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Influence of Steric Symmetry and Electronic Dissymmetry on the Enantioselectivity in Palladium-Catalyzed Allylic Substitutions

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Chiral P,N-ligands with pseudo-C_2 and pseudo-C_s symmetry based on chiral pyrrolidine and phospholane rings or on dinaphthatodihydroazepino and dinaphthatodihydrophosphepino moieties were prepared and assessed in the palladium-catalyzed allylic substitutions of allylic acetates. Higher selectivity was achieved with pseudo-C_2-symmetric ligands based on the binaphthyl skeleton than with the analogous C_2-symmetric P,P- and N,N-analogues. Pseudo-C_2-type ligands had properties superior to those of pseudo-meso-type ligands when 1,3-diphenyl-2-propenyl acetate was used as a substrate, whereas the reverse situation was found for 3-cyclohexenyl acetate. Chirally flexible ligands, prepared by substitution of one of the rigid binaphthyl skeletons for a flexible biphenyl system, were found to induce chirality to the same extent as a 1:1 mixture of the rigid ligands.

Introduction

Control of the steric and electronic properties of chiral ligands employed in asymmetric metal catalysis is a requirement for efficient transfer of chirality, and factors responsible for those properties thus need to be considered in ligand design and preparation.[1] Ligands with C_2 symmetry have been extensively employed in asymmetric catalysis.[2] The success of such ligands originates in a reduction of the number of catalyst−substrate interactions and, as a consequence, the number of competing reaction pathways. There is, however, no fundamental rule stating that ligands with 2-fold rotational symmetry must always exert enantiocontrol superior to those lacking elements of symmetry. In bidentate C_2-symmetric ligands, the two donor atoms have, by definition, to be identical, and therefore, the enantiodiscrimination in asymmetric reactions involving such ligands relies solely on the steric properties of the enantiocontrolling catalytic intermediates. Introduction of electronic dissymmetry destroys the rotational symmetry, and in C_2-symmetric ligands differences in trans influence and π-back-donation of the donor atoms can thus not be exploited.

The palladium-catalyzed substitution of symmetrical allylic acetates and carbonates constitutes one example of reactions where C_2- as well as C_1-symmetric ligands have been shown to result in high enantioselectivity.[3] Nucleophilic attack occurs on an intermediate π-allyl palladium complex outside the coordination sphere of the metal and is directed via ligand−substrate interactions. Ligands with C_2 symmetry have the advantage of providing a reduced number, with symmetrical substrates often one single, of diastereoisomeric π-allyl palladium complexes, whereas with asymmetric ligands, electronic dissymmetry may contribute to control nucleophilic attack.

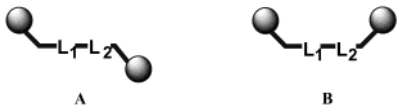

FIGURE 1. Ligands with C_2 or pseudo-C_2 symmetry (A) and C_s or pseudo-C_s symmetry (B).

We wished to exploit the behavior of "sterically symmetric" ligands (possessing a mirror plane or a 2-fold rotational axis) which are being electronically desymmetrized. Systematic studies have previously been made of the effect of electronic properties of ligands on the enantioselectivity,[4] but the ligands studied have at the same time usually been "sterically dissymmetric", containing differently substituted donor atoms. To our knowledge, the effect of pure electronic dissymmetry has previously been studied in only a few cases. A pseudo-C_2-symmetric ligand was shown to afford higher enantioselectivity than truly C_2-symmetric analogues,[5] and a "pseudo-meso" ligand with the asymmetry in the ligand backbone was found to induce chirality in the catalytic process.[6]

Two types of structures, A and B (Figure 1), fulfilling our needs may be distinguished. The arrangement A has

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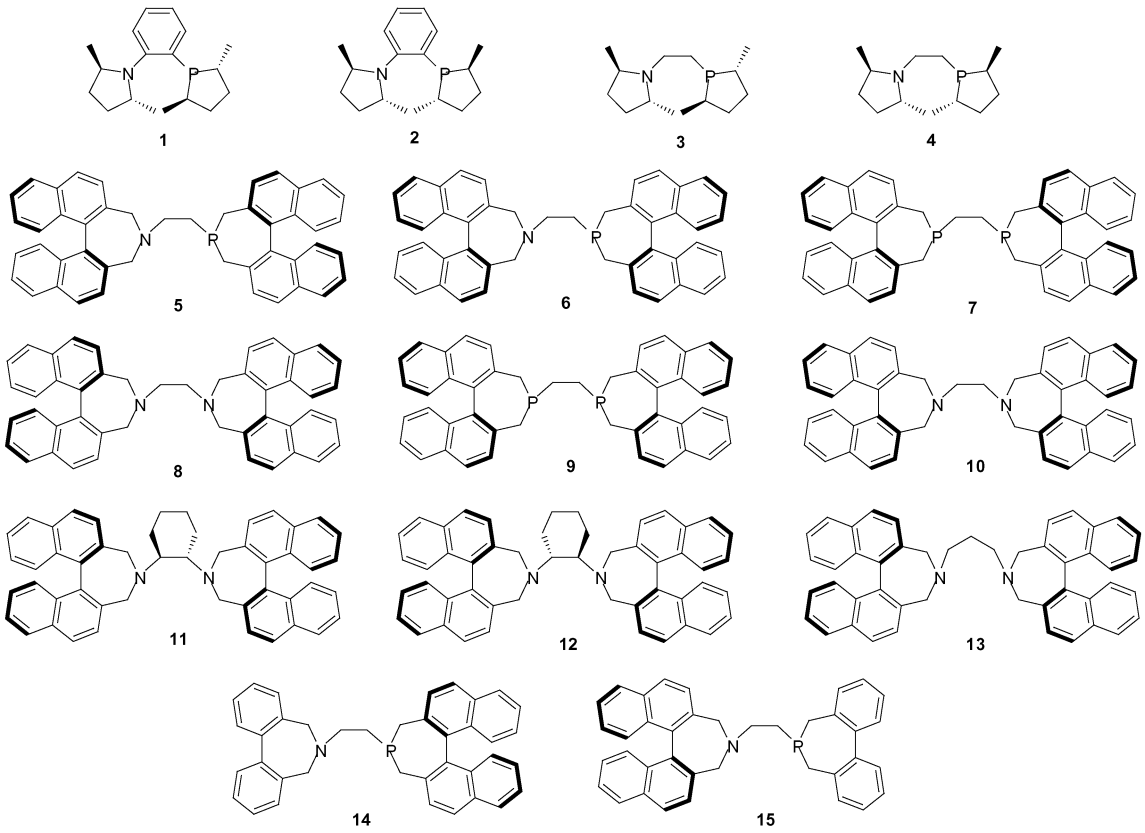
CHART 1



C_2 symmetry when L_1 is equal to L_2 and C_1 symmetry when L_1 is different from L_2, whereas B is achiral (meso compound) when L_1 is equal to L_2 but asymmetric when L_1 is different from L_2. In a preliminary study, we reported results from initial investigations of the two types of ligands where we demonstrated that a ligand of type B exhibited higher reactivity and resulted in higher enantioselectivity in reactions of a substrate reacting via an anti-anti π-allyl palladium complex, while those with structure A were preferred for syn-syn complexes.[7] We now report on further studies of the use of ligands with different steric and electronic symmetry properties in palladium catalyzed allylation reactions.

Results

Ligand Design and Preparation. Ligands based on rigid, conformationally restricted scaffolds, which have proven to exhibit high enantiodiscrimination in catalytic reactions, were selected for the present study. Trans-2,5-disubstituted five-membered nitrogen and phosphorus[8] heterocycles on one hand and dinaphthatodihydroazepino[9] and dinaphthatodihydrophosphepino derivatives[10] on the other hand were considered to satisfy our requirements and were selected as appropriate chiral motifs for the construction of suitable N,N-, N,P-, and P,P-ligands. The two moieties containing the heteroatom donors were connected with different linkers to allow for structural diversity and variation of the steric and geometric parameters (ligands **1**−**15**, Chart 1).

For the construction of 1-substituted *trans*-dialkylphospholanes, two synthetic strategies have been described. One involves reaction of a lithio *trans*-2,5-dialkylphospholane, obtained from a *trans*-2,5-dialkyl-1-phenylphospholane via *P*-aryl bond cleavage with lithium[11] or from lithium bis(trimethylsilyl)phosphide and a cyclic sulfate,[12] with a suitable electrophile, whereas the key step in the second strategy is the reaction of the cyclic sulfate of an (*R**,*R**)-1,4-alkanediol with an appropriate lithiophosphido derivative.[13] For the preparation of the pyrrolidine part of the ligands a variety of suitable methods are available, including N-alkylation of a preformed pyrrolidine as well as alkylation of a primary amine with an electrophile derived from 2,5-hexanediol.[14] The route finally selected for the preparation of **1** and **2** started with 2-bromoaniline (**16**), which was treated with (*S*,*S*)-2,5-hexanediol cyclic sulfate (**17**, Scheme 1), obtained via Baker's yeast reduction of hexane-2,5-dione.[15] Bromine lithium exchange of the resulting pyrrolidine (**18**, 71%) followed by reaction with

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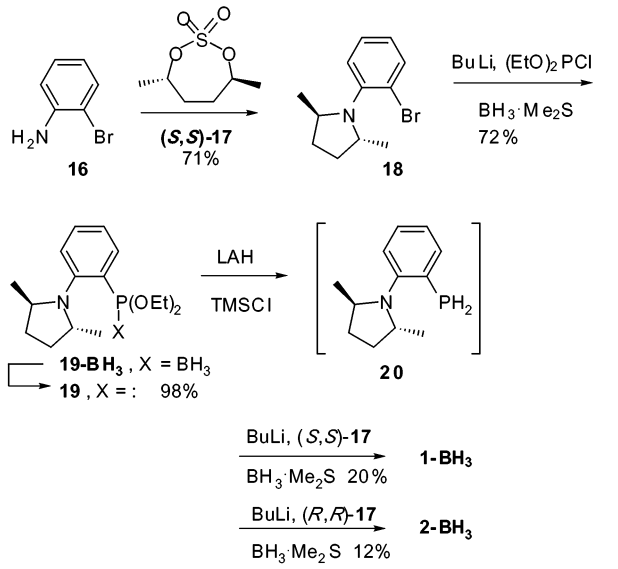
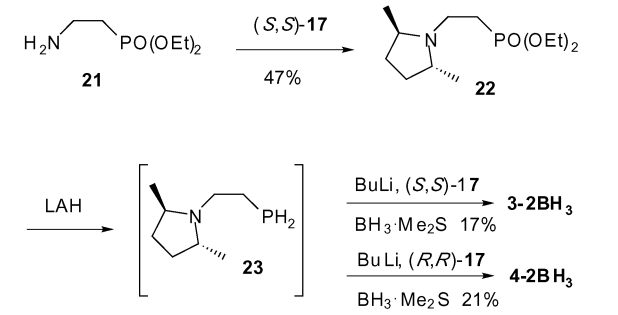
SCHEME 1



SCHEME 2



diethylchlorophosphite yielded a phosphinite, which was isolated as its borane adduct **19**−BH_3 (72%). Deprotection using DABCO[16] (to yield **19**), subsequent reduction (LAH/TMSCl), and lithiation of the phosphine (**20**) obtained afforded a monolithiophosphide that was reacted with (*S*,*S*)-2,5-hexanediol cyclic sulfate or (*R*,*R*)-2,5-hexanediol cyclic sulfate. A second litiation completed the ring closure, yielding **1** and **2**, respectively (20 and 12% yield from **19**−BH_3), isolated as their borane adducts. Compound **1** and its four-membered ring analogue were recently prepared in low yields by an alternative procedure.[17]

Ligands **3** and **4**, with more electron-rich phosphorus and nitrogen atoms, were obtained via reaction of (2-aminoethyl)phosphonic acid diethyl ester (**21**) with (*S*,*S*)-2,5-hexanediol cyclic sulfate (**17**) to yield **22** (47%), which was reduced by LAH[18] to the corresponding phosphine (**23**). Lithiation and treatment with a (*S*,*S*)- or (*R*,*R*)-2,5-hexanediol cyclic sulfate, followed by BH_3·Me_2S, afforded the desired borane protected ligands **3** (17% from **22**) and **4** (21% from **22**, Scheme 2); 2 equiv of BH_3·Me_2S was required as the first equivalent was trapped by the electron-rich nitrogen atom. The four-membered ring analogue of **3** was recently prepared via a similar procedure.[17]

Ligands **5** and **6**,[7] based on 4,5-dihydro-3*H*-dinaphtho-[1,2-*c*:2′,1′-*e*]azepino and 4,5-dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]phosphepino skeletons, were prepared as previously described via a route analogous to that used for the preparation of **3** and **4**, by reaction of (*R*)-2,2′-bis-(bromomethyl)-1,1′-binaphthyl ((*R*)-**24**),[19] obtained together with its enantiomer from BINOL via resolution,[20] with (2-aminoethyl)phosphonic acid diethyl ester (**21**) followed by reduction to the primary phosphine. Protection with borane followed by alkylation of the protected phosphine with (*R*)-**24** or (*S*)-**24** gave the desired ligands as their borane adducts. Attempts to alkylate on phosphorus prior to protection, using **24** and a variety of bases, resulted in lower yields of products. Selective deprotection at nitrogen gave proligands **5**−BH_3 and **6**−BH_3 (59 and 61%, respectively, from **24**), which could be fully deprotected or used directly in the catalytic reactions.

