Nitrogen-Based Chirality Effects in Novel Mixed Phosphorus/Nitrogen Ligands Applied to Palladium-Catalyzed Allylic Substitutions

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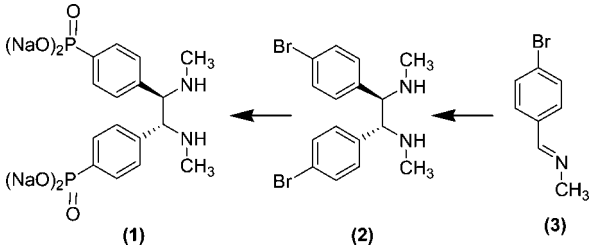
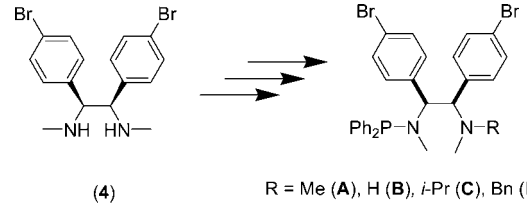
A novel series of chiral P,N-ligands was obtained by desymmetrization of the achiral *meso-N,N′*-dimethyl-1,2-diphenylethane-1,2-diamine backbone and resolution of the resulting adducts. This transformation was achieved by the selective introduction of a diphenylphosphine moiety on one of the two nitrogen centers. The resulting palladium complexes were used for the catalytic enantioselective allylic alkylation of 1,3-diphenyl-1-acetoxy-2-propene with dimethyl malonate. In some cases, high conversions (up to 98% after 1 h) along with good chiral inductions (up to 95% e.e.) were obtained, as a result of a control of the inversion of the stereogenic center formed at nitrogen upon coordination to palladium.

Scheme 1



Scheme 2



Introduction

In a previous study, we have reported the synthesis of new chiral diamines **1** (Scheme 1) based on the *N,N′*-dimethyl-1,2-diphenylethane-diamine backbone and modified by phosphonate groups (PO_3Na_2) to achieve solubility of the ligand in water.[1] The key step for the preparation of the diamine-bisphosphonate **1** consisted of the synthesis of the bisbromo analogue **2** by reductive dimerization of imine **3**, using the combination of zinc and chlorotrimethylsilane (Scheme 1).

Besides the formation of racemic *d,l*-**2**, this reaction also led to the *meso*-diamine **4** in a 1:1 ratio. We found that the backbone present in compounds **2** and **4** was an ideal scaffold to access novel mixed N,P ligands **A**−**D** (Scheme 2) for asymmetric catalysis.

In the literature, many mixed bidentate donor ligands have been successfully used for the palladium-catalyzed asymmetric allylic substitution with carbon nucleophiles, providing high enantiomeric excesses.[2−4] Mixed N,P ligands represent one of the most intensively studied systems containing dissimilar donor atoms combining hard and soft centers, and studies have largely concentrated on the design of novel series of such hemilabile ligands and the scope of asymmetric reactions achievable using the resulting transition-metal-based catalysts.[5,6] Early studies in allylic substitution of 1,3-diphenylpropenyl acetate were based on the use of chiral ligands containing C_2 symmetry in order to reduce the number of diastereomeric intermediates.[7−10] However, non-C_2-symmetric ligands can also afford excellent stereoinduction. The most famous example is the use of phosphine-oxazolines first described by Pfaltz.[11] In that case, combining strong phosphorus and weaker nitrogen donors influences both the stability and reactivity of the diastereomeric intermediates during the reaction, and it is generally well agreed that nucleophilic addition occurs trans to phosphorus.[12−16] However, in the case of mixed phosphine/alkylamine ligands,

