	**11**	15	1.2:1
3	**12**	68	1.8:1[c]
4	**13**	11	1.1:1
5	**14**	18	1.2:1
6	**17**	18	1.2:1
7	**18**	14	1.3:1
8	**19**	97	1.0:1

[a] Conversions were determined by ^{1}H NMR with an internal standard. [b] Enantiomeric ratios were determined by chiral HPLC or SFC. [c] The (*R*) enantiomer was predominant.

proposed whereby the phosphine moiety (soft site) binds to the ethylcopper species and that the phosphine oxide (hard site) preferentially binds to ethylzinc triflate[43] (Figure 2).[44]

As such, the chirality on the hard site would not be required to achieve enantioinduction. This is well demonstrated with ligands **10** and **16a**,**b**. Furthermore, it seems that the Lewis basicity of the hard site is highly important in the catalytic process (ligand **16b** vs **16c**).

Conclusion

In conclusion, we have developed new hemilabile ligands with the following general structure: chiral phospholane−linker−labile coordinating group. These were tested in the copper-catalyzed addition of diethylzinc to the *N*-phosphinoylimine **1**. The degree of lability of the hard site had a huge impact on the catalytic activity with the phosphine oxide moiety proving to be the optimal group. Furthermore, this study revealed that ligands bearing only one chiral phospholane and an achiral phosphine oxide (compared to **2**) led to high levels of enantioselectivities. In addition, the corresponding aliphatic (**15**) and aromatic (**16**) series of diphosphine monoxides could be potential ligands for other applications. This work is currently underway in our laboratories and will be reported in due course.

Experimental Section[45]

1,3,2-Dioxathiepane 2,2-dioxide (25). 1,3,2-Dioxathiepane 2-oxide[46] (5.0 g, 36.7 mmol) was dissolved in CCl_4 (26 mL), followed by MeCN (26 mL) and distilled H_2O (41 mL) and cooled to 0 °C. $RuCl_3 \cdot xH_2O$ (52 mg, 0.25 mmol) was added in one portion, and then $NaIO_4$ (11.8 g, 55.0 mmol) was added portionwise. The reaction was stirred for 1 h and then transferred to a separatory funnel where the organic layer was separated. The aqueous layer was extracted with Et_2O (3 × 25 mL). The combined organic layers were washed with brine (20 mL) and dried over Na_2SO_4. Concentration under vacuum gave the crude material which was purified by flash chromatography on silica gel (40% EtOAc/hexane) to afford cyclic sulfate **25** as a white solid (5.0 g, 89%): mp 40−41 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.51−4.31 (m, 4H), 2.09−2.01 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 71.7 (2 C), 27.4 (2 C). All spectral data are consistent with the literature values.[47]

Diethyl 2-bromophenylphosphonate (30). $Pd(OAc)_2$ (449 mg, 2.0 mmol), PPh_3 (5.2 g, 20.0 mmol), 1-bromo-2-iodobenzene (12.8 mL, 100.0 mmol), diethylphosphite (64.4 mL, 500.0 mmol), distilled DIPEA (108.9 mL, 625.0 mmol), and distilled/degassed EtOH (400

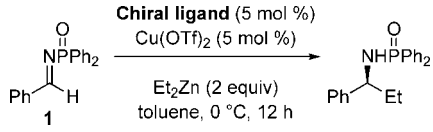
(44) (a) It has been previously demonstrated that the reaction follows a first-order kinetics in catalyst, see ref 18. (b) Charette, A. B.; Côté, A.; Desrosiers, J.-N.; Bonnaventure, I.; Lindsay, V. N. G.; Lauzon, C.; Tannous, J.; Boezio, A. *Pure Appl. Chem.* **2008**, *80*, 881.

(45) Presented in the Experimental Section are the experimental procedures and spectral data for the new ligands **10** and **16a**,**b** and their intermediates. Complete experimental procedures and spectral data for all new compounds are presented in the Supporting Information.

(46) This material was synthesized according to the literature procedure: Berridge, M. S.; Franceschini, M. P.; Rosenfeld, E.; Tewson, T. J. *J. Org. Chem.* **1990**, *55*, 1211.

(47) This material was synthesized according to the literature procedure: Burk, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 8518.

TABLE 3. Study of the Lability of Various Phosphine Oxide-Based Hard Sites



entry	chiral ligand	conversion (%)[a]	er (%)[b]
1	**2**	85	49.0:1
2	**15a**	75	19.0:1
3	**15b**	10	1.0:1
4	**15c**	36	4.0:1
5	**16a**	91	13.3:1
6	**16b**	84	32.3:1
7	**16c**	49	2.2:1

[a] Conversions were determined by ^{1}H NMR with an internal standard. [b] Enantiomeric ratios were determined by chiral HPLC or SFC.