To enable comparison of the asymmetric ligands with C_2-symmetric analogues, the P,P- and N,N-ligands **7** and **8** were also synthesized. The former ligand (**7**) was obtained from reaction of (*S*)-**24** with ammonium phosphinate[21] (to give **25**, 42%), followed by reduction with phenylsilane[22] to give **26**,[23] isolated as its borane adduct (43%, Scheme 3). Disubstitution of ethylene glycol ditosylate with **26**−BH_3 resulted in a low yield of product, and as this route can give access to only one diastereoisomer it was not considered useful. Instead, conjugate addition of **26**−BH_3 to diethyl vinylphosphonate (**27**) gave **28**−BH_3 (83%), which was subjected to LAH reduction to give **29**−BH_3 (71%). Treatment of **28**−BH_3 with an additional 1 equiv of borane gave the bisborane adduct of **29**, which afforded protected ligand **7** (51%) after reaction with (*S*)-**24**. An alternative procedure affording **7**, employing reaction of bis(1,2-dichlorophosphine)ethane with bis(lithiomethyl)-1,1′-binaphthyl, was also recently described.[24] Ligand **8** was prepared in one step from (*R*)-2,2′-bis(bromomethyl)-1,1′-binaphthyl and 1,2-diaminoethane according to a published procedure (Scheme 4).[25] Meso ligands **9** and **10**,[25] which were desired in order to enable comparison of the reactivity of the asymmetric ligands with that of analogues with different steric properties, were prepared via treatment of (*R*)-**24** with **29**-2BH_3 and **31**, respectively, the latter obtained by reacting (*S*)-**24** with a large excess of 1,2-diaminoethane.

To assess the importance of the length and structure of the tether connecting the coordinating parts of the ligands, the N,N-ligands **11**−**13** were prepared via reaction of (*R*)-2,2′-bis(bromomethyl)-1,1′-binaphthyl with the

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(18) Gali, H.; Prabhu, K. R.; Karra, S. R.; Katti, K. V. *J. Org. Chem.* **2000**, *65*, 676−680.
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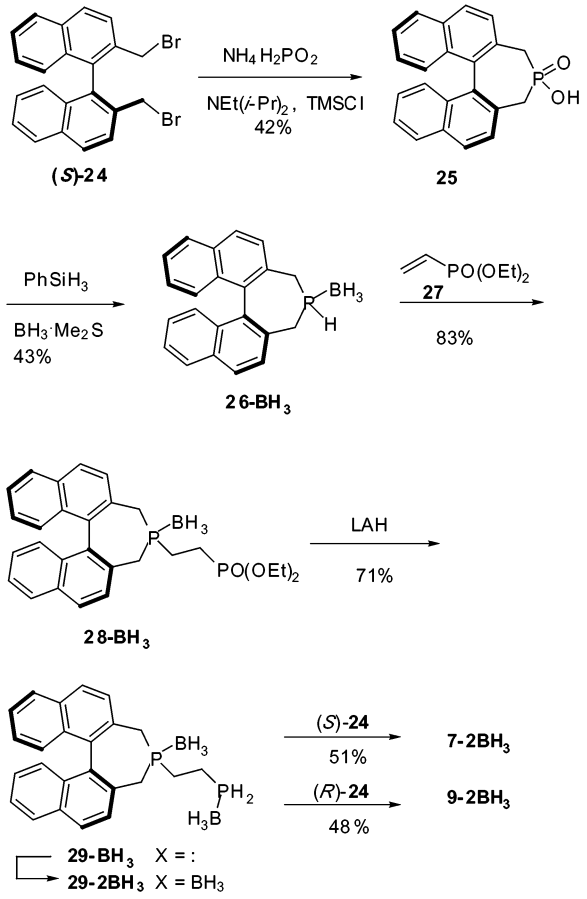
SCHEME 3



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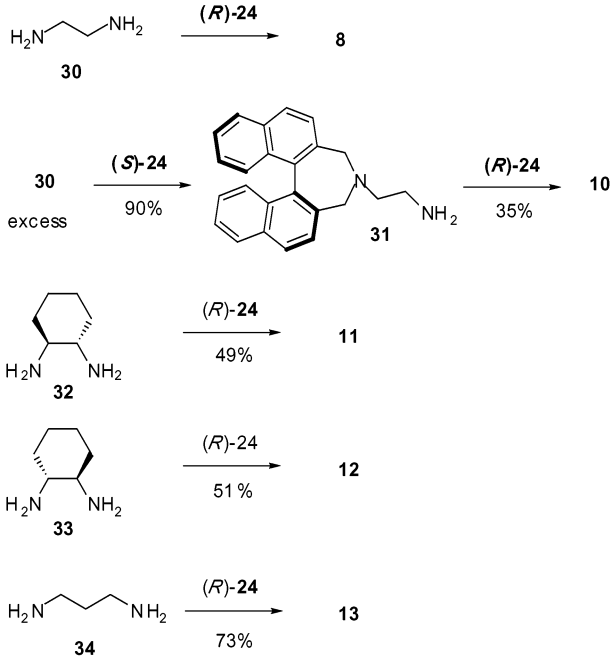
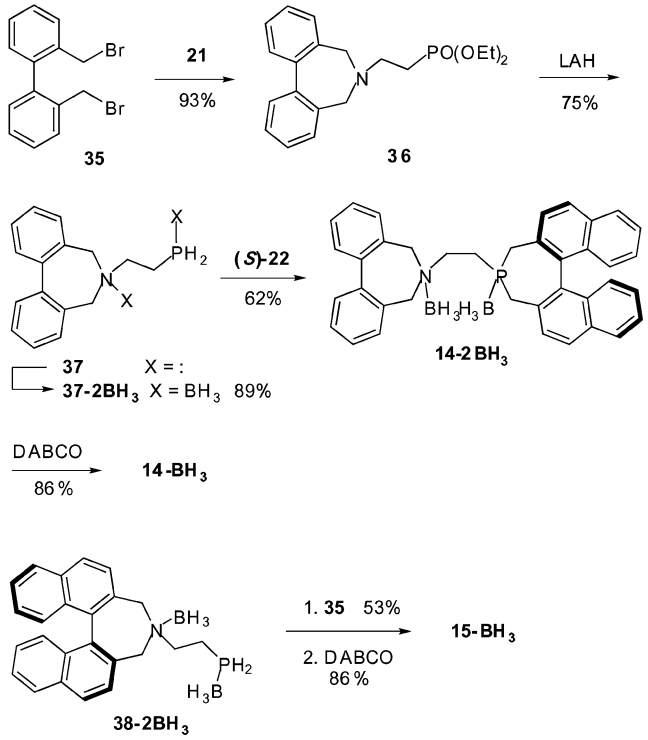


appropriate diamine (**32**−**34**, Scheme 4). Finally, the chirally flexible ligands **14** and **15** were prepared by procedures similar to those applied for the preparation of **7** and **9**, employing 2,2′-bis(bromomethyl)-1,1′-biphenyl[26] (**35**) in place of either binaphthyl derivative (Scheme 5). Thus, treatment of **35** with **21** afforded **36**, which was

SCHEME 5



reduced by LAH to afford **37** and, after protection, **37**-2BH_3. Reaction with (*S*)-**22** afforded **14**-2BH_3, which was chemoselectively deprotected to the desired compound **14**−BH_3. Protected ligand **15**−BH_3 was obtained via an analogous procedure from **38**−2BH_3. As expected, in the ^{1}H NMR spectra of **5** and **6**, the methylene protons in the azepino and phosphepino rings gave rise to separate AB patterns, whereas in **14**−BH_3 a singlet was observed from the methylene protons of the nitrogen part of the ligand, demonstrating that interconversion of the atropisomers, via rotation around the biphenyl axis, is rapid on the NMR time scale.

Allylic Alkylations with 1,3-Diphenyl-2-propenyl Acetate. Deprotection of the BH_3-protected ligands was achieved either with DABCO prior to the catalytic reaction or in situ with palladium acetate,[27] at the same time employed as the palladium source for the catalytic reaction.[28] Pseudo-C_2-symmetric ligand **1** and pseudo-meso ligand **2** were employed in the alkylation of *rac*-(*E*)-1,3-diphenyl-2-propenyl acetate (**39**) with malonate using palladium acetate as the palladium source in the presence of bis(trimethylsilyl)acetamide (BSA) and KOAc[29] (eq 1). Surprisingly, from both reactions the product was obtained with 37% ee, but with different absolute configurations of the major isomer (Table 1, entries 1 and 2). The reason for this might be that the nitrogen atom is too electron-poor to take part in coordination to the metal and that the ligand coordinates in a monodentate

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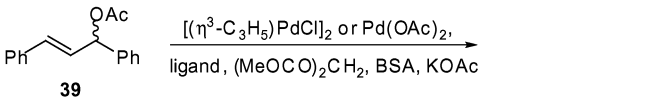
TABLE 1. Alkylation of 1,3-Diphenyl-2-propenyl Acetate with Malonate (Eq 1) Using N,P-Ligands 1−4

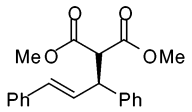
entry	ligand	Pd source	time (h)	convn (%)	ee (%)
1	**1**−BH_3	$Pd(OAc)_2$	1	100	37 (*R*)
2	**2**−BH_3	$Pd(OAc)_2$	1	100	37 (*S*)
3	**3**−$2BH_3$	$Pd(OAc)_2$	7	100	81 (*S*)
4	**4**−$2BH_3$	$Pd(OAc)_2$	7	100	67 (*R*)

TABLE 2. Alkylation of 1,3-Diphenyl-2-propenyl Acetate with Malonate (Eq 1) Using N,P-Ligands 5 and 6: Variation of Temperature and Ligand Metal Ratio

entry	ligand	Pd source	Pd/L	*T* (°C)	time (h)	yield (%)	ee (%)
1	**5**−BH_3	$Pd(OAc)_2$	1:1	20	6	100	98 (*S*)
2	**6**−BH_3	$Pd(OAc)_2$	1:1	20	72	95	37 (*R*)
3	**5**−BH_3	$Pd(OAc)_2$	1:1	0	8	10	98 (*S*)
4	**5**−BH_3	$Pd(OAc)_2$	1:1	−20	24	0	
5	**6**−BH_3	$Pd(OAc)_2$	1:1	−20	24	0	
6	**5**	$[(\eta^3\text{-}C_3H_5)PdCl]_2$	1:2	20	8	100	98 (*S*)
7	**6**	$[(\eta^3\text{-}C_3H_5)PdCl]_2$	1:2	20	8	100	59 (*S*)

fashion. This assumption is supported by the results from the same catalytic reaction employing monodentate (*R*,*R*)-2,5-dialkyl-1-phenylphospholane, which was reported to give the product with 37% ee.[30]





(1)

Different results were obtained when ligands **3** and **4** were employed in the same catalytic process. In these reactions, the protected ligands and palladium acetate were used. The pseudo-C_2-symmetric ligand **3** afforded the product from reaction of *rac*-(*E*)-1,3-diphenyl-2-propenyl acetate with malonate with 81% ee and with the (*S*)-product dominating (Table 1, entry 3), whereas the (*R*)-product was obtained with lower selectivity, 67% ee, using **4** as the ligand (entry 4). Full conversion was achieved with both ligands within 6−7 h.