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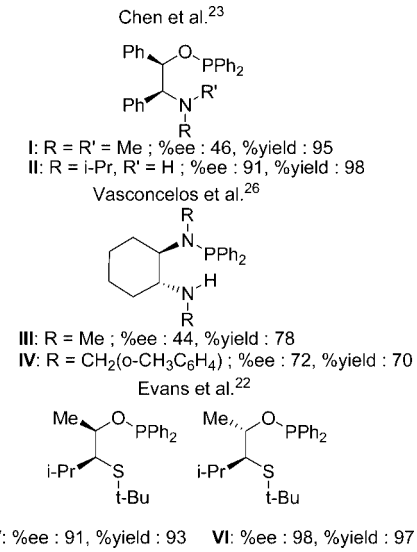

Figure 1. Pd-catalyzed allylic alkylation of rac-(E)-1,3-diphenyl-3-acetoxyprop-1-ene with dimethylmalonate, using mixed phosphorus/nitrogen and phosphorus/sulfur ligands closely related to amino-phosphines **A**−**D**.

there are still many mechanistic issues to be addressed, and our present system offers the possibility of investigating the influence of various parameters. This includes the relative configuration of the two chiral benzylic carbon atoms and more importantly the role of the stereogenic center formed at nitrogen upon coordination. While the role of the control of *N*-chirality in asymmetric induction has been investigated, especially in the case of 1,2-diamines,[17−20] relay of stereochemical information to nitrogen was presumed in the case of mixed phosphine/alkylamine ligands[21] but has never been studied thoroughly, in a way similar to that reported by Evans et al.[22] in the case of mixed phosphorus/sulfur ligands (Figure 1).

In addition, the steric bulk of the coordinating nitrogen can be easily tailored in our case. Chen first described good enantioselectivities in palladium-mediated allylic substitution, using amino-phosphinite ligands (Figure 1). In this respect, the effects of both nitrogen substitution and stereochemistry of the 1,2-diphenyl-2-aminoethanol backbone were studied, although the differences observed between the ligands and the role of the nitrogen chirality, in particular, have yet to be elucidated.

In the present article, the enantioselective Pd-catalyzed allylic substitution of 1,3-diphenylpropenyl acetate with dimethyl malonate was selected to compare the catalytic properties of our ligands **A**−**D**, obtained from *meso*-diamine **4** via a desymmetrization route. The performances of the best ligands (**B**) were compared with that of their diastereoisomers (**E**) and the marked differences observed between the two series of diastereoisomers were found to arise from the control of the inversion of the *N*-chiral center, which was more effective in the case of **B**. Indeed, a suitable stereochemical model was proposed, supported by NMR, molecular modeling, and X-ray crystallographic studies.

Table 1. Results of the Reaction of Chlorodiphenylphosphine with Diamines *d*, *l*-2, or 4 in Various Conditions

entry	diamine	solvent	*T* (°C)	time	result[c]
1	*d*, *l*-**2**[a]	toluene	r.t.	30 min	100/0/0
2	**4**[a]	toluene	r.t.	30 min	100/0/0
3	**4**[a]	toluene	reflux	12 h	67/33/0
4	**4**[a]	CH_2Cl_2	r.t.	12 h	50/50/0
5	**4**[a]	CH_2Cl_2	r.t.	30 min	50/50/0
6	**4**[b]	toluene	r.t.	30 min	65/0/35
7	**4**[b]	toluene	r.t.	12 h	100/0/0
8	**4**[b]	CH_2Cl_2	r.t.	30 min	22/0/78
9	**4**[b]	CH_2Cl_2	r.t.	12 h	28/0/72

[a] Diamine (1 equiv), chlorodiphenylphosphine (2 equiv), triethylamine (4 equiv), solvent (60 mL). [b] Diamine (1 equiv), chlorodiphenylphosphine (1 equiv), triethylamine (4 equiv), solvent (60 mL). [c] Product distribution: monophosphine/diphosphine/**2** or **4**.