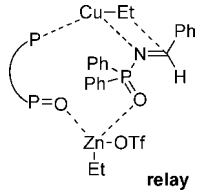


FIGURE 2. Putative intermediate.

mL) were placed in a 1 L flask equipped with a condenser. The reaction was heated to reflux for 48 h (monitored by TLC). The reaction was cooled to rt, diluted with Et_2O (200 mL), and washed with a solution of HCl (1 M). The aqueous layer was then extracted with Et_2O (3 × 200 mL). The combined organic layers were washed with a solution of NaOH (2.5 M, 50 mL) and brine (50 mL) and dried over $MgSO_4$. Concentration under vacuum gave the crude material which was purified by flash chromatography on silica gel (hexane:acetone:Et_3N (70:29:1)) to afford phosphonate **30** as a pale yellow oil (21.8 g, 74%): R_f 0.23 (30% acetone/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05−7.96 (m, 1H), 7.70−7.62 (m, 1H), 7.43−7.33 (m, 2H), 4.28−4.04 (m, 4H), 1.35 (td, J = 7.1, 0.5 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.2 (d, J_{C-P} = 8.3 Hz), 134.2 (d, J_{C-P} = 11.2 Hz), 133.5 (d, J_{C-P} = 2.7 Hz), 129.3 (d, J_{C-P} = 192.0 Hz), 126.8 (d, J_{C-P} = 13.6 Hz), 125.1 (d, J_{C-P} = 3.9 Hz), 62.5 (d, J_{C-P} = 5.6 Hz), 16.2 (d, J_{C-P} = 6.6 Hz); ^{31}P NMR (121 MHz, $CDCl_3$) δ 15.4; IR (neat) 2981, 2905, 1579, 1422, 1244, 1140, 1017, 967, 759 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{15}BrO_3P$ (M + H)$^+$ 292.9937, found 292.9940.

(2-Bromophenyl)phosphine (31). A solution of phosphonate **30** (7.9 g, 27.0 mmol) in dry Et_2O (30 mL) was cannulated to a suspension of LAH (2.6 g, 67.4 mmol) in dry Et_2O (100 mL) at 0 °C. The reaction was stirred for 1 h. The mixture was cannulated over $Na_2SO_4 \cdot 10H_2O$ (65 g) at 0 °C and stirred for 1 h at rt. The mixture was filtered under argon and washed with Et_2O. The solvent was distilled off at atmospheric pressure, and the residue was finally distilled (50 °C, 0.1 mmHg) to afford the primary phosphine **31** as a colorless oil (1.5 g, 29%): ^{1}H NMR (400 MHz, C_6D_6) δ 7.21−7.13 (m, 1H), 7.03−6.96 (m, 1H), 6.68−6.60 (m, 1H), 6.57−6.49 (m, 1H), 3.88 (dd, J = 203.8, 1.9 Hz, 2H); ^{31}P NMR (162 MHz, C_6D_6) δ −119.0.

[1-(2-Bromophenyl)phospholanium-1-yl](trihydrido)borate(1-) (32•BH$_3$). *t*-BuOK (374 mg, 3.3 mmol) was added to a solution of primary phosphine **31** (600 mg, 3.2 mmol) in distilled THF (32 mL) at −30 °C (internal temperature). The orange solution was allowed to warm slowly to 0 °C (1 h) and was cannulated to a solution of cyclic sulfate **25** (483 mg, 3.2 mmol) in distilled THF (3.2 mL) at rt and stirred for 2 h. *t*-BuOK (374 mg, 3.3 mmol) was added to the solution at rt, and the reaction was stirred for 48 h. The resulting yellow solution was treated with $BH_3 \cdot$DMS (10 M, 480 μL, 4.7 mmol) at rt and stirred for 2 h. The reaction was then concentrated under vacuum to give a solid residue which was triturated with CH_2Cl_2 and filtered on Celite. Concentration under vacuum gave the crude material which was purified by flash chromatography on silica gel (5% EtOAc/hexane) to afford borane adduct **32•BH$_3$** as a white solid (572 mg, 74%): R_f 0.19 (5% EtOAc/hexane); mp 82−84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (ddd, J = 11.4, 7.6, 1.8 Hz, 1H), 7.64 (ddd, J = 7.9, 2.7, 1.2 Hz, 1H), 7.39 (tt, J = 7.6, 1.4 Hz, 1H), 7.32 (tt, J = 7.8, 1.4 Hz, 1H), 2.52−2.37 (m, 2H), 2.19−1.99 (m, 6H), 1.36−0.37 (br m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.6 (d, J_{C-P}= 11.2 Hz), 134.3 (d, J_{C-P} = 5.3 Hz), 132.5 (d, J_{C-P} = 1.7 Hz), 130.6 (d, J_{C-P} = 44.3 Hz), 127.4 (d, J_{C-P} = 9.3 Hz), 126.7 (d, J_{C-P} = 2.9 Hz), 26.6 (d, J_{C-P} = 2.8 Hz), 25.3, 24.9; ^{31}P NMR (162 MHz, $CDCl_3$) δ 38.0 (br d_{app}, J_{P-B} = 63.3 Hz); IR (neat) 2955, 2406, 2325, 1452, 1425, 1408, 1127, 1112, 1050, 1022, 858, 733, 702 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{15}BBrNaP$ (M + Na)$^+$ 279.0089, found 279.0080. Anal. Calcd for $C_{10}H_{15}BBrP$: C, 46.75; H, 5.88. Found: C, 46.91; H, 5.81.