The behavior of binaphthyl derivatives **5** and **6**, employed as their borane protected adducts, differed to an even larger extent. With pseudo-C_2-symmetric ligand **5** total conversion was achieved after 6 h at ambient temperature and an enantiomeric excess of 98% in favor of the (*S*)-enantiomer was observed (Table 2, entry 1), whereas 3 days of stirring were necessary to obtain 95% conversion to the product with moderate enantioselectivity (37% of the (*R*)-enantiomer) when the *pseudo-meso* ligand **6** was used (entry 2). The catalytic reaction was also attempted at lower temperature. However, at 0 °C low conversion was observed for the more reactive ligand (entry 3), without alteration of the enantiomeric excess, and at −20 °C no reaction occurred (entries 4 and 5).

To allow a study of the influence of the ratio between metal and ligand on the outcome of the catalytic process, deprotection of the ligand precursors **5**−BH_3 and **6**−BH_3, to obtain the free ligands, was required. This was achieved using two equivalents of DABCO in toluene (Table 2).[7] When an excess of **5** was employed, results identical to those obtained with a Pd/ligand ratio of 1:1 were obtained (entry 6). The catalytic reaction in the presence of 2 equiv of **6** afforded the product having opposite absolute configuration with higher ee (59%, entry 7) than that obtained using a 1:1 ratio. These results suggest that the catalytically active species derived from **5** does not change with the metal/ligand ratio, but that a 2:1 complex with only phosphorus binding to palladium is involved in the reaction employing an excess of **6**. That type of complex is expected to yield the product with opposite absolute configuration (see Mechanistic Considerations).

TABLE 3. Alkylation of 1,3-Diphenyl-2-propenyl Acetate with Malonate (Eq 1) Using N,P-Ligands 5 and 6: Influence of the Counterion

entry	ligand	Pd source	salt	time (h)	yield (%)	ee (%)
1	**5**−BH_3	$Pd(OAc)_2$	KOAc	6	100	98 (*S*)
2	**6**−BH_3	$Pd(OAc)_2$	KOAc	24	40	37 (*R*)
3	**5**−BH_3	$Pd(OAc)_2$	NaOAc	6	100	98 (*S*)
4	**6**−BH_3	$Pd(OAc)_2$	NaOAc	24	40	37 (*R*)
5	**5**−BH_3	$Pd(OAc)_2$	CsF	6	100	98 (*S*)
6	**6**−BH_3	$Pd(OAc)_2$	CsF	12	100	37 (*R*)
7	**5**−BH_3	$Pd(OAc)_2$	LiOAc	6	100	98 (*S*)
8	**6**−BH_3	$Pd(OAc)_2$	LiOAc	8	60	4 (*S*)

With symmetrical substrates, the nucleophilic addition constitutes the enantiodiscriminating step. To achieve high enantioselectivity with racemic substrates, the rate of interconversion between diastereomeric allyl complexes must be rapid relative to the nucleophilic addition. Decreased enantioselectivity may also be achieved due to the presence of unsymmetrical ion pairs leading to memory effects.[31] It is therefore not surprising that the nature of the ion pair containing the nucleophilic anion, and thus the counterion of the nucleophile, may influence the enantioselectivity of the catalytic reaction.[32] The effect of that ion on the reactions employing ligands **5** and **6** was therefore studied. The results are reported in Table 3. Reactions employing pseudo-C_2-symmetric ligand **5** were found to be insensitive to whether lithium, sodium, potassium, or cesium was employed as the counterion, and good conversion and high enantioselectivity was always achieved (entries 1, 3, 5, and 7). In contrast, the nucleophilic species turned out to play an important role upon the outcome of reactions involving the pseudo-meso ligand **6**. Replacing KOAc (entry 2) with NaOAc (entry 4) or CsF (entry 6) did not affect the enantioselectivity (37% ee of the (*R*)-product), whereas in the presence of LiOAc (entry 8) merely 4% ee was achieved. It has also previously been observed that the smaller cation lithium affords higher amounts of the *ent*-product.[6] This is probably due to increased rate of nucleophilic attack. In the reactions with ligand **6**, increased reactivity was observed with nucleophiles having cesium and lithium as counterions.

Allylic substitutions using C_2-symmetric P,P-ligand **7** and N,N-ligand **8** were next studied. Attempts to deprotect **7** using a large excess of diethylamine removed the

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TABLE 4. Alkylation of 1,3-Diphenyl-2-Propenyl Acetate with Malonate (Eq 1) Using N,N- and P,P-Ligands 7−13

entry	ligand	Pd source	time (h)	convn (%)	ee (%)
1	**7**	$[(\eta^3\text{-}C_3H_5)PdCl]_2$	3	90	73 (*S*)
2	**7**−$2BH_3$	$Pd(OAc)_2$	4	100	94 (*S*)
3	**8**	$[(\eta^3\text{-}C_3H_5)PdCl]_2$	2	100	99 (*R*)
4	**9**−$2BH_3$	$Pd(OAc)_2$	4	20	
5	**10**	$[(\eta^3\text{-}C_3H_5)PdCl]_2$	24	2	
6	**11**	$[(\eta^3\text{-}C_3H_5)PdCl]_2$	72	0	
7	**12**	$[(\eta^3\text{-}C_3H_5)PdCl]_2$	72	98	94 (*R*)
8	**13**	$[(\eta^3\text{-}C_3H_5)PdCl]_2$	72	0	

borane according to ^{1}H NMR, but a well resolved ^{31}P NMR spectrum could not be recorded. The ligand obtained was, however, assessed in the palladium-catalyzed allylic substitution. After 4 h, the reaction was complete and a product with an enantiomeric excess of 73% (*S*) was isolated (Table 4, entry 1). We suspected that a significant amount of mono-oxidized ligand was present, which is probably detrimental for the reaction as the oxidized ligand might coordinate in a monodentate fashion yielding a complex leading to the opposite enantiomer, thus decreasing the ee of the catalytic reaction. It has previously, indeed, been demonstrated that oxidation of one phosphorus atom in dppe yields a ligand which coordinates in a monodentate fashion.[33] We therefore decided to repeat the method applied to the P,N-ligands, using $Pd(OAc)_2$ to generate the catalyst from P,P-ligand **7**-$2BH_3$. Under these conditions, the catalytic reaction was complete after 4 h and the (*S*) enantiomer was obtained with 94% excess (entry 2). It was still difficult to completely avoid oxidation of the ligand, and this is probably the reason that higher enantioselectivity was achieved when P,N-ligand **5** was used, as oxidation of phosphorus in that case leads to a monodentate N-ligand which probably is inactive in the catalytic process. It is interesting to note that **5**, having pseudo-C_2 symmetry, required nearly twice as long reaction time as C_2-symmetric **7** for full conversion, suggesting the formation of about equal amounts of two complexes from the former, of which only one reacts. The N,N-ligand **8**, which has previously not found use in catalytic applications,[10] was found, in addition to high enantioselectivity, to exhibit remarkably high reactivity, affording full conversion to product within less than 2 h at room temperature (entry 3). Meso ligands **9** and **10**, obviously resulting in racemic products, were found to exhibit considerably lower reactivity than the C_2- or pseudo-C_2-symmetric ligands, P,P-ligand **9** requiring 4 h at room temperature for 20% conversion, whereas only 2% of product was obtained after 24 h using N,N-ligand **10** (entries 4 and 5).

The reactivity and selectivity of the catalytically active complex was found to be strongly affected by the structure of the spacer connecting the binaphthyl moieties. Thus, whereas no product was obtained upon use of **11** (entry 6), derived from (*S*,*S*)-diaminocyclohexane, the diastereomer **12** afforded 98% yield of a product consisting mainly of the (*R*) enantiomer (94% ee) within 72 h at ambient temperature (Table 4, entry 7). A catalytic reaction employing ligand **13**, resulting in a six-membered chelate with palladium, resulted in precipitation of palladium, and no product was isolated (entry 8).

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TABLE 5. Alkylation of 1,3-Diphenyl-2-propenyl Acetate with Malonate (Eq 1) Using Chirally FlexibleLigands 14 and 15

entry	ligand	Pd source	*T* (°C)	time (h)	convn (%)	ee (%)
1	**14**−BH_3	$Pd(OAc)_2$	20	4	60	87 (*S*)
2	**14**−BH_3	$Pd(OAc)_2$	5	24	40	87 (*S*)
3	**15**−BH_3	$Pd(OAc)_2$	20	5	55	78 (*S*)
4	**15**−BH_3	$Pd(OAc)_2$	5	24	55	81 (*S*)
5	**5**−BH_3/**6**−BH_3 1:1	$Pd(OAc)_2$	20	4	65	79 (*S*)

Chirally Flexible Ligands. The addition of a chiral enantiopure diamine to a racemic mixture of ruthenium(II) complexes with chirally flexible (proatropisomeric) biphenylphosphine ligands has been shown to result in a mixture of diastereomeric complexes undergoing slow stereomutation to finally yield one single diastereomer.[34] We considered that, instead of combining one rigid and one flexible ligand, the incorporation of one rigid and one chirally flexible moiety in the same ligand[35] would give rise to a system which, according to the reaction conditions, would exhibit either pseudo-C_2 or pseudo-C_s configuration. We thus decided to design ligands bearing one fixed element of chirality and a potentially flexible element capable of adopting either (*R*) or (*S*) absolute configuration. For this purpose, two ligands, **14** and **15**, were designed (Scheme 5). Each ligand is able to adopt two configurations, as rotation around the single bond connecting the aromatic rings in the biphenyl part of the molecules is possible, although the rate of interconversion between this two diastereoisomeric conformations may be different.

The two ligands were assessed in the palladium-catalyzed allylic substitution of 1,3-diphenyl-2-propenyl acetate with dimethylmalonate and the results compared with those obtained from a catalytic reaction employing a 1:1 mixture of the pseudo-C_2 and pseudo-meso ligands (Table 5). The 1:1 mixture of **5** and **6** gave the product with (*S*) absolute configuration in 79% enantiomeric excess (entry 5), showing the reactivity of **5** to be seven times higher than that of **6**. Ligand **15**, being chirally flexible at the phosphorus part of the molecule, behaved essentially like the 1:1 mixture of **5** and **6** (78% ee at room temperature, 81% ee at 5 °C), indicating that interconversion between the two diastereomeric conformations is slow compared to the rate-determining step of the catalytic reaction (Table 5, entries 3 and 4). Use of **14** led to higher enantioselectivity (87% at room temperature as well as at 5 °C), although not higher than expected for a than the 1:1 mixture of *ent*-**5** and **6** (entries 1 and 2). These results suggest that the barrier to interconversion between the diastereomeric conformations is high compared to the activation barriers leading to nucleophilic addition, and thus that reactions using **14** and **15** do not occur under Curtin−Hammet conditions.