Results and Discussion

Ligand Synthesis. The reaction of chlorodiphenylphosphine with bis-nitrogen ligands or amino-alcohols for their derivatization into chelating diphosphines is well documented,[23−27] with good yields as evidenced by Fiorini et al. and Alper et al. in the case of *d* or *l*-*N*,*N*′-dimethyl-1,2-diphenylethane-diamine.[28,29] This reaction is usually performed in refluxing benzene or toluene. We have found that the selective monofunctionalization of the parent diamines *d*,*l*-**2** and *meso*-**4**[1] was taking place with good yields for short reaction times (30 min) in toluene at room temperature (Table 1, entries 1,2). Under such conditions, although two equivalents of chlorodiphenylphosphine were used, no formation of the diphosphine adduct was observed, unless longer reaction times and/or higher temperatures (entry 3), or a different solvent were used (entries 4,5). However, we can use 1 equiv of chlorodiphenylphosphine by increasing the reaction time in toluene (entry 7). In this case, even with dichloromethane we never observed the formation of the diphosphine, but the conversion was low even after 12 h (entries 8,9). A very similar phenomenon was recently reported in the case of (*R*,*R*)-*N*,*N*′-dialkyl-1,2-cyclohexanediamine[26] or *N*,*N*′-dimethyl urea,[30] when treated with chlorodiphenylphosphine in the presence of triethylamine.

Thus, the selective introduction of a diphenylphosphine group on one of the two nitrogen atoms of the *meso*-diamine **4** was performed in good conditions, and by subsequent reaction with sulfur,[31] the racemic mixture of the corresponding phosphine sulfide **5** was isolated (76% yield, Scheme 3). Then, the resolution of **5** was carried out using L-(+)-tartaric acid and D-(−)-tartaric acid successively, according to an optimized

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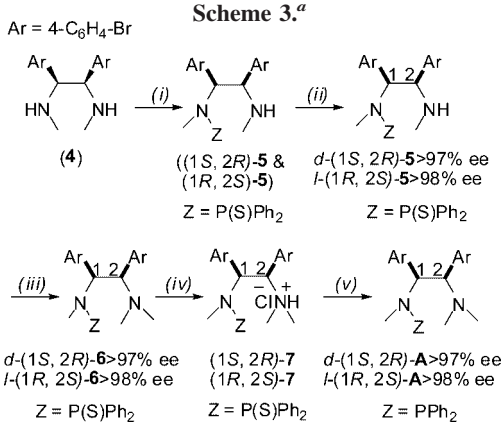
Scheme 3.[a]



[a] (i) (a) Et_3N, $ClPPh_2$, toluene; (b) S_8, toluene (76%). (ii) L- or D-tartaric acid, 97% EtOH (90% for *d*-5; 75% for l-5). (iii) 37% aqueous CH_2O, HCO_2H, 80 °C (95 %). (iv) 37% HCl, THF (98%). (v) (a) MeOTf, CH_2Cl_2; (b) $P(NMe_2)_3$, (89 %).

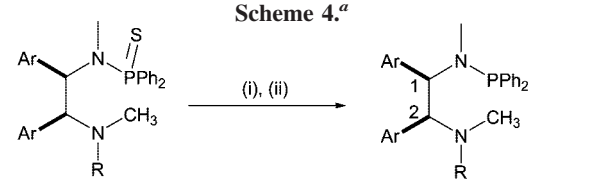
protocol derived from Alexakis et al. [32] to give (1*R*, 2*S*)-**5** (ee >98%) or (1*S*, 2*R*)-**5** (ee >97%) in good yields (75% and 90%, respectively), while the enantiomeric purities for the two compounds were determined by HPLC assay on a chiral column. The tartrate salt formed using L-tartaric acid was obtained as crystalline needles. X-ray analysis carried out on the resulting crystals [composition: *d*-**5**: L-(HO_2C-CHOH-CHOH-CO_2H): 3 H_2O] showed that the corresponding enantiomer *d*-**5** had (1*S*, 2*R*) configuration,[33] where carbon 1 represents the benzylic position bonded to the methyl-aminophosphine sulfide group. Reductive amination of *l*-(1*R*, 2*S*)-**5** or *d*-(1*S*, 2*R*)-**5** using an Eschweiler−Clark procedure[34] gave *l*-(1*R*, 2*S*)-**6** (ee >98%) or *d*-(1*S*, 2*R*)-**6** (ee >97%) in 95% yield, without epimerization of the stereogenic centers. Attempts to reduce the phosphine sulfide using Raney nickel were unsuccessful. Finally, desulfuration of (1*R*, 2*S*)-**7** or (1*S*, 2*R*)-**7** through S-methylation followed by treatment with HMPT[35] afforded *l*-(1*R*, 2*S*)-**A** (ee >98%) or *d*-(1*S*, 2*R*)-**A** (ee >97%) in 89% yield. Preliminary protection of the dimethylamino group in l-(1*R*, 2*S*)-**6** or d-(1*S*, 2*R*)-**6** as the corresponding chlorhydrate (1*R*, 2*S*)-**7** or (1*S*, 2*R*)-**7** (98% yield) proved to be necessary to achieve selective alkylation of the phosphine sulfide moiety (Scheme 3).