1-(2-Bromophenyl)phospholane (32). DABCO (375 mg, 3.3 mmol) and borane adduct **32•BH$_3$** (572 mg, 2.2 mmol) were placed in a 50 mL flask which was purged with argon. Dry PhH (20 mL) was then added, and the reaction was stirred at 50 °C for 20 h. The reaction was then cooled to rt and concentrated under vacuum. The crude material was purified by filtering quickly (care should be taken at that stage to avoid oxidation of the ligand by air) through a short pad of silica gel (degassed 5% EtOAc/hexane) to afford phospholane **32** as a colorless oil (521 mg, 96%): R_f 0.29 (5% EtOAc/hexane); ^{1}H NMR (400 MHz, C_6D_6) δ 7.37 (ddd, J = 7.9, 2.9, 1.2 Hz, 1H), 6.93 (dt, J = 7.6, 1.6 Hz, 1H), 6.85 (td, J = 7.3, 1.1 Hz, 1H), 6.69−6.63 (td, J = 7.6, 1.7 Hz, 1H), 1.89−1.64 (m, 4H), 1.50−1.32 (m, 4H); ^{31}P NMR (162 MHz, C_6D_6) δ −10.7.

Diethyl 2-(1-oxidophospholan-1-yl)phenylphosphonate (33). *n*-BuLi (3.05 M in hexane, 767 μL, 2.3 mmol) was added dropwise to a solution of phospholane **32** (542 mg, 2.2 mmol) in distilled THF (22 mL) at −78 °C while keeping the internal temperature below −75 °C. The yellow solution was stirred for 30 min at −78 °C. Diethyl chlorophosphate (354 μL, 2.4 mmol) was then added at −78 °C while keeping the internal temperature below −75 °C. The resulting solution was then allowed to warm to rt and stirred overnight. The solution was treated with $BH_3 \cdot$DMS (10 M, 450 μL, 4.5 mmol) at rt and stirred for 1 h. The reaction was then concentrated under vacuum to give a solid residue which was triturated with CH_2Cl_2 and filtered on Celite. Concentration under vacuum gave the crude material which was purified by flash chromatography on silica gel (40−50% EtOAc/hexane) to afford the borane adduct as a colorless oil (540 mg, 77%).

DABCO (290 mg, 2.6 mmol) and the borane adduct (540 mg, 1.7 mmol) were placed in a 50 mL flask which was purged with argon. Dry PhH (17 mL) was then added, and the reaction was stirred at 50 °C for 16 h (monitored by TLC). The reaction was then cooled to rt and concentrated under vacuum. The crude material was taken up in THF (15 mL), and H_2O_2 (34% in H_2O) (240 μL, 2.6 mmol) was added at rt. The reaction was stirred for 2 h, then slowly quenched with a saturated solution of Na_2SO_3 (5 mL) and transferred to a separatory funnel. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried over $MgSO_4$. The crude material was purified by flash chromatography on silica gel (0−30% MeOH/EtOAc) to afford phosphonate **33** as a white solid (500 mg, 92%): R_f 0.32 (30% MeOH/EtOAc); mp 77−79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07−7.97 (m, 1H), 7.92−7.84 (m, 1H), 7.57−7.44 (m, 2H), 4.16−3.99 (m, 4H), 2.44−2.28 (m, 2H), 2.10−1.82 (m, 6H), 1.23 (t, J = 7.1 Hz, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 137.2 (dd, J_{C-P} = 80.9, 14.2 Hz), 134.2 (t_{app}, J_{C-P} = 8.8 Hz), 133.2 (dd, J_{C-P} = 14.9, 9.5 Hz), 131.6 (dd, J_{C-P} = 10.4, 2.7 Hz), 130.7 (dd, J_{C-P} = 13.5, 1.9 Hz), 130.4 (dd, J_{C-P} = 187.8, 8.9 Hz), 62.4 (d, J_{C-P} = 5.8 Hz), 29.2 (d, J_{C-P} = 69.2 Hz), 24.0 (d, J_{C-P} = 8.5 Hz), 16.0 (d, J_{C-P} = 6.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 63.6 (d, J_{P-P} = 9.5 Hz, P = O), 16.3 (d, J_{P-P} = 9.5 Hz, P(O)(OEt)$_2$); IR (neat)

2952, 1449, 1403, 1256, 1171, 1139, 1130, 1010, 968, 852, 794, 776, 710, 679 cm^{-1}; LRMS (APCI) calcd for $C_{14}H_{23}O_4P_2$ $(M + H)^+$ 317.1, found 317.1. Anal. Calcd for $C_{14}H_{22}O_4P_2$: C, 53.17; H, 7.01. Found: C, 53.11; H, 6.96.