Cyclic Substrates. The study of this new class of ligands was also extended to sterically less demanding substrates. Thus, **3** and **4** were tested as ligands in the

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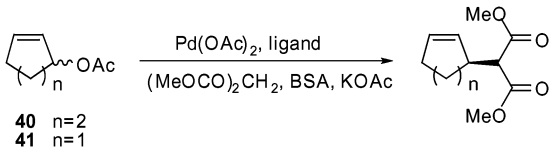
TABLE 6. Alkylation of 3-Cyclopentenyl Acetate (n = 1) and 3-Cyclohexenyl Acetate (n = 2) with Malonate (Eq 2) Using Ligands 3−6

entry	ligand	n	Pd source	T (°C)	time (h)	convn (%)	ee (%)
1	**3**−2BH$_3$	2	Pd(OAc)$_2$	20	120	0	
2	**4**−2BH$_3$	2	Pd(OAc)$_2$	20	192	73	24 (*R*)
3	**5**−BH$_3$	2	Pd(OAc)$_2$	40	24	40	12 (*R*)
4	**6**−BH$_3$	2	Pd(OAc)$_2$	40	24	70	26 (*R*)
5	**3**−2BH$_3$	1	Pd(OAc)$_2$	20	25	100	13 (*S*)
6	**4**−2BH$_3$	1	Pd(OAc)$_2$	20	17	100	12 (*R*)
7	**5**−BH$_3$	1	Pd(OAc)$_2$	20	24	100	27 (*R*)
8	**6**−BH$_3$	1	Pd(OAc)$_2$	20	24	100	26 (*R*)

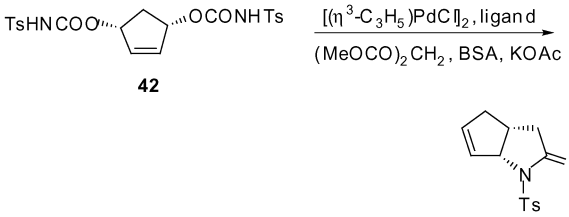
palladium mediated substitution of *rac*-3-cyclohexenyl (**40**) and *rac*-3-cyclopententyl acetate (**41**) with dimethyl malonate as the nucleophile (eq 2), employing metal/ligand ratios of 1:1 (Table 6). From the reaction with cyclohexenyl acetate, using pseudo-C_2-symmetric ligand **3**, no product was isolated even after a reaction time of 120 h (entry 1). The pseudo-meso ligand **4** exhibited higher reactivity, resulting in 73% conversion to the (*R*)-product with 24% ee after 192 h (entry 2). The same substrate was transformed to the (*R*)-product employing ligands **5** (40% conversion after 24 h, 12% ee, entry 3) and **6** (70% conversion after 24 h, 26% ee, entry 4). Interestingly, in contrast to the situation with 1,3-diphenyl-2-propenyl acetate, use of pseudo-meso ligands **4** and **6** thus resulted in somewhat higher enantioselectivity and higher reactivity in the substitution of cyclohexenyl acetate than use of the diastereoisomeric compounds **3** and **5**. With cyclopentenyl acetate as the substrate, a smaller difference in reactivity between the two types of ligands was observed, **3** requiring 25 h for full conversion and **4** 17 h, and both ligands led to the same level of enantioselectivity ((*S*)-product with 13% ee, entry 5, and (*R*)-product with 12% ee, entry 6 respectively). With ligands **5** and **6** full conversion to the (*R*)-product (27 and 26% ee, respectively) was achieved after 24 h (entries 7 and 8).



40 n=2
41 n=1

(2)

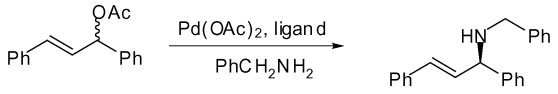
Substrate with Enantiotopic Leaving Groups. We have also explored the possibility for the two ligands **5** and **6** to desymmetrize a *meso*-diacetyl compound employing 3,5-cyclopentenyl bisurethane **42** as substrate (eq 3). High enantioselectivity has been observed in this type of process with different types of ligands, including the C_2-symmetric Trost diphosphine[3c] as well as some asymmetric ligands.[36] In this particular reaction, the enantiodetermining step is the oxidative addition of the allylic acetate to Pd(0).[37] Although electronic dissymmetry might be expected to influence the ionization of the acetate, discrimination of the enantiotopic leaving groups was not achieved with the present catalytic systems and no enantioselectivity was thus observed.



42

(3)

Nitrogen Nucleophiles. Benzylamine was explored as a nucleophile in the substitution of 1,3-diphenyl-2-propenyl acetate using **5** as a ligand (eq 4). Whereas essentially no enantioselectivity (4% ee) was achieved at room temperature, a 39% ee of the product with (*R*) absolute configuration was surprisingly observed when the reaction was run at 45 °C, at which temperature full conversion was achieved within 48 h. This suggests that the rate-determining step is not the same at the two temperatures. Under the same conditions, ligand **6** resulted in 10% conversion to a racemic product. When potassium phthalimide was used as nitrogen source no reaction with 1,3-diphenyl-2-propenyl acetate was observed, even at 50 °C.



(4)

Mechanistic Considerations

Several features concerning the mechanism of palladium-catalyzed allylic alkylations are known.[3] The first step is the oxidative addition of the allylic acetate to Pd(0), which has been shown to be a reversible process.[38] For symmetrically substituted substrates, the enantiodiscriminating step is the attack of the nucleophile on the π-allyl palladium complex, from the side trans to phosphorus, to form a palladium(0) olefin complex. Depending on whether this step is endothermic or exothermic, the reactivity of the reacting π-allyl palladium(II) complex or the stability of the π-olefin palladium(0) complex resulting from nucleophilic attack should be considered in order to rationalize the enantiodiscrimination of the catalytic process.[39] Late, product-like, transition states have recently been suggested as a result of experimental[40] as well as theoretical studies,[41] although under different conditions, an early transition state has been demonstrated.[42] In processes with late transition states, the enantiodiscrimination is assumed to be a result of the most favorable conversion of the allyl complex into an olefin complex, as recently illustrated by for example Morimoto.[43] The steric as well as the electronic properties of the ligand−metal complex are

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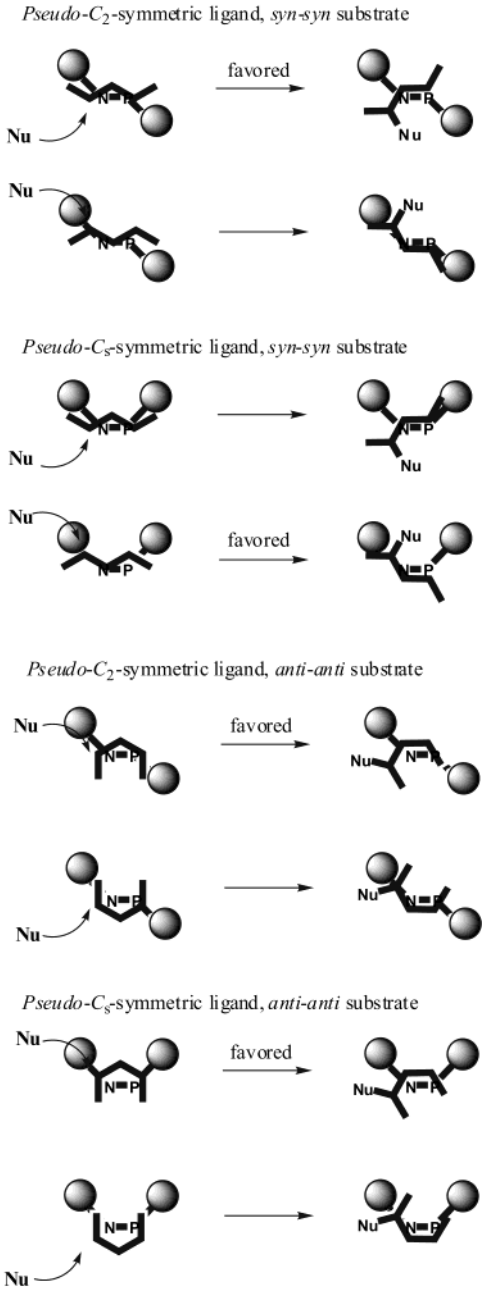
SCHEME 6



crucial for the enantioselectivity, although the origin of the enantiocontrol using aminophosphine ligands has been claimed to depend mainly on steric factors, electronic factors being important only for cyclic substrates.[44]

The situation for the two types of ligands presented here is illustrated in Scheme 6. A late transition state for the step involving addition of the nucleophile is assumed, although the same conclusions would result from a consideration of processes with early transition states. As the ligands are devoid of symmetry, up to eight diastereomeric allyl palladium complexes may form from 1,3-diphenyl-2-propenyl acetate. In the case of the pseudo-C_2 ligand **5**, two out of these, the M- and W-shaped (endo, exo) syn-syn complexes, are assumed to have similar stabilities. Nucleophilic attack on these two complexes is assumed to represent the major reaction routes, as the anti-anti and anti-syn complexes would give rise to either products with *Z*-olefinic bonds, not observed in the product mixtures, or to the opposite enantiomer, and therefore can be present only in a low amount, or at least lead to product only to a minor extent. Nucleophilic attack trans to phosphorus is generally preferred[45] but occurs readily only for one of the complexes, as formation of an olefin complex is sterically unfavorable for the other. The observation that the major product has (*S*) absolute configuration when ligands with *Pr* chirality (**3**, **5**, **7**, **14**, **15**) are employed and that the opposite enantiomer is preferentially formed from reactions employing a ligand with *Mr* chirality (**8**, **12**) is in accordance with the proposed model.[43] Likewise, from pseudo-meso ligand **6** the formation of two major allyl palladium complexes is assumed to occur, although in this case this assumption has less strong support from experimental data. The two syn-syn complexes are believed to have different energies due to different sterical situations, the formation of product via nucleophilic attack trans to phosphorus on the complex assumed to be the most stable one being in accordance with experiments. These suggestions are also in accordance with the formation of products with different absolute configurations from the two types of ligands (**3** and **5** on one hand, and **4** and **6** on the other), and with the fact that **5** exhibits only about half the reactivity of C_2-symmetric ligand **7**.

The low reactivity of **11** and **13** as compared to **8** and **12** probably originates in different steric situations. Inspection of molecular models suggests that a smaller chiral pocket is available for the substrate in the former ligands, resulting in more labile metal complexes; attempted reaction employing **13** even resulted in the precipitation of palladium.

The results obtained upon alkylation of cyclic substrates can be rationalized analogously. Only two π-allyl palladium complexes are possible, as only two diastereomeric anti-anti complexes may form. Nucleophilic attack trans to phosphorus on the complexes leading to products with (*R*) absolute configuration is expected to be favored, in accordance with the results from experiments employing ligands **4**, **5**, and **6**, although from the reaction of cyclopentenyl acetate using ligand **3**, the opposite enantiomer was isolated with low ee. The model also suggests that larger enantiodiscrimination for cyclic substrates should occur for nucleophilic attack at the complex with the pseudo-meso ligands **4** and **6** as compared to those with ligands **3** and **5**, although this is observed experimentally only in the alkylation of cyclohexenyl acetate. The observation of products with different absolute configuration from reactions employing a 1:1 and 1:2 **6**/Pd ratio is in accordance with a change from a pseudo-meso structure of the palladium allyl complex to one with *Pr* chirality.

Only few ligands induce high enantioselectivity in alkylations of small aliphatic substrates. One factor which seems to be crucial in reactions with this type of substrate is the bite angle, but other factors may be important as well. We are presently undertaking further

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studies of the present type of ligands in order to optimize the structure for a wider range of substrates.

Conclusions

N,P-, N,N-, and P,P-ligands with pseudo-C_2, pseudo-C_s, C_2, and C_s symmetry were prepared and evaluated in palladium-catalyzed allylic alkylations; in ligands with pseudo-C_s symmetry, the chirality originates in different donor atoms only. With substrates preferring syn-syn conformation, C_2- and pseudo-C_2-symmetric ligands proved to induce higher enantioselectivity than those having pseudo-C_s symmetry (those with C_s symmetry evidently resulting in racemic products), whereas the reverse situation was found for a cyclohexenyl substrate, forced to have an anti-anti structure. Depending on the substrate, a ligand with either pseudo-C_2 or pseudo-C_s symmetry should thus be selected for the allylic alkylation. The nature of the spacer connecting the two donor parts of the bidentate ligands proved to be crucial for the selectivity as well as for the reactivity of the catalysts.

Experimental Section

General Remarks. All air-sensitive reactions were performed in oven-dried glassware under argon or nitrogen atmosphere using freshly distilled solvents. Tetrahydrofuran and diethyl ether were distilled from sodium−benzophenone under nitrogen. Methylene chloride was distilled from CaH_2 or P_2O_5. Hexanes, dimethylformamide, and methanol were dried over molecular sieves, unless otherwise stated. Column chromatography was performed using EM silica gel 60 (230−400 mesh), Merck silica gel 60 H, or SDS silica gel 60 A. ^{1}H NMR spectra were recorded at 500, 400, or 300 MHz, ^{13}C spectra at 125 and 100 MHz, and ^{31}P spectra at 202 MHz. The ^{1}H and ^{13}C chemical shifts are reported relative to $CHCl_3$, and the ^{31}P chemical shifts are reported relative to H_3PO_3 (external). Melting points are uncorrected. Elemental analyses were performed by Analytische Laboratorien, Lindlar, Germany. HRMS analyses were performed at the University of Lund, Sweden. Handling of the cyclic sulfates and the manipulation of the primary phosphines should be conducted with **caution** (well ventilated fume hood). Compounds **5**,[7] **6**,[7] **8**,[14] and **38**-$2BH_3$[7] were prepared via previously described procedures.