Then, analogues of compound **A** were prepared, in which the substitution of the amine block was tuned (i.e., NMeR, with R = H (**B**), i-Pr (**C**), or Bn (**D**)) to generate a stereogenic center at nitrogen upon coordination and vary its bulkiness. This transformation was successfully performed following a similar strategy, starting from compounds **5**, **8**, and **9**, respectively (Scheme 4).

Compounds **8** (65% yield) and **9** (85% yield) were derived from product **5**, by reductive amination using acetone and benzaldehyde, respectively.

Asymmetric Allylic Alkylation Reactions. Ligands **A**−**D** were then evaluated in the palladium-catalyzed allylic alkylation

Scheme 4.[a]



[a] (i) 37% HCl, THF, (ii) (a) MeOTf, CH_2Cl_2, (b) $P(NMe_2)_3$.

Table 2. Pd-Catalyzed Allylic Alkylation of rac-1,3-Diphenyl-3-acetoxyprop-1-ene Using Ligands A−D

ligand[a]	% conversion[b]	% ee[c]
1*R*,2*S*-**A**	0	
1*R*,2*S*-**B**	98	93 (*S*)
1*R*,2*S*-**C**	0	
1*R*,2*S*-**D**	0	

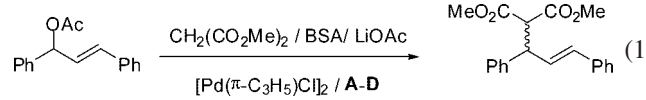
[a] Conditions: 1.5 mol % $[Pd(\pi\text{-}C_3H_5)Cl]_2$, 3 mol % ligand, 48 h, toluene, 3 equiv of $CH_2(CO_2Me)_2$ and BSA, 0.12 equiv of LiOAc, and room temperature. [b] Measured by ^1H NMR. [c] Determined by HPLC (Chiracel OD-H). Absolute configuration is shown in parentheses.

Table 3. Pd-Catalyzed Allylic Alkylation of rac-1,3-Diphenyl-3-acetoxyprop-1-ene Using Ligands A−C in CH_2Cl_2

ligand	% conversion[d]	% ee[e]
1*R*,2*S*-**B**[a]	98[f]	93 (*R*)[f]
1*S*,2*R*-**B**[a]	93	95 (*S*)
1*R*,2*S*-**A**[b]	24	0
1*R*,2*S*-**C**[c]	6	69 (*R*)

[a] Conditions: 1.5 mol % $[Pd(\pi\text{-}C_3H_5)Cl]_2$, 3 mol % ligand, and 12 h. [b] Conditions: 1.5 mol % $[Pd(\pi\text{-}C_3H_5)Cl]_2$, 3 mol % ligand, and 20 h. [c] Conditions: 1.5 mol % $[Pd(\pi\text{-}C_3H_5)Cl]_2$, 3 mol % ligand, 5 days, CH_2Cl_2, 3 equiv of $CH_2(CO_2Me)_2$ and BSA, 0.12 equiv of LiOAc, and room temperature. [d] Measured by ^1H NMR. [e] Determined by HPLC (Chiracel OD-H). Absolute configuration shown in parentheses. [f] Same yield and ee after 1 h when performed at 37 °C.

of 1,3-diphenylpropenyl acetate with dimethyl malonate, using *N*,*O*-bis(trimethylsilyl)acetamide (BSA) as the base in the presence of LiOAc at room temperature, and 3 mol % of Pd and ligand (eq 1).