{(2*R*,5*R*)-2,5-Dimethyl-1-[2-(1-oxidophospholan-1-yl)phenyl]phospholanium-1-yl}(trihydrido) borate(1-) (29). A solution of phosphonate **33** (450 mg, 1.4 mmol) in dry THF (2 mL) was cannulated to a suspension of LAH (135 mg, 3.5 mmol) in dry Et_2O (12 mL) at −78 °C. The resulting suspension was allowed to warm to −45 °C (internal temperature) and stirred for 30 min at −45 °C. (It was crucial to maintain the internal temperature below −40 °C to avoid excessive reduction and decomposition.) The mixture was cannulated over $Na_2SO_4 \cdot 10H_2O$ (3 g) at −78 °C and stirred for 1 h at rt. The mixture was filtered under argon and washed with dry Et_2O. The solvent was pumped off to yield a colorless oil, and distilled THF (2 mL) was added. An aliquot was taken: a mixture of starting material **33** (∼35%), desired primary phosphine **34** (∼35%), **41** (∼18%), and **42** (∼12%) was obtained: ^{31}P NMR (162 MHz, C_6D_6) δ 60.6 (d, J = 5.2 Hz, P(V)═O (**34**)), −115.1 (P(III) (**34**)); 58.7 (d, J = 9.1 Hz, P═O (**33**)), 16.2 (d, J = 9.1 Hz, P(O)$(OEt)_2$ (**33**)); 54.2 (**42**); −20.9 (d, J = 99.3 Hz, P(III) (**41**)), −126.2 (d, J = 99.2 Hz, PH_2 (**41**))).

t-BuOK (159 mg, 1.4 mmol) was added to a solution of phosphines (1.4 mmol) in distilled THF (15 mL) at −30 °C (internal temperature). The orange solution was allowed to warm slowly to 0 °C (1 h) and was cannulated to a solution of cyclic sulfate **24**[47] (255 mg, 1.4 mmol) in distilled THF (2 mL) at rt and stirred for 2 h. *t*-BuOK (159 mg, 1.4 mmol) was added to the solution at rt and stirred for 48 h. The resulting white solution was treated with $BH_3 \cdot$DMS (10 M, 200 μL, 2.0 mmol) at rt and stirred for 2 h. The reaction was then concentrated under vacuum to give a solid residue which was triturated with CH_2Cl_2 and filtered on Celite. Concentration under vacuum gave the crude material which was purified by flash chromatography on silica gel (60 to 90 to 100% EtOAc/hexane then 5% MeOH/EtOAc) to afford borane adduct **29** as a white solid (20.8 mg, 5%): R_f 0.15 (100% EtOAc); mp 100−102 °C; $[\alpha]^{20}_D$ −101.8 (*c* 1.7, PhH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (t_{app}, J = 8.8 Hz, 1H), 7.61−7.41 (m, 3H), 3.15−2.86 (m, 2H), 2.54−1.78 (m, 10H), 1.73−1.52 (m, 2H), 1.34 (dd, J = 14.2, 6.9 Hz, 3H), 0.98 (dd, J = 14.9, 7.3 Hz, 3H), 1.08−0.27 (br m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0 (dd, J_{C-P} = 85.5, 7.8 Hz), 134.8 (t_{app}, J_{C-P} = 9.0 Hz), 133.3 (dd, J_{C-P} = 34.8, 7.4 Hz), 131.0 (dd, J_{C-P} = 8.2, 2.8 Hz), 130.9 (dd, J_{C-P} = 12.2, 6.3 Hz), 130.2 (dd, J_{C-P} = 11.9, 2.1 Hz), 33.7 (d, J_{C-P} = 37.0 Hz), 32.2 (d, J_{C-P} = 14.2 Hz), 31.8 (dd, J_{C-P} = 36.7, 6.0 Hz, 2 C), 31.0, 29.9 (d, J_{C-P} = 35.0 Hz), 25.2 (dd, J_{C-P} = 20.3, 8.4 Hz, 2 C), 18.9 (d, J_{C-P} = 5.9 Hz), 13.8 (d, J_{C-P} = 2.4 Hz); ^{31}P NMR (121 MHz, $CDCl_3$) δ 64.1 (d, J_{P-P} = 5.8 Hz, P(V)═O), 49.6 (br d_{app}, J_{P-P} = 59.3 Hz, P(III)); IR (neat) 2922, 2852, 2355, 1455, 1262, 1162, 1125, 1058, 753, 680, 630 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{27}BONaP_2$ $(M + Na)^+$ 331.1534, found 331.1522.