(2*R*,5*R*)-1-(2-Bromophenyl)-2,5-dimethylpyrrolidine (18). (2*S*,5*S*)-Hexanediol cyclic sulfate ((*S*,*S*)-**17**, 2.0 g, 11.1 mmol) was mixed with 2-bromoaniline (**16**, 9.56 g, 55.5 mmol). The flask containing the mixture was degassed and sealed before it was heated for 22 h at 75 °C. The reaction mixture was cooled to room temperature and the resulting solid treated with 5 M NaOH (150 mL), followed by extraction with pentane (4 × 75 mL). The combined organic phases were dried over Na_2SO_4 and concentrated at reduced pressure. The crude product was purified by column chromatography on silica gel (pentane) to give **18** (2.0 g, 71%) as a colorless oil: $[\alpha]^{25}_D$ +132.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (dd, J = 7.9, 1.5 Hz, 1H), 7.20 (td, J = 7.7, 1.5 Hz, 1H), 6.97 (dd, J = 8.0, 1.3 Hz, 1H), 6.81 (td, J = 7.6, 1.5 Hz, 1H), 4.44 (m, 1H), 3.79 (m, 1H), 2.22 (m, 1H), 2.10 (m, 1H), 1.57 (m, 1H), 1.47 (m, 1H), 1.1 (J = 5.8 Hz, 3H), 0.75 (d, J = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.8, 133.6, 127.1, 123.8, 122.6, 119.8, 55.4, 53.6, 33.1, 32.6, 19.5, 19.4. Anal. Calcd for $C_{12}H_{16}NBr$: C, 56.71; H, 6.34; N, 5.51. Found: C, 56.65; H, 6.36; N, 5.62.

Diethyl (2*R*,5*R*)-[2-(2,5-Dimethylpyrrolidinyl)phenyl]-phosphinite−Borane (19−BH_3). *tert*-Butyllithium (5.1 mL, 1.7 M in pentane, 8.6 mmol) was added dropwise (5 min) at −95 °C to a degassed solution of **18** (1.0 g, 3.9 mmol) in diethyl ether (20 mL). The mixture was stirred for 45 min before diethyl chloro phosphite (0.69 mL, 4.7 mmol) was added at −78 °C and then stirred for an additional 5 h, while the temperature was allowed to slowly raise to 0 °C. The flask was cooled to −78 °C, and BH_3·SMe_2 (2.4 mL, 2 M in THF, 4.8 mmol) was added. The flask was degassed, and the reaction mixture was stirred overnight at room temperature. The slurry was filtered through a short plug of silica and concentrated. The crude product was purified by column chromatography on silica gel (pentane/diethyl ether 97:3) to give an oil, which was further purified by recrystallization from pentane at −78 °C to give **19**−BH_3 (882 mg, 72%) as a white solid: mp 35−36 °C; $[\alpha]^{25}_D$ +163.6 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (ddd, J = 11.3, 7.8, 1.6 Hz, 1H), 7.42 (app t, J = 7.7 Hz, 1H), 7.13−7.04 (m, 2H), 4.28−4.18 (m, 1H), 4.18−3.96 (m, 4H), 3.82−3.71 (m, 1H), 2.32−2.21 (m, 1H), 2.13−2.02 (m, 1H), 1.69−1.57 (m, 1H), 1.50−1.40 (m, 1H), 1.34 (ddd, J = 14.1, 7.0, 0.4 Hz, 6H), 1.07 (d, J = 5.9 Hz, 3H), 0.75 (d, J = 6.4 Hz, 3H), 1.02−0.30 (br, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.0 (d, J_{CP} = 9.9 Hz), 133.5 (d, J_{CP} = 8.8 Hz), 132.3 (d, J_{CP} = 1.2 Hz), 127.3 (d, J_{CP} = 74.5 Hz), 124.4 (d, J_{CP} = 7.3 Hz), 122.0 (d, J_{CP} = 9.0 Hz), 63.0 (d, J_{CP} = 5.2 Hz), 62.6 (d, J_{CP} = 5.3 Hz), 59.1, 53.3, 32.5, 31.7, 18.9, 18.5, 16.4 (d, J_{CP} = 6.3 Hz), 16.3 (d, J_{CP} = 6.4 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 130.7 (br m). Anal. Calcd for $C_{16}H_{29}BNO_2P$: C, 62.15; H, 9.45; N, 4.53. Found: C, 61.96; H, 9.50; N, 4.50.

Diethyl (2*R*,5*R*)-[2-(2,5-Dimethylpyrrolidinyl)phenyl]-phosphinite (19). DABCO (123.4 mg, 1.1 mmol) was added to a degassed solution of **19**−BH_3 (309.2 mg, 1.0 mmol) in toluene (600 μL) at −78 °C. The mixture was degassed and warmed to room temperature before the flask was sealed and heated at 45 °C for 48 h. The flask was cooled to room temperature, and the toluene was removed at reduced pressure. The residue was washed with degassed hexanes (3 × 1 mL). The organic phases were combined and concentrated at reduced pressure to give 289 mg of an air-sensitive oil which was used without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74−7.72 (m, 1H), 7.35−7.28 (m, 1H), 7.06−7.01 (m, 2H), 4.19 (br s, 1H), 4.07−3.95 (m, 1H), 3.94−3.84 (m, 1H), 3.83−3.70 (m, 2H), 3.62−3.50 (m, 1H), 2.23 (br s, 1H), 2.09 (br s, 1H), 1.54−1.43 (br m, 2H), 1.31 (ddd, J = 14.1, 7.0, 0.3 Hz, 3H), 1.19 (ddd, J = 14.1, 7.0, 0.4 Hz, 3H), 1.03 (br s, 3H), 0.79 (br s, 3H);^{13}C NMR (125 MHz, $CDCl_3$) δ 149.9 (d, J_{CP} = 21.8 Hz), 136.6 (d, J_{CP} = 23.0 Hz), 130.4 (d, J_{CP} = 3.9 Hz), 130.1, 123.0 (d, J_{CP} = 2.1 Hz), 122.1, 62.7 (d, J_{CP} = 16.1 Hz), 61.2 (d, J_{CP} = 7.9 Hz), 58.7, 58.6, 32.6, 32.0, 19.6, 18.5, 17.2 (d, J_{CP} = 5.6 Hz), 17.0 (d, J_{CP} = 5.1 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 152.3; GC−MS 295 (M^+), 266, 252, 238, 224, 172, 158.

1-[(2*R*,5*R*)-2,5-Dimethylphospholanylborane]-2-[(2*R*,5*R*)-2,5-dimethylpyrrolidinyl]benzene (1−BH_3). Chlorotrimethylsilane (38 μL, 3.0 mmol) was added dropwise to a degassed slurry of LAH (114 mg, 3.0 mmol) in THF (10 mL) at −78 °C with stirring. The suspension was stirred for 3 h at room temperature. Phosphonite **19** (289 mg, 1.0 mmol) in degassed THF (2 mL) was slowly added at −78 °C. The reaction mixture was allowed to reach room temperature slowly, and stirring was continued for an additional 15 h. The reaction was quenched by the addition of degassed absolute MeOH (640 μL) followed by degassed THF (15 mL) at −78 °C. The reaction mixture was stirred at room temperature for 1 h and 20 min and then filtered. The filter cake was washed with degassed THF (3 mL). The solvents were carefully removed at reduced pressure. The residue, consisting of **20**, was dissolved in 5 mL of degassed THF, and *n*-butyllithium (300 μL, 2.5 M in hexane, 0.75 mmol) was added dropwise at −78 °C. The resulting yellow solution was stirred at room temperature for 1 h. (2*S*,5*S*)-Hexanediol cyclic sulfate ((*S*,*S*)-**17**, 135 mg, 0.75 mmol) in degassed THF (1 mL) was added at −78 °C. The solution was stirred at room temperature for 1.5 h. *n*-Butyllithium (300 μL, 2.5 M in hexane, 0.75 mmol) was added dropwise at −78 °C, resulting in a yellow color. The reaction mixture was then stirred at room temperature for 18 h. BH_3·Me_2S (375 μL, 2 M in THF, 0.75 mmol) was added at −78 °C and the reaction mixture stirred at room temperature

for 2 h. The reaction was quenched by the addition of water (100 μL). The mixture was diluted with $CHCl_3$ (25 mL) and filtered through a plug of Na_2SO_4. Concentration of the solvent resulted in a white sticky material that was purified by column chromatography on silica gel ($CHCl_3$/hexanes 4:6) to give **1**−BH_3 (60 mg, 20%) as a white solid. An analytically pure sample was obtained by recrystallization from hexanes: mp 118−119 °C; $[\alpha]^{25}_D$ +35.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (ddd, J = 9.7, 7.9, 1.6 Hz, 1H), 7.39 (split t, J = 7.7 Hz, 1H), 7.15−7.11 (m, 2H), 4.01−3.89 (m, 1H), 3.75−3.63 (m, 1H), 3.50−3.34 (m, 1H), 2.55−2.42 (m, 1H), 2.33−2.04 (m, 4H), 1.75−1.60 (m, 1H), 1.59−1.42 (m, 3H), 1.36 (dd, J = 15.8, 6.9 Hz, 3H), 1.02 (d, J = 6.0 Hz, 3H), 0.88 (dd, J = 13.9, 7.3 Hz, 3H), 0.75 (d, J = 6.5 Hz, 3H), 1.15−0.25 (br, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.4 (d, J_{CP} = 2.1 Hz), 136.0 (d, J_{CP} = 10.9 Hz), 130.9 (d, J_{CP} = 2.5 Hz), 125.5 (d, J_{CP} = 6.0 Hz), 125.1-(d, J_{CP} = 38.7 Hz), 123.6 (d, J_{CP} = 10.5 Hz), 59.9, 52.9, 35.1 (d, J_{CP} = 37 Hz), 33.7 (d, J_{CP} = 4.2 Hz), 32.9 (d, J_{CP} = 7.6 Hz), 32.2, 30.7, 29.7 (d, J_{CP} = 35.7 Hz), 19.3, 17.1, 15.8 (d, J_{CP} = 4.1 Hz), 14.6 (d, J_{CP} = 3.7 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 41.2 (br m). Anal. Calcd for $C_{18}H_{31}BNP$: C, 71.30; H, 10.30; N, 4.62. Found: C, 71.14; H, 10.34; N, 4.51.

1-[(2*S*,5*S*)-2,5-Dimethylphospholanylborane]-2-[(2*R*,5*R*)-2,5-dimethylpyrrolidinyl]benzene (2−BH_3). Ligand **2** was prepared analogously to **1** from **19** using (2*R*,5*R*)-hexanediol cyclic sulfate: yield 12%, as a white solid; mp 96−97 °C; $[\alpha]^{25}_D$ +141.9 (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (ddd, J = 9.2, 7.9, 1.6 Hz, 1H), 7.35 (split t, J = 9.6 Hz, 1H), 7.13−7.07 (m, 2H), 3.78−3.60 (m, 3H), 2.36−2.04 (m, 5H), 1.64−1.41 (m, 4H), 1.37 (dd, J = 16.3, 7.2 Hz, 3H), 1.08 (d, J = 5.9 Hz, 3H), 0.85 (dd, J = 13.5, 7.2 Hz, 3H), 0.67 (d, J = 6.5 Hz, 3H), 1.03−0.21 (br, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.8 (d, J_{CP} = 1.5 Hz), 135.7 (d, J_{CP} = 10.0 Hz), 130.5 (d, J_{CP} = 2.3 Hz), 124.5 (d, J_{CP} = 5.6 Hz), 123.7 (d, J_{CP} = 39.2 Hz), 122.9 (d, J_{CP} = 10.3 Hz), 61.1, 51.9, 36.3 (d, J_{CP} = 36.1 Hz), 34.5 (d, J_{CP} = 2.9 Hz), 33.9 (d, J_{CP} = 5.0 Hz), 32.3, 31.3 (d, J_{CP} = 34.3 Hz), 30.5, 19.4, 17.2, 16.0 (d, J_{CP} = 4.4 Hz), 15.9 (d, J_{CP} = 3.9 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 42.1 (br m). Anal. Calcd for $C_{18}H_{31}BNP$: C, 71.30; H, 10.30; N, 4.62. Found: C, 71.10; H, 10.38; N, 4.55.