(1)

We first studied the effect of the ligand architecture obtained from the *meso*-diamine backbone **4**, and the yields and enantiomeric excesses shown in Table 2 indicate that the catalytic activity is affected by the nature of the nitrogen substituents. In the case of a secondary amine bound to carbon 2 (ligand **B**), excellent yield and enantioselectivity were observed, in contrast to tertiary amine analogues (ligands **A**, **C**−**D**) for which no conversion was obtained after 48 h in toluene.

Changing the solvent from toluene to dichloromethane strongly enhanced the reaction rates, reducing the time of the reaction from 48 to 12 h, in the case of ligand **B**. Under such conditions, low but observable conversions were obtained for ligands **A** and **C**, after 20 h and 5 days, respectively, and most importantly, the absence of stereogenic nitrogen (ligand **A**) resulted in no enantioselectivity in the allylic alkylation (Table 3).

This is in strong contrast with results from the literature[23] for the closely related *N*,*N*-dimethyl ligand **I** (Figure 1), which showed high yields (>95%) along with some stereoinduction, although moderate (ee <50%), for the same reaction. The

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(33) CCDC-679468 contains the supplementary crystallographic data for this paper. These data can be obtained free ofcharge via www.ccdc-.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK. Fax: (+44) 1223-336-033. E-mail: deposit@ccdc.cam.ac.uk.)

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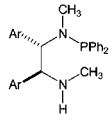
Table 4. Pd-Catalyzed Allylic Alkylation of rac-1,3-Diphenyl-3-acetoxyprop-1-ene Using Ligand E in Toluene and CH_2Cl_2

Ligand **E**	% conversion[c]	%ee[d]
		
1*R*,2*R*-**E**[a]	38	19 (*R*)
1*S*,2*S*-**E**[a]	37	23 (*S*)
1*R*,2*R*-**E**[b]	99	19 (*R*)
1*S*,2*S*-**E**[b]	99	23 (*S*)

[a] Conditions: 1.5 mol % $[Pd(\pi\text{-}C_3H_5)Cl]_2$, 3 mol % ligand in toluene (48 h). [b] Conditions: 1.5 mol % $[Pd(\pi\text{-}C_3H_5)Cl]_2$, 3 mol % ligand in CH_2Cl_2 (12 h), 3 equiv of $CH_2(CO_2Me)_2$ and BSA, 0.12 equiv of LiOAc, room temperature. [c] Measured by ^1H NMR. [d] Determined by HPLC (Chiracel OD-H). Absolute configuration is shown in parentheses.

influence of the stereochemistry of the ligand backbone was then investigated under the same reaction conditions. Therefore, diastereoisomers **E** corresponding to ligand **B** were prepared by selective introduction of a diphenylphosphine group on one of the two nitrogen atoms of the enantiomerically pure forms of diamine **2** (*d*-**2** or *l*-**2**).

Surprisingly, when compared to their analogues **B**, ligands **E** showed low yields (ca. 40%) and low enantioselectivities (ca. 20%) in the allylic alkylation when performed in toluene (Table 4). Once again, using dichloromethane as the solvent increased the reaction rate leading to quantitative yields after only 12 h, but no change of the enantioselectivity was observed, confirming that the solvent has no effect on the stereoinduction. While the precise mechanism leading to these effects has to be investigated, these data suggest that a lower control of the nitrogen chirality during the palladium complex formation might be present in the case of ligand **E**.