(2*R*,5*R*)-2,5-Dimethyl-1-[2-(1-oxidophospholan-1-yl)phenyl]phospholane (10). DABCO (12 mg, 0.11 mmol) and borane adduct **29** (21 mg, 0.07 mmol) were placed in a 5 mL flask which was purged with argon. Dry PhH (1 mL) was then added, and the reaction was stirred at 50 °C for 8 h (monitored by TLC). The reaction was then cooled to rt. Concentration under vacuum (care should be taken at that stage to avoid oxidation of the ligand by air) gave the crude material which was purified quickly by flash chromatography on silica gel (5 to 10% degassed MeOH/EtOAc) to afford ligand **10** as a sticky oil (14.9 mg, 75%): R_f 0.24 (100% EtOAc); ^{1}H NMR (400 MHz, C_6D_6) δ 7.88−7.77 (m, 1H), 7.39 (d, J = 6.9 Hz, 1H), 7.14−7.03 (m, 2H), 2.54−2.34 (m, 2H), 2.34−2.15 (m, 1H), 2.16−1.43 (m, 9H), 1.43−1.28 (m, 1H), 1.21 (dd, J = 18.4, 7.1 Hz, 3H), 1.22−1.13 (m, 1H), 0.88 (dd, J = 9.5, 7.1 Hz, 3H); ^{31}P NMR (162 MHz, C_6D_6) δ 58.2 (d, J = 10.3 Hz, P(V)═O), 2.0 (d, J = 10.3 Hz, P(III)).

{(2*R*,5*R*)-1-[2-(Diphenylphosphoryl)phenyl]-2,5-dimethylphospholanium-1-yl}(trihydrido) borate(1-) (16a·BH_3). *t*-BuOK (342 mg, 3.0 mmol) was added to a solution of diphenyl(2-phosphinophenyl)phosphine (853 mg, 2.9 mmol) in distilled THF (30 mL) at −30 °C (internal temperature). The orange solution was allowed to warm slowly to 0 °C (1 h) and was cannulated to a solution of cyclic sulfate **24**[47] (523 mg, 2.9 mmol) in distilled THF (3 mL) at rt and stirred for 2 h. The reaction was diluted with distilled THF (30 mL), and *t*-BuOK (342 mg, 3.0 mmol) was added to the solution at rt and stirred for 48 h. The resulting white solution was treated with $BH_3 \cdot$DMS (10 M, 580 μL, 5.8 mmol) at rt and stirred for 2 h. Concentration under vacuum gave the crude material which was taken up in THF and stirred with silica gel for 7 h. Concentration under vacuum gave a dry pack which was purified by flash chromatography on silica gel (10% EtOAc/hexane) to afford borane adduct **40** as a white solid (400 mg, 34%).

The borane adduct **40** (100 mg, 0.26 mmol) was then dissolved in THF (3 mL), and H_2O_2 (34% in H_2O) (72 μL, 0.65 mmol) was added at rt. The reaction was stirred at rt until completion. Then a saturated solution of Na_2SO_3 was slowly added at 0 °C, and the mixture was stirred for 30 min at rt. The suspension was then filtered and washed with EtOAc. Concentration under vacuum gave borane adduct **16a•BH_3** as a white solid (105 mg, quantitative): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (ddd, J = 12.2, 7.4, 3.7 Hz, 1H), 7.68−7.34 (m, 12H, Ar-*H*), 7.25−7.12 (m, 1H), 3.71−3.50 (m, 1H), 2.62−2.46 (m, 1H), 2.25−1.89 (m, 3H), 1.74−1.53 (m, 1H), 1.05 (dd, J = 15.1, 7.2 Hz, 3H), 0.58 (dd, J = 16.1, 6.9 Hz, 3H), 1.21−0.19 (br m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.5 (dd, J = 17.1, 10.5 Hz), 135.2 (dd, J = 15.8, 7.8 Hz), 135.6 (d, J = 97.6 Hz), 133.9 (d, J = 13.4 Hz), 132.9 (d, J = 35.7 Hz), 132.7 (d, J = 8.6 Hz), 132.2 (d, J = 9.7 Hz, 2 C), 132.1−131.9 (m), 131.6 (d, J = 9.6 Hz, 2 C), 131.6−131.4 (dd, J = 11.5, 2.6 Hz, 2 C), 129.7 (dd, J = 12.5, 1.9 Hz), 128.7 (d, J = 12.1 Hz, 2 C), 128.5 (d, J = 12.3 Hz, 2 C), 35.1 (d, J = 37.8 Hz), 34.1 (d, J = 10.0 Hz), 32.8, 31.0 (d, J = 33.7 Hz), 16.4 (d, J = 4.1 Hz), 12.2 (d, J = 3.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 52.0−50.0 (br m, PBH_3), 33.7 (d, J = 4.9 Hz, P(V)).