Diethyl [2-(2*R*,5*R*)-(2,5-Dimethylpyrrolidinyl)ethyl]-phosphinite (22). A degassed mixture of (2*S*,5*S*)-hexanediol cyclic sulfate ((*S*,*S*)-**17**, 600 mg, 3.33 mmol) and (2-aminoethyl)-phosphonic acid diethyl ester (**21**, 1.80 g, 9.94 mmol) was heated at 75 °C for 48 h. Water (5 mL) and NEt_3 (1 mL) were added, and the mixture was extracted with pentane. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure to give 416 mg (47%) of **22** as a yellow oil, which was used further without additional purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.06 (m, 4H), 3.00 (br s, 2H), 2.86 (m, 1H), 2.60 (m, 1H), 2.06−1.82 (m, 4H), 1.37−1.27 (m, 8H), 0.94 (d, J = 6.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 61.4 (dd, J_{CP} = 10.3 Hz), 54.9, 40.8, 30.7, 25.6 (d, J_{CP} = 137.9 Hz), 16.5, 16.4 (d, J_{CP} = 6.0 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 31.8.

1-[(2*R*,5*R*)-2,5-Dimethylphospholanylborane]-2-[(2*R*,5*R*)-2,5-dimethylpyrrolidinylborane]ethane (3−2BH_3). LAH (151 mg, 3.98 mmol) was slowly added to a degassed solution of phosphonite **22** (349 mg, 1.33 mmol) in diethyl ether (10 mL, stirring at 0 °C for 10 min). After being stirred at 0 °C for 30 min, the reaction mixture was allowed to reach room temperature and then stirred at this temperature for a further 2 h. The reaction was quenched with a saturated aqueous solution of Na_2SO_4 and the organic phase dried over Na_2SO_4. Removal of the solvents under reduced pressure gave **23** (125 mg) as a yellow oil, which was diluted with degassed THF (5 mL). *n*-Butyllithium (0.39 mL, 2.5 M, 0.98 mmol) was added at −78 °C. The reaction mixture was allowed to reach room temperature and, after being stirred at this temperature for a further 30 min, added to a solution of (2*S*,5*S*)-hexanediol cyclic sulfate ((*S*,*S*)-**17**, 142 mg, 0.79 mmol) in THF (15 mL) at −78 °C. The reaction mixture was allowed to reach room temperature and then stirred at this temperature for a further 3 h, whereafter an additional amount of *n*-butyllithium (0.39 mL, 2.5 M, 0.98 mmol) was added at −78 °C. The reaction mixture was allowed to reach room temperature and then stirred at this temperature for a further 19 h. BH_3·SMe_2 (1.56 mL, 2 M, 3.12 mmol) was added, and the reaction mixture was stirred at ambient temperature for 1 h. Liquid chromatography on neutral alumina (column 2.5 × 15 cm, eluent: 100 mL of hexane followed by 200 mL of hexane/Et_2O 2:1) yielded 61 mg (17%, white crystals) of **3**−2BH_3: $[\alpha]^{25}_D$ −55.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65−3.59 (m, 1H), 3.12−3.03 (m, 1H), 2.88−2.76 (m, 2H), 2.46−2.32 (m, 2H), 2.23−2.01 (m, 5H), 1.91−1.82 (m, 1H), 1.9−0.9 (br, 3H), 1.79−1.69 (m, 1H), 1.48−1.34 (m, 3H), 1.32 (d, J = 6.5 Hz, 3H), 1.24 (dd, J = 6.9, 2.4 Hz, 3H), 1.20 (d, J = 6.8 Hz, 3H), 1.14 (d, J = 6.9 Hz, 3H), 0.36 (br q, J = 109.2, 80.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 65.2, 63.6, 50.7 (d, J_{CP} = 6.9 Hz), 34.9 (d, J_{CP} = 3.3 Hz), 34.2, 33.7 (d, J_{CP} = 37.1 Hz), 32.0 (d, J_{CP} = 3.5 Hz), 28.9, 28.6, 17.5 (d, J_{CP} = 27.7 Hz), 16.0, 15.8 (d, J_{CP} = 4.7 Hz), 15.2, 13.4 (d, J_{CP} = 2.7 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 38.1 (br s). Anal. Calcd for $C_{14}H_{34}B_2NP$: C, 62.50; H, 12.74; N, 5.21. Found: C, 62.37; H, 12.57; N, 5.25.

2-[(2*S*,5*S*)-2,5-Dimethylphospholanyl-borane]-1-[(2*R*,5*R*)-2,5-dimethylpyrrolidinylborane]ethane (4−2BH_3). Compound **4**−2BH_3 was synthesized using the procedure employed for the preparation of **3**−2BH_3 by using (2*R*,5*R*)-hexanediol cyclic sulfate instead of (2*S*,5*S*)-hexanediol cyclic sulfate (21% of **4**-2BH_3, white crystals): $[\alpha]^{25}_D$ −26.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.18−3.09 (m, 1H), 3.66−3.58 (m, 1H), 2.94−2.86 (m, 1H), 2.77−2.68 (m, 1H), 2.42−2.25 (m, 2H), 2.20−2.00 (m, 5H), 1.9−0.9 (br, 3H), 1.85−1.73 (m, 2H), 1.52−1.35 (m, 3H), 1.31 (d, J = 6.6 Hz, 3H), 1.26 (dd, J = 13.9, 6.8 Hz, 3H), 1.23 (dd, J = 16.2, 6.9 Hz, 3H), 1.17 (d, J = 6.9 Hz, 3H), 0.35 (br q, J = 102.2, 86.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 65.3, 63.3, 50.2 (d, J_{CP} = 6.8 Hz), 34.6 (d, J_{CP} = 3.5 Hz), 34.4, 33.8 (d, J_{CP} = 36.1 Hz), 33.1 (d, J_{CP} = 35.1 Hz), 28.8, 28.7, 17.8 (d, J_{CP} = 27.1 Hz), 16.2, 15.5, 15.2 (d, J_{CP} = 4.5 Hz), 13.7 (d, J_{CP} = 2.8 Hz); ^{31}P NMR δ (202 MHz, $CDCl_3$) 38.4 (br m). Anal. Calcd for $C_{14}H_{34}B_2NP$: C, 62.50; H, 12.74; N, 5.21. Found: C, 62.60; H, 12.87; N, 5.13.

(*S*)-4,5-Dihydro-5-hydroxy-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]-phosphepine 5-Oxide (25). Diisopropylethylamine (2.6 mL, 14.9 mmol) was added to a suspension of ammonium phosphinate (340 mg, 4.1 mmol) in dichloromethane (25 mL) at 0 °C. After the mixture was stirred for 20 min, chlorotrimethylsilane (1.9 mL, 15 mmol) was added at 0 °C. The mixture was stirred for 2 h at room temperature, a solution of (*S*)-2,2′-di(bromomethyl)-1,1′-binaphthyl ((*S*)-**24**, 1.19 g, 2.7 mmol) in dichloromethane (5 mL) was added at 0 °C, and the mixture was stirred for additional 24 h. The reaction was carefully quenched with water (5 mL) at 0 °C, and the organic phase washed twice with aqueous HCl (10%, 5 mL) and with water (5 mL). The organic layer was dried over magnesium sulfate and concentrated to give, after flash chromatography on silica gel using CH_2Cl_2/MeOH (95:5) as eluent, **25** as a brown pale solid (392 mg, 42%): $[\alpha]^{20}_D$ −97.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.4 Hz, 4H), 7.45 (d, J = 8.2 Hz, 2H), 7.36 (t, J = 6.7 Hz, 2H), 7.13 (m, 4H), 3.02 (quint, J = 16.9 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.7, 132.7, 132.1, 130.2, 129.1, 128.2, 128.1, 126.9, 126.3, 125.5, 35.2 (d, J_{HP} = 90 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 67.7.

(*S*)-4,5-Dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]phosphepine−Borane (26−BH_3). A mixture of phosphinic acid **25** (365 mg, 1.06 mmol) and phenylsilane (0.26 mL, 2.12 mmol) was heated at 90 °C for 6 h under argon, and the excess of phenylsilane was removed under reduced pressure. THF (1 mL) was added followed by a solution of BH_3·Me_2S (2N in THF, 0.6 mL), and the mixture was stirred for 2 h at room temperature. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel using CH_2Cl_2/hexane (50:50) as eluent to give **26**−BH_3 as a white solid (148 mg, 43%): $[\alpha]^{20}_D$ = +195 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93−7.86 (m, 4H), 7.51

(dd, J = 8.6, 1.6 Hz, 1H), 7.43−7.39 (m, 2H), 7.27−7.21 (m, 3H), 7.13 (d, J = 8.0 Hz, 1H), 7.08 (d, J = 8.6 Hz, 1H), 5.15 (dm, J = 375 Hz, 1H), 3.03 (ddd, J = 18.7, 13.3, 5.8 Hz, 1H), 2.95 (dt, J = 14.5, 3.6 Hz, 1H), 2.84 (d, J = 13.4 Hz, 1H), 2.67 (ddd, J = 10.5, 12.2, 14.1 Hz, 1H), 0.9−0.0 (br, 3H).

Diethyl (*S*)-2-[(*S*)-4,5-Dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]phosphepinoborane]ethylphosphonate (28−BH_3). KO-*t*-Bu (5 mg, 0.045 mmol) was added to a solution of the phosphine−borane **26**−BH_3 (148 mg, 0.45 mmol) and diethyl vinylphosphonate (**27**, 74 mg, 0.45 mmol) in THF (1 mL), and the reaction mixture was stirred for 12 h at room temperature. Evaporation of the solvent and purification of the residue by flash chromatography on silica gel using CH_2Cl_2/MeOH (98:2) as eluent gave **28**−BH_3 (183 mg, 83%) as a colorless oil: $[\alpha]^{20}_D$ +126 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (m, 4H), 7.37 (d, J = 8.8 Hz, 1H), 7.30 (d, J = 7.1 Hz, 1H), 7.28 (d, J = 7.5 Hz, 1H), 7.23 (d, J = 8.5 Hz, 1H), 7.10−7.00 (m, 3H), 6.95 (d, J = 8.5 Hz, 1H), 3.92 (m, 4H), 2.72 (d, J = 13.1 Hz, 1H), 2.61 (m, 2H), 2.44 (dd, J = 12.8, 16.4 Hz, 1H), 1.88−1.52 (m, 4H), 1.14 (dt, J = 9.9, 7.1 Hz, 6H), 0.7−0.1 (br, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.8, 133. 2, 133.1, 132.2, 132.0, 130.1, 130.0, 129.9, 129.8, 129.0, 128.9, 128.4, 128.3, 127.1, 126.8, 126.5, 126.3, 125.9, 125.7, 62.0 (d, J = 6.5 Hz), 29.7 (d, J = 46.0 Hz), 28.7 (d, J = 29.5 Hz), 20.0, 18.6, 16.4 (d, J = 6 Hz), 16.1 (d, J = 5.2 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 50.3 (br), 30.5 (dt, J = 56.5, 8.1 Hz).

2-[(*S*)-4,5-Dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]phosphepinoborane]ethylphosphine (29−BH_3). LAH (44 mg, 1.11 mmol) was added in small portions to a solution of **28**−BH_3 (180 mg, 0.37 mmol) in THF (3 mL) at 0 °C. After 30 min of stirring, saturated aqueous sodium sulfate (40 μL) was added with caution. The crude product was filtered through a plug of silica to give, after evaporation of the solvent, **29**−BH_3 (101 mg, 71%) as a white solid which was directly used in the next step: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01−7.88 (m, 4H), 7.58 (d, J = 8.3 Hz, 1H), 7.48 (m, 2H), 7.41 (d, J = 8.2, 1H), 7.30−7.22 (m, 3H), 7.15 (d, J = 8.4, 1H), 2.94 (d, J = 12.9 Hz, 1H), 2.85 (dt, J = 195.0, 6.8 Hz, 2H), 2.82 (m, 2H), 2.62 (dd, J = 16.0, 12.9 Hz, 1H), 1.87−1.69 (m, 4H), 0.94−0.05 (br, 3H).