Mechanistic Considerations. Investigation of the control of stereochemistry at coordinated nitrogen was performed, using X-ray crystallography, NMR spectroscopic analysis, and molecular modeling of palladium−ligand complexes derived from ligands **B** and **E**, respectively. (*l*-**B**)$PdCl_2$ crystals suitable for X-ray structure determination were obtained from CH_2Cl_2/Et_2O, showing a half-chair geometry for the chelate,[36] while the methyl substituent on the coordinating nitrogen and the adjacent 4-bromophenyl group were oriented anti to each other (Figure 2).

As expected, the stronger trans influence of the phosphine (versus the secondary amine) was confirmed on the basis of the markedly different Pd−Cl bond lengths trans to phosphorus (2.38 Å) and trans to nitrogen (2.28 Å). The presence of only one diastereomeric complex at nitrogen in solution, as observed in the solid state, was evidenced by recording ^1H and ^{31}P NMR spectra of (**B**)$PdCl_2$ from −50 °C to +40 °C. For example, only one phosphorus signal ($\delta^{31}P$ = 71.6 ppm) was present over this temperature range, unlike (**E**)$PdCl_2$ for which a 1:0.4 mixture of diastereomeric complexes ($\delta^{31}P$ = 73.4 and 63.4 ppm, respectively) was apparent. Geometry optimizations performed at the PM6[37] level using MOPAC2007[38] led to a similar conclusion. Indeed, in the case of (**B**)$PdCl_2$, optimization of the anti geometry between the methyl group of the nitrogen and the adjacent 4-bromophenyl group versus the syn geometry, showed a difference in energy of 7.7 kcal/mol in favor of the anti complex. Similar calculations were carried out in the case of (**E**)$PdCl_2$, resulting in a very low energy difference (0.8 kcal/mol) between the trans and syn geometries, but this time in favor of the syn complex, accounting for the poor control of the stereochemistry at the coordinated nitrogen, for this ligand.

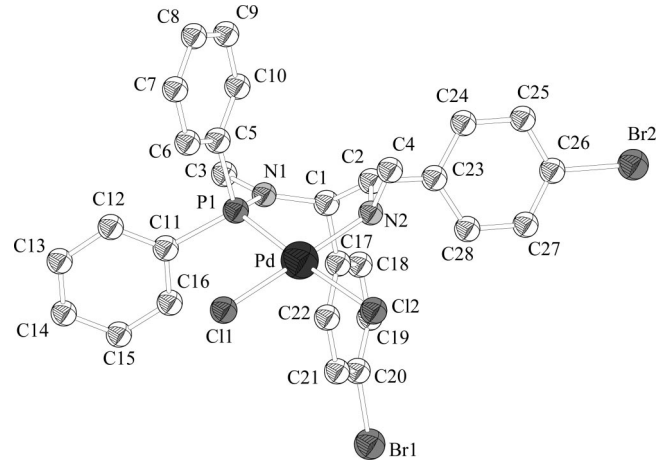


Figure 2. ORTEP view of (*l*-**B**)$PdCl_2$. Displacement ellipsoids are drawn at the 50% probability level. Hydrogen atoms were omitted for clarity.

As a result, NMR studies of the solution dynamics of the π-allyl complexes obtained from **B** should lead to the observation of a mixture of two diastereomeric complexes in rapid equilibrium, as a result of π-allyl isomerization, while a more complex mixture (i.e., 4 species) might be anticipated in the case of **E**, arising from both π-allyl isomerization and nitrogen inversion. The coordination of ligands **B** and **E** with $[Pd(1,3\text{-diphenylpropenyl})Cl]_2$[39] was thus investigated. An X-ray crystal structure of [Pd(*l*-**B**)(1,3-diphenylpropenyl)](SbF_6) was obtained (Figure 3),[40] showing a conformation very similar to that observed in (*l*-**B**)$PdCl_2$.