(2*R*,5*R*)-1-[2-(Diphenylphosphoryl)phenyl]-2,5-dimethylphospholane (16a). DABCO (40 mg, 0.35 mmol) and borane adduct **16a·BH_3** (95 mg, 0.23 mmol) were placed in a 10 mL flask which was purged with argon. Dry PhH (2.3 mL) was then added, and the reaction was stirred at 50 °C for 17 h (monitored by TLC). The reaction was then cooled to rt and concentrated under vacuum. The crude material was purified quickly by flash chromatography on silica gel (70% degassed EtOAc/hexane) to afford ligand **16a** as a white solid (74.3 mg, 82%): R_f 0.36 (70% EtOAc/hexane); mp 124−126 °C; $[\alpha]^{20}_D$ −12.8 (*c* 1.8, PhH); ^{1}H NMR (400 MHz, C_6D_6) δ 7.88−7.75 (m, 4H), 7.52−7.38 (m, 2H), 7.13−6.96 (m, 7H), 6.93−6.86 (m, 1H), 2.58−2.29 (m, 2H), 1.98−1.72 (m, 2H), 1.41−1.25 (m, 1H), 1.16−1.05 (m, 1H), 1.02 (d, J = 7.9 Hz, 3H), 0.99 (dd, J = 10.2, 7.4 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 144.5 (dd, J_{C-P} = 40.2, 11.0 Hz), 141.7 (dd, J_{C-P} = 102.9, 30.9 Hz), 136.5 (dd, J_{C-P} = 104.0, 2.1 Hz), 135.5 (d, J_{C-P} = 102.4 Hz), 134.7 (dd, J_{C-P} = 11.3, 2.7 Hz), 134.1 (dd, J_{C-P} = 13.3, 8.7 Hz), 132.9 (dd, J_{C-P} = 9.1, 0.6 Hz, 2 C), 132.1 (dd, J_{C-P} = 9.6, 3.3 Hz, 2 C), 131.2 (d, J_{C-P} = 2.6 Hz), 130.7 (dd, J_{C-P} = 12.6, 2.5 Hz, 2 C), 128.4 (d, J_{C-P} = 11.7 Hz, 2 C), 128.2 (d, J_{C-P} = 12.2 Hz, 2 C), 127.7 (d, J_{C-P} = 12.4 Hz), 36.9 (d, J_{C-P} = 2.2 Hz), 36.5 (d, J_{C-P} = 4.4 Hz), 35.4 (d, J_{C-P} = 13.0 Hz), 35.1 (d, J_{C-P} = 15.2 Hz), 20.0 (d, J_{C-P} = 37.1 Hz), 17.5 (d, J_{C-P} = 2.9 Hz); ^{31}P NMR (162 MHz, C_6D_6) δ 28.3 (d, J_{P-P} = 15.6 Hz, P(V)═O), 3.1 (d, J_{P-P} = 15.6 Hz, P(III)); IR (neat) 3053, 2920, 2860, 1479, 1436, 1193, 1113, 729, 717, 693, 678 cm^{-1}; LRMS (APCI) calcd for $C_{24}H_{27}O_2P_2$ $(M(O) + H)^+$ 409.1, found 409.1. Anal. Calcd for $C_{24}H_{26}OP_2$: C, 73.46; H, 6.68. Found: C, 73.19; H, 6.70.

[(2*R*,5*R*)-1-(2-Bromophenyl)-2,5-dimethylphospholanium-1-yl](trihydrido)borate(1-) (36). *t*-BuOK (623 mg, 5.6 mmol) was added to a solution of primary phosphine **31** (1.0 g, 5.3 mmol) in distilled THF (53 mL) at −30 °C (internal temperature). The orange solution was allowed to warm slowly to 0 °C (1 h) and was cannulated to a solution of cyclic sulfate **24**[47] (953 mg, 5.3 mmol) in distilled