2-[(*S*)-4,5-Dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]phosphepinoborane]ethylphosphine−Borane (29−$2BH_3$). A solution of BH_3·Me_2S (2 N in THF, 0.14 mL) was added to a solution of **29**−BH_3 (101 mg, 0.26 mmol) in THF (2 mL), and the mixture was stirred for 1 h at room temperature. The solvent was removed under reduced pressure and the residue filtered through a plug of silica to give **29**−$2BH_3$ (83 mg, 81%) as a white solid: $[\alpha]^{20}_D$ +100.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08−7.99 (m, 4H), 7.62 (d, J = 8.1 Hz, 1H), 7.55 (d, J = 7.6 Hz, 1H), 7.51 (d, J = 8.2 Hz, 1H), 7.47 (d, J = 6.5 Hz. 1H), 7.32−7.27 (m, 3H), 7.20 (d, J = 7.8 Hz, 1H), 4.76 (dm, J_{PH} = 370 Hz, 1H), 4.63 (dm, J_{PH} = 370 Hz, 1H), 3.00 (d, J = 12.8 Hz, 1H), 2.87 (m, 2H), 2.71 (app t, J = 14.8 Hz, 1H), 2.16 (m, 2H), 1.97 (m, 1H), 1.78 (m, 1H), 0.2−0.9 (br, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.3 (d, J = 3.0 Hz), 133.7 (d, J = 4.4 Hz), 133.6, 133.4, 132.7 (d, J = 1.5 Hz), 132.4 (d, J = 2.3 Hz), 130.1, 129.9, 129.8, 129.5, 129.5, 128.9, 128.6, 128.6, 127.3 (d, J = 2.2 Hz), 127.2, 127.0, 126.9, 126.5, 126.3, 30.2 (d, J = 32.3 Hz), 29.1 (d, J = 30.0 Hz), 19.9 (dd, J = 26.0, 3.7 Hz), 10.9 (d, J = 34.5 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 50.5, −46.7 (t, J = 470 Hz).

1,2-Bis[(*S*)-4,5-dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]phosphepinoborane]ethane (7−$2BH_3$). Sodium hydride (4.2 mg, 0.175 mmol) was added in one portion to a solution of phosphine−borane **29**−$2BH_3$ (30 mg, 0.075 mmol) and (*S*)-2,2′-di(bromomethyl)-1,1′-diphenyl ((*S*)-**24**, 33 mg, 0.075 mmol) in THF (0.3 mL) and the mixture was stirred for 2 h at room temperature. The solid was filtered off and the filtrate concentrated to give, after flash chromatography on silica gel using CH_2Cl_2/hexane (1:1) as eluent, **7**-$2BH_3$ (26 mg, 51%) as a white solid: $[\alpha]^{20}_D$ +39.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.3 Hz, 2H), 7.95 (app q, J = 7.3 Hz, 6H), 7.52−7.43 (m, 8H), 7.27−7.21 (m, 4H), 7.19 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 8.4 Hz, 2H), 2.83 (m, 6H), 2.61 (dd, J = 16.8, 13.0 Hz, 2H), 1.90 (m, 2H), 1.68 (m, 2H), −0.1- -0.8 (br, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.2, 133.7, 133.6, 133.4, 132.7, 132.5, 130.3, 130.0, 129.7, 129.4, 128.9, 128.8, 128.6, 127.7, 127.2, 127.1, 127.0, 126.8, 126.4, 126.2, 29.9 (d, J = 32.2 Hz), 29.3 (d, J = 29.8 Hz), 17.0 (d, J = 26.4 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 50.3 (br); HRMS (FAB+Na) *m*/*z* calcd for $C_{46}H_{42}B_2NaP_2$ 701.2846, found 701.2853.

1-[(*S*)-4,5-Dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]phosphepinoborane]-2-[(*R*)-4,5-dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]phosphepinoborane]ethane (9−$2BH_3$). Compound **9**−$2BH_3$ was prepared by the method described for **7**−$2BH_3$ using **29**−$2BH_3$ (25 mg, 0.062 mmol) and (*R*)-2,2′-di(bromomethyl)-1,1′-dinaphthyl ((*R*)-**24**, 27 mg, 0.062 mmol): yield 48% (20 mg, white solid); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.6 Hz, 2H), 7.87 (d, J = 8.3 Hz, 2H), 7.83 (d, J = 8.1 Hz, 2H), 7.67 (d, J = 8.3 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 7.8 Hz, 2H), 7.38 (d, J = 7.8 Hz, 2H), 7.22 (d, J = 8.6 Hz, 2H), 7.16 (m, 4H), 7.07 (t, J = 9.8 Hz, 4H), 2.86 (d, J = 13.1 Hz, 2H), 2.72 (dd, J = 15.1, 3.2 Hz, 2H), 2.64 (d, J = 15.1 Hz, 2H), 2.57 (dd, J = 16.4, 12.9 Hz, 2H), 1.74 (m, 2H), 1.67 (m, 2H), 0.75- -0.1 (br, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.2, 133.7, 133.6, 133.4, 132.7, 132.4, 130.2, 129.6, 129.4, 128.9, 128.8, 128.7, 127.4, 127.2, 127.0, 126.8, 126.4, 126.2, 30.4 (d, J = 32.9 Hz), 28.6 (d, J = 35.9 Hz), 17.2 (d, J = 27.4 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 50.7 (br); HRMS (FAB+Na) *m*/*z* calcd for $C_{46}H_{42}B_2NaP_2$ 701.2846, found 701.2853.

2-[(*S*)-4,5-Dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]azepino]-ethylamine (31). Ethylenediamine (1.8 g, 30 mmol) and triethylamine (1.39 g, 13.7 mmol) in toluene (0.5 mL) were added to (*S*)-2,2′-dibromoethyl-1,1′-binaphthyl ((*S*)-**24**, 104 mg, 0.236 mmol). The flask was sealed and heated to 60 °C for 24 h. Water and diethyl ether were added. The organic layer was separated and dried (Na_2SO_4) and concentrated under vacuum to give **31** (72 mg, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.21 Hz, 4H), 7.46−7.28 (m, 6H), 7.19−7.10 (m, 2H), 3.55 and 3.10 (AB, J = 12.2 Hz, 4H), 2.85−2.72 (m, 2H), 2.66−2.56 (m, 1H), 2.38−2.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.0, 133.4, 133.1, 131.3, 128.3, 128.2, 127.7, 127.4, 125.7, 125.4, 58.0, 55.4, 39.7.

1-[(*R*)-4,5-Dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]azepino]-2-[(*S*)-4,5-dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]azepino]-ethane (10). Compound (*R*)-**24** (74.7 mg, 0.170 mmol) and triethylamine (1 mL) were added to compound **31** (57 mg, 0.168 mmol) in toluene (1 mL), and the mixture was heated at 60 °C for 24 h. After the mixture was cooled to room temperature, the solvent was evaporated and the remaining solid was dissolved in chloroform. The organic phase was washed with water and dried (Na_2SO_4): yield 35%. The ^{1}H NMR spectrum of the product obtained was in agreement with that published.[25b]

(1*S*,2*S*)-1,2-Bis[(*R*)-4,5-dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]azepino]cyclohexane (11). (*R*)-2,2′-Dibromoethyl-1,1′-binaphthyl ((*R*)-**24**, 443.5 mg, 1.0 mmol) and (1*S*,2*S*)-1,2-diaminocyclohexane (57.5 mg, 0.5 mmol) were mixed with toluene (5 mL) and triethylamine (420 μL, 3.0 mmol). The resulting slurry was degassed at −78 °C and then warmed to room temperature before the flask was sealed and heated at 60 °C for 60 h. The flask was cooled to room temperature, and THF (5 mL) was added. The liquid was decanted, and the residue was washed with THF (2 × 5 mL). The combined liquids were filtered through a glass frit (P2) and concentrated at reduced pressure. The crude product was recrystallized from $CHCl_3$/*tert*-butyl methyl ether to give **11** (164 mg, 49%) as a white powder: mp 293−294 °C; $[\alpha]^{25}_D$ −185.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.1 Hz, 4H), 7.74 (d, J = 8.2 Hz, 4H), 7.44−7.37 (m, 12H), 7.24−7.20 (m, 4H), 3.70 and 3.52 (AB, J = 12.3 Hz, 8H), 2.85 (br d, J = 8.5 Hz, 2H), 1.91 (br d, J = 13.1 Hz, 2H), 1.76−1.66 (br m, 2H), 1.39−1.28 (br m, 2H), 1.24−1.16 (br m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.3, 134.6, 132.7, 131.5, 128.3, 128.2, 128.1, 127.4, 125.4, 125.0, 66.0, 51.7, 28.9, 25.8; MS (EI, direct inlet) 670 (M^+),

391, 377, 308, 293, 266. HRMS (FAB+H) *m/z* calcd for $C_{50}H_{43}N_2$ 671.3426, found 671.3434.

(1*R*,2*R*)-1,2-Bis[(*R*)-4,5-dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]azepino]cyclohexane (12). Compound **12** was prepared analogously to **11** using (1*R*,2*R*)-1,2-diaminocyclohexane: yield 51% (white powder); mp 286−288 °C; $[\alpha]^{25}_D$ −314.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.0 Hz, 4H), 7.85 (d, J = 8.2 Hz, 4H), 7.47−7.39 (m, 12H), 7.27−7.23 (m, 4H), 3.85 and 3.59 (AB, J = 11.7 Hz, 8H), 2.97 (br d, J = 8.1 Hz, 2H), 1.88 (br d, J = 10.7 Hz, 2H), 1.71−1.63 (br m, 2H), 1.33−1.15 (br m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.7, 134.6, 132.8, 131.3, 128.5, 128.23, 128.17, 127.5, 125.4, 125.0, 66.7, 51.8, 29.0, 25.7; MS (EI, direct inlet) 670 (M^+), 391, 377, 308, 293, 265; HRMS (FAB+H) *m/z* calcd for $C_{50}H_{43}N_2$ 671.3426, found 671.3423.

1,3-Bis[(*S*)-4,5-dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]azepino]propane (13).[46] Compound **13** was prepared similarly to **11** using 1,2-diaminopropane but was purified by column chromatography on basic alumina (CH_2Cl_2/MeOH 9:1): yield 73% (pale yellow powder); mp 221−223 °C; $[\alpha]^{25}_D$ −172.6 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.2 Hz, 8H), 7.58 (d, J = 8.2 Hz, 4H), 7.52−7.45 (m, 8H), 7.29−7.25 (m 4H), 3.76 and 3.21 (AB, J = 12.3 Hz, 8H), 2.68−2.62 (m, 2H), 2.51−2.44 (m, 2H), 2.03−1.96 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.0, 133.4, 133.1, 131.3, 128.29, 128.27, 127.8, 127.4, 125.7, 125.3, 55.3, 53.2, 26.9; MS (EI, direct inlet) 630 (M^+), 308, 293, 266.

Diethyl 2-[4,5-Dihydro-3*H*-dibenzo[c−e]azepino]ethylphosphonate (36). A solution of (2-aminoethyl)phosphonic acid diethyl ester (**21**, 216 mg, 1.2 mmol) in THF (2.5 mL) was added dropwise to a solution of 2,2′-di(bromomethyl)-1,1′-diphenyl[26] (**35**, 408 mg, 1.2 mmmol) and triethylamine (0.37 mL, 2.7 mmol) in THF (5 mL), and the mixture was stirred for 8 h at 50 °C. The salt was filtered off and the filtrate concentrated under reduced pressure to give, after purification by flash chromatography on silica gel using $CHCl_3$/MeOH (99:1) as eluent, **36** (405 mg, 93%) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 7.6 Hz, 2H), 7.41 (t, J = 6.3 Hz, 2H), 7.37−7.32 (m, 4H), 4.18 (m, 4H), 3.46 (s, 4H), 2.92 (app q, J = 8.3 Hz, 2H), 2.18 (m, 2H), 1.16 (t, J = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 134.7, 130.1, 128.3, 128.2, 128.0, 62.0 (d, J = 5.7 Hz), 55.5, 48.9, 25.8 (d, J = 138 Hz), 16.9 (d, J = 6 Hz).