THF (5.3 mL) at rt and stirred for 2 h. *t*-BuOK (623 mg, 5.6 mmol) was added to the solution at rt, and the reaction was stirred for 48 h. The resulting yellow solution was treated with BH_3·DMS (10 M, 600 μL, 6.0 mmol) at rt and stirred for 2 h. The reaction was then concentrated under vacuum to give a solid residue which was triturated with CH_2Cl_2 and filtered on Celite. Concentration under vacuum gave the crude material which was purified by flash chromatography on silica gel (5% EtOAc/hexane) to afford borane adduct **36** as a white solid (1.2 g, 78%): R_f 0.28 (5% EtOAc/hexane); mp 65−68 °C; $[\alpha]^{20}_D$ −40.7 (*c* 2.87, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (ddd, *J* = 12.8, 7.7, 1.6 Hz, 1H), 7.66 (ddd, *J* = 7.9, 2.3, 1.3 Hz, 1H), 7.42 (tt, *J* = 7.7, 1.3 Hz, 1H), 7.38−7.32 (m, 1H), 3.50−3.33 (m, 1H), 2.68−2.51 (m, 1H), 2.40−2.18 (m, 2H), 2.11−1.95 (m, 1H), 1.79−1.62 (m, 1H), 1.28 (dd, *J* = 16.4, 6.9 Hz, 3H), 1.10 (dd, *J* = 14.7, 7.3 Hz, 3H), 1.03−0.25 (br, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8 (d, J_{C-P} = 14.8 Hz), 134.6 (d, J_{C-P} = 4.8 Hz), 132.8 (d, J_{C-P} = 1.9 Hz), 128.0 (d, J_{C-P} = 38.0 Hz), 127.5 (d, J_{C-P} = 10. Six Hz), 127.2, 35.0 (d, J_{C-P} = 37.6 Hz), 34.3 (d, J_{C-P} = 15.4 Hz), 34.2 (d, J_{C-P} = 9.5 Hz), 29.5 (d, J_{C-P} = 35.2 Hz), 14.9 (d, J_{C-P} = 4.2 Hz), 14.3 (d, J_{C-P} = 4.2 Hz); ^{31}P NMR (121 MHz, $CDCl_3$) δ 49.5 (br dd_{app}, *J* = 117.5, 47.6 Hz); IR (neat) 2928, 2868, 2373, 1451, 1416, 1051, 1022, 747, 673 cm^{-1}; LRMS (APCI) calcd for $C_{12}H_{17}{}^{79}BrP$ $(M(-BH_3) + H)^+$ 271.0, found 271.1; calcd for $C_{12}H_{17}{}^{81}BrP$ $(M(-BH_3) + H)^+$ 273.0, found 273.1. Anal. Calcd for $C_{12}H_{19}BBrP$: C, 50.58; H, 6.72. Found: C, 50.80; H, 6.86.

((2*R*,5*R*)-1-{2-[Bis(4-methoxyphenyl)phosphoryl]phenyl}-2,5-dimethylphospholanium-1-yl) (trihydrido)borate(1-) (16b·BH_3). *n*-BuLi (3.03 M in hexane, 122 μL, 0.37 mmol) was added dropwise to a solution of borane adduct **36** (100 mg, 0.35 mmol) in distilled THF (3.5 mL) at −78 °C while keeping the internal temperature below −75 °C. The purple solution was stirred for 15 min at −78 °C. A solution of bis(4-methoxyphenyl)phosphinous chloride[48] (108 mg, 0.38 mmol) in distilled THF (1 mL) was then added at −78 °C while keeping the internal temperature below −75 °C. The resulting yellow solution was then allowed to warm to rt and stirred overnight. The resulting mixture was quenched with a saturated solution of NH_4Cl (5 mL). The aqueous layer was extracted with EtOAc (3 × 10 mL), washed with brine (10 mL), and dried over $MgSO_4$. Concentration under vacuum gave the crude material which was redissolved in THF (3 mL), and H_2O_2 (34% in H_2O) (43 μL, 0.42 mmol) was added at 0 °C. The reaction was stirred at rt until completion (2 h). Then a saturated solution of Na_2SO_3 (5 mL) was slowly added at 0 °C, and the mixture was stirred for 10 min. The mixture was then transferred to a separatory funnel, where the aqueous layer was extracted with EtOAc (3 × 10 mL), and the combined organic layers were dried over $MgSO_4$. Concentration under vacuum gave the crude material which was purified by flash chromatography on silica gel (40 to 50% EtOAc/hexane) to afford borane adduct **16b•BH_3** as a white solid (74.5 mg, 46%): R_f 0.28 (50% EtOAc/hexane); mp 73−75 °C; $[\alpha]^{20}_D$ −123.9 (*c* 1.26, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57−8.42 (m, 1H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.52−7.31 (m, 5H), 7.18 (dd, *J* = 13.9, 7.7 Hz, 1H), 7.03−6.90 (m, 4H), 3.82 (d, *J* = 4.5 Hz, 6H), 3.79−3.61 (m, 1H), 2.65−2.44 (m, 1H), 2.29−1.87 (m, 3H), 1.75−1.56 (m, 1H), 1.13−0.26 (br m, 3H), 1.03 (dd, *J* = 15.1, 7.2 Hz, 3H), 0.63 (dd, *J* = 16.1, 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4 (d, J_{C-P} = 2.5 Hz, 2 C), 139.5 (dd, J_{C-P} = 17.5, 10.7 Hz), 136.6 (d, J_{C-P} = 101.6 Hz), 135.1 (dd, J_{C-P} = 14.0, 6.1 Hz), 134.1 (d, J_{C-P} = 11.0 Hz, 2 C), 133.5 (d, J_{C-P} = 11.2 Hz, 2 C), 132.7 (dd, J_{C-P} = 31.5, 8.7 Hz), 131.3 (dd, J_{C-P} = 11.7, 2.5 Hz), 129.6 (dd, J_{C-P} = 12.5, 2.0 Hz), 125.5, 124.3 (d, J_{C-P} = 7.6 Hz), 114.2 (d, J_{C-P} = 18.5 Hz, 2 C), 114.0 (d, J_{C-P} = 18.8 Hz, 2 C), 55.3 (d, J_{C-P} = 2.9 Hz, 2 C), 35.2 (d, J_{C-P} = 38.0 Hz), 34.2 (d, J_{C-P} = 9.8 Hz), 32.9, 31.0 (d, J_{C-P} = 33.8 Hz), 16.4 (d, J_{C-P} = 4.1 Hz), 12.5 (d, J_{C-P} = 4.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 52.30−49.65 (br s, *P*BH_3), 33.1 (d, J_{P-P} = 4.8 Hz, *P*(V)=O); IR (neat) 2928, 2374, 1595, 1502, 1455, 1293, 1253, 1177, 1113, 1059, 1023, 829, 801, 742, 659 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{33}BO_3NaP_2$ $(M + Na)^+$ 489.1890, found 489.1894.

(2*R*,5*R*)-1-{2-[Bis(4-methoxyphenyl)phosphoryl]phenyl}-2,5-dimethylphospholane (16b). DABCO (27 mg, 0.24 mmol) and borane adduct **16b·BH_3** (74 mg, 0.16 mmol) were placed in a 10 mL flask which was purged with argon. Dry PhH (1.6 mL) was then added, and the reaction was stirred at 50 °C for 23 h (monitored by TLC). The reaction was then cooled to rt and concentrated under vacuum. The crude material was purified quickly by flash chromatography on silica gel (0−5% MeOH/EtOAc) to afford ligand **16b** as a white solid (69.5 mg, 96%): R_f 0.26 (100% EtOAc); ^{1}H NMR (400 MHz, C_6D_6) δ 7.82−7.71 (m, 4H), 7.57−7.47 (m, 2H), 7.21−7.11 (m, 1H), 6.99 (t, *J* = 7.2 Hz, 1H), 6.68 (ddd, *J* = 13.7, 8.7, 1.9 Hz, 4H), 3.19 (s, 3H), 3.16 (s, 3H), 2.68−2.49 (m, 1H), 2.47−2.34 (m, 1H), 1.98−1.76 (m, 2H), 1.44−1.29 (m, 1H), 1.23−1.11 (m, 1H), 1.08 (dd, *J* = 12.9, 7.0 Hz, 3H), 1.05 (dd, *J* = 7.0, 3.9 Hz, 3H); ^{31}P NMR (162 MHz, C_6D_6) δ 28.3 (d, *J* = 14.6 Hz, *P*(V)=O), 3.5 (d, *J* = 14.5 Hz, *P*(III)).

General Procedure for the Addition of Diethylzinc to *N*-[(Phenyl)methylene]-*P*,*P*-diphenylphosphinic amide (1). Neat diethylzinc (34−100 μL, 0.33−0.96 mmol, 2.00 equiv) was added to a solution of $Cu(OTf)_2$ (2.9−10.5 mg, 0.008−0.029 mmol, 0.05 equiv) in dry PhMe (500 μL) at −45 °C. The resulting yellow solution was stirred and kept below −40 °C for 15 min. A solution of the chiral ligand (0.008−0.014 mmol, 0.05 equiv) in dry PhMe (500 μL) was added at −40 °C, and the resulting solution was warmed slowly to rt for 50 min. The solution was then cooled to 0 °C, and a suspension of amide **1**[49] (50−147 mg, 0.16−0.48 mmol, 1.00 equiv) in dry PhMe (1−4 mL) was cannulated (Teflon cannula). After stirring for 12 h at 0 °C, 1,3,5-trimethoxybenzene (internal standard) (0.1 M in PhH, 200 μL) was added. The reaction was then quenched with a saturated solution of NH_4Cl (5 mL), and the aqueous layer was extracted rapidly with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried over Na_2SO_4. Concentration under vacuum gave the crude material which was analyzed by ^{1}H NMR. The crude material was then purified by flash chromatography on silica gel (90% EtOAc/hexane). Enantiomeric ratio was determined either by HPLC analysis (Chiralpak) AD-H, 80:20 hexane: *i*-PrOH, 1.0 mL/min: (major enantiomer) t_r = 9.6 min, (minor enantiomer) t_r = 12.7 min or by SFC analysis (Chiralpak) AD, 200 bar, 2 mL/min, 40 °C, modifier 30% *i*-PrOH: (minor enantiomer) t_r = 5.6 min, (major enantiomer) t_r = 7.7 min.

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Supporting Information Available: Experimental procedures for the preparation of all the compounds and characterization data for each reaction and detailed structural assignment as well as crystallographic data of compounds **6** and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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