2-[4,5-Dihydro-3*H*-dibenzo[c−e]azepino]ethylphosphine (37). Compound **37** was prepared by LAH reduction of **36** (130 mg, 0.36 mmol) in THF according to the procedure used for the preparation of **29**−BH_3: yield 75% (white solid, 69 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41(d, J = 7.6 Hz, 2H), 7.35 (td, J = 6.8, 1.6 Hz, 2H), 7.30−7.23 (m, 4H), 3.32 (s, 4H), 2.64 (dd, J = 14.4, 5.9 Hz, 2H), 2.61 (dt, J = 195, 8.2 Hz, 2H), 1.73 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 134.9, 130.1, 128.5, 128.14, 128.06, 58.5 (d, J = 3.0 Hz), 55.5, 13.2 (d, J = 8.8 Hz).

2-[4,5-Dihydro-3*H*-dibenzo[c−e]azepinoborane]ethylphosphine−Borane (37−2BH$_3$). Compound **37**−$2BH_3$ was prepared from **37** (120 mg, 0.47 mmol) using a solution of BH_3·Me_2S (2M in THF): yield 89% (white solid, 117 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52−7.48 (m, 4H), 7.42−7.35 (m, 4H), 4.62 (dsext, J = 365, 7.1 Hz, 2H), 3.69 (d, J = 12.4 Hz, 2H), 3.32 (br s, 2H), 2.99 (dd, J = 16.3, 7.3 Hz, 2H), 2.53 (oct, J = 5.7 Hz, 2H), 1.0−0.6 (br, 3H), 0.6−0.1 (br, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 132.4, 131.2, 130.2, 128.7, 128.6, 61.5 (br), 56.9, 12.6 (d, J = 35 Hz).

1-[4,5-Dihydro-3*H*-dibenzo[c−e]azepinoborane]-2-[(*S*)-4,5-dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]phosphepinoborane]ethane (14−2BH$_3$). Compound **14**−$2BH_3$ was prepared in analogy to **7** from **37**-$2BH_3$ (50 mg, 0.18 mmol) and (*S*)-2,2′-di(bromomethyl)-1,1′-dinaphthyl ((*S*)-**24**, 79 mg, 0.18 mmol): yield 62% (white solid, 62 mg); $[\alpha]^{20}_D$ +52.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.3 Hz, 1H), 7.88 (t, J = 8.9 Hz, 3H), 7.54 (d, J = 8.3 Hz, 1H), 7.50−7.36 (m, 10H), 7.22−7.09 (m, 5H), 3.74 (br d, J = 12.7 Hz, 1H), 3.55 (br d, J = 11.8 Hz, 1H), 3.30 (br, 2H), 3.02 (m, 2H), 2.86 (d, J = 12.9 Hz, 1H), 2.79 (s, 1H), 2.77 (d, J = 4.3 Hz, 1H), 2.68 (dd, J = 16.8, 13.1 Hz, 1H), 2.49 (qd, J = 12.9, 4.2 Hz, 1H), 2.01 (qd, J = 11.3, 6.3 Hz, 1H), 1.7−1.2 (br, 3H), 0.7−0.0 (br, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 134.2, 134.2, 133.9, 133.6, 133.5, 132.6, 132.5, 130.5, 130.4, 130.1, 130.0 (d, J = 6 Hz), 129.7, 129.3, 128.9, 128.8, 128.8, 128.7, 128.7, 128.5, 128.0, 127.2, 127.1, 126.8, 126.4, 126.2, 55.8, 55.1, 53.9, 30.5 (d, J = 34 Hz), 29.2 (d, J = 30 Hz), 18.6 (d, J = 27 Hz). Anal. Calcd for $C_{38}H_{38}B_2NP$: C, 81.31; H, 6.82; N, 2.50. Found: C, 81.19; H, 6.67; N, 2.35.

1-[4,5-Dihydro-3*H*-dibenzo[c−e]azepino]-2-[(*S*)-4,5-dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]phosphepinoborane]ethane (14−BH$_3$). Compound **14**−BH_3 was prepared from **14**−$2BH_3$ (56 mg, 0.1 mmol) and DABCO (12 mg, 0.1 mmol) by stirring under argon atmosphere for 12 h at room temperature. Flash chromatography on silica gel using CH_2Cl_2/AcOEt (98:2) as eluent gave **14**−BH_3 in 86% yield (47 mg, white solid): $[\alpha]^{20}_D$ +80.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91−7.84 (m, 4H), 7.51 (d, J = 8.3 Hz, 1H), 7.44−7.34 (m, 7H), 7.28 (td, J = 7.3, 1.3 Hz, 2H), 7.22 (d, J = 6.6 Hz, 2H), 7.20−7.16 (m, 2H), 7.14 (d, J = 6.6 Hz, 1H), 7.06 (dd, J = 8.6 Hz, 1H), 3.32 (s, 4H), 2.93 (dd, J = 13.3, 2.0 Hz, 1H), 2.86 (dd, J = 14.6, 5.1 Hz, 1H), 2.81 (m, 2H), 2.76 (dd, J = 14.6, 9.3 Hz, 1H), 2.66 (dd, J = 17.1, 13.3 Hz, 1H), 1.92 (m, 1H), 1.74 (m, 1H), 0.9−0.0 (br, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) MHz δ 141.5, 134.4, 133.7, 133.6, 133.5, 133.3, 132.8, 132.4, 131.2, 130.8, 130.7, 130.1, 129.2, 128.9, 128.9, 128.8, 128.7, 128.7, 128.3, 128.1, 127.8, 127.3, 127.0, 126.7, 126.3, 126.0, 55.5, 49.2, 30.9 (d, J = 33.0 Hz), 30.3 (d, J = 30.5 Hz), 22.7 (d, J = 25.5 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 47.2 (br).

1-[(*S*)-4,5-Dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]azepinoborane]-2-[4,5-dihydro-3*H*-dibenzo[c−e]phosphepinoborane]ethane (15−2BH$_3$). Compound **15**−$2BH_3$ was prepared by the method described for **14**−BH_3 using **38**−$2BH_3$ (55 mg, 0.14 mmol) and 2,2′-di(bromomethyl)-1,1′-diphenyl (**35**, 48 mg, 0.14 mmol): yield 53% (white solid, 42 mg): $[\alpha]^{20}_D$ +207 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 7.9 Hz, 0.5H), 8.05−7.96 (m, 3.5H), 7.78 (d, J = 8.3 Hz, 0.5H), 7.71 (d, J = 7.9 Hz, 0.5H), 7.62 (J = 8.6 Hz, 0.5H), 7.59−7.27 (m, 14.5H), 4.02 (d, J = 11.2 Hz, 0.5H), 3.92 (d, J = 11.7 Hz, 0.5H), 3.81 (s, 1H), 3.73 (d, J = 13.6 Hz, 0.5H), 3.64 (J = 13.6 Hz, 0.5H), 3.26 (d, J = 11.2 Hz, 0.5H), 3.21 (d, J = 11.7 Hz, 0.5H), 3.10−2.60 (m, 6H), 2.17 (m, 2H), 1.75−1.45 (br, 3H), 0.8−0.1 (br, 3H); ^{31}P NMR (202 MHz, $CDCl_3$) δ 44.14 (br). Anal. Calcd for $C_{38}H_{38}B_2NP$: C, 81.31; H, 6.82; N, 2.50. Found: C, 81.09; H, 6.68; N, 2.42.

1-[(*S*)-4,5-Dihydro-3*H*-dinaphtho[1,2-*c*:2′,1′-*e*]azepino]-2-[4,5-dihydro-3*H*-dibenzo[c−e]phosphepinoborane]ethane (15−BH$_3$). Compound **15**−BH_3 was prepared by the method employed for the preparation of **14**−BH_3 from **15**−$2BH_3$ (40 mg, 0.071 mmol): yield 86% (white solid, 34 mg); $[\alpha]^{20}_D$ +110.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82−7.74 (m, 4H), 7.39 (d, J = 8.4 Hz, 1H), 7.34−7.06 (m, 14.5 H), 6.93 (d, J = 7.8 Hz, 0.5H), 3.53 (d, J = 12.4 Hz, 1H), 3.52 (d, J = 12.2 Hz, 1H), 3.05 (d, J = 12.4 Hz, 1H), 3.01 (d, J = 12.2 Hz, 1H), 2.81 (m, 1H), 2.73−2.44 (m, 5H), 1.81 (m, 1H), 1.61 (m, 1H), 0.8- -0.1 (br, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.4, 139.7, 134.9, 133.2, 131.3, 130.4, 129.8, 129.2, 128.5 (2C), 128.2, 128.1, 128.0, 127.8 (2C), 127.5, 127.4, 125.8, 125.5, 55.1 (d, J = 24 Hz), 48.8 (d, J = 24 Hz), 29.7 (d, J = 36 Hz), 29.1 (d, J = 13 Hz), 22.6 (d, J = 27.0 Hz), 22.2 (d, J = 29.0 Hz).

Typical Procedure for Catalytic Asymmetric Allylic Substitution Using Palladium Acetate as Palladium Source. Ligand (*S,S*)-**5**−BH_3 (5 mg, 0.0077 mmol) and *rac*-1,3-diphenyl-2-propenyl acetate (78 mg, 0.31 mmol) were mixed in degassed CH_2Cl_2 (0.7 mL) in a dry flask. Palladium

(46) This compound has previously been reported (electronic publication in Japanese): Nakada, M. *Asahi Garasu Zaidan Josei Kenkyu Seika Hokoku* 1998; *Chem. Abstr.* **1998**, *132*, 193960.

acetate (1.73 mg, 0.0077 mmol) was added, and the solution was degassed and stirred for 15 min at room temperature. A solution of dimethyl malonate (91.8 mg, 0.69 mmol) and BSA (189 mg, 0.93 mmol) in degassed CH_2Cl_2 (0.7 mL) was added at −78 °C. Potassium acetate (a few crystals) was added, and the solution was degassed and stirred at room temperature. After complete reaction (monitored by HPLC), a saturated solution of NH_4Cl in water was added, and the aqueous layer was extracted with Et_2O. The organic phases were combined, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with hexane/EtOAc (4:1) as eluent to give the product (95%, 98.5% ee (*S*)) as a white solid. The enantiomeric excess was measured using HPLC (chiralcel OD-H, flow rate = 0.5 mL/min, hexane/2-propanol = 99:1, t_R = 21.30 min, t_S = 22.85 min.

The same procedure was used for the dimethyl(3-cyclohexenyl)malonate, but the product was purified by flash chromatography on silica gel with hexane/EtOAc (95:5) as eluent. The enantiomeric excess was mesured using GC: Chrompack Permethyl-β-CD.

Typical Procedure for Catalytic Asymmetric Allylic Substitution Using Allylpalladium Chloride Dimer as Palladium Source. To a degassed solution of (*S*,*S*)-**1**−BH_3 (7.15 mg, 11 μmol) in toluene (0.3 mL) was added a degassed solution of DABCO (2.5 mg, 22.1 μmol) in toluene (0.1 mL), and the mixture was stirred for 8 h at 80 °C. The solvent was removed under reduced pressure. CH_2Cl_2 (0.5 mL) was added, the solution was degassed, allylpalladium chloride dimer (1.05 mg, 2.9 μmol) was added, and the solution was stirred at room temperature for 20 min. *rac*-1,3-Diphenyl-2-propenyl acetate (138.8 mg, 0.55 mmol) in degassed CH_2Cl_2 (0.6 mL) was added at −78 °C, followed by a solution of dimethyl malonate (163 mg, 1.24 mmol) and BSA (335 mg, 1.65 mmol) in degassed CH_2Cl_2 (0.8 mL). Potassium acetate (a few crystals) was added, and the solution was degassed and stirred at room temperature. After complete reaction, a saturated solution of NH_4Cl in water was added, and the aqueous layer was extracted with diethyl ether. The organic phases were combined, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with hexane/EtOAc (4:1) as eluent to give the product (93%, 98.4% ee (*S*)) as a white solid.

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Supporting Information Available: NMR spectra for obtained compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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