In addition, the bond length of the Pd−C bond trans to phosphorus (Pd−C5 = 2.28 Å) compared to the Pd−C bond trans to the nitrogen (Pd−C3 = 2.16 Å) reflected the stronger trans influence of the phosphine moiety and a more electrophilic π-allyl terminus at C5. While strongly rotated allyl moieties have been reported in crystal structures of different kinds of mixed donor ligand−palladium π-allyl complexes,[16,41,42] in the present case only a very small twist of the allyl phenyl group was observed. However, the bond length difference between C3−C4 (1.42 Å) and C4−C5 (1.39 Å) is consistent with a σ

(36) CCDC-679469 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc-.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK. Fax: (+44) 1223-336-033. E-mail: deposit@ccdc.cam.ac.uk).

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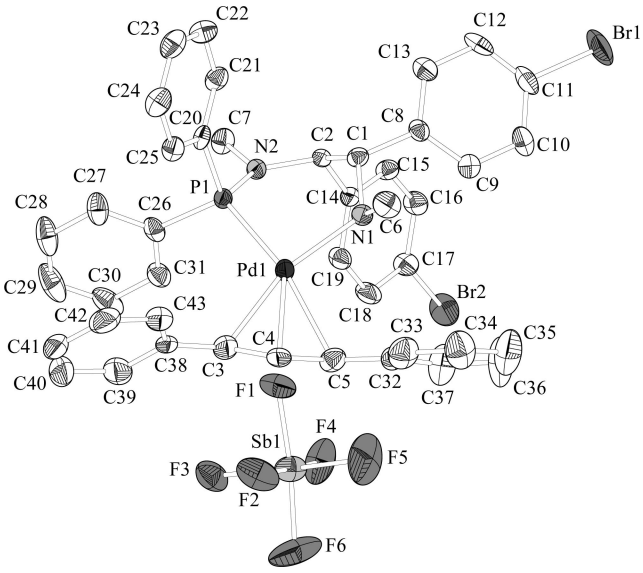

Figure 3. ORTEP view of [Pd(*l*-**B**)(1,3-diphenylpropenyl)](SbF_6). Displacement ellipsoids are drawn at the 50% probability level. Hydrogen atoms were omitted for clarity.

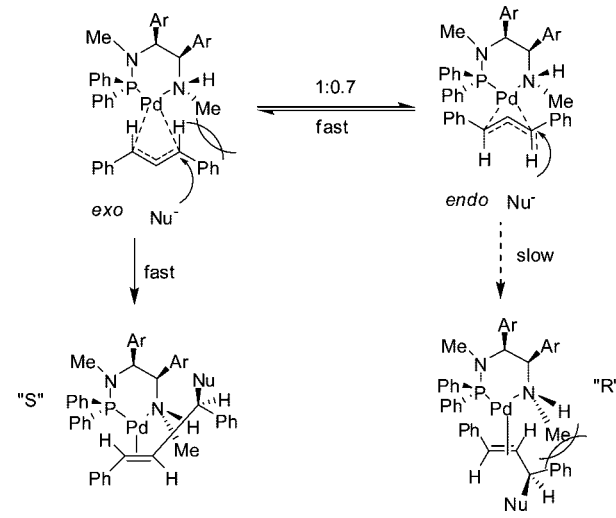

Figure 4. Proposed model for the Pd-catalyzed allylic alkylation of rac-1,3-diphenyl-3-acetoxyprop-1-ene using ligands **B**.

bond character of the Pd−C3 bond and an η^2 bond between Pd and C4−C5, confirming that the reaction pathway can be rationalized by a nucleophilic addition trans to phosphorus.

Although the X-ray structure of [Pd(*l*-**B**)(1,3-diphenylpropenyl)](SbF_6) corresponded only to the exo isomer of the π-allyl complex, as expected the ^{1}H and ^{31}P NMR spectra recorded in $CDCl_3$ showed a mixture of diastereomeric complexes ($\delta^{31}P$ = 73.1 and 80.9 ppm, respectively, in a 1:0.7 ratio) in rapid equilibrium, driven by the well-known fast isomerization of the palladium π-allyl between the exo and the endo species in solution.[43] According to data reported by Helmchen et al.,[44] the chemical shifts related to the three protons of the π-allyl in the major product could be assigned to the exo isomer. Moreover, crystals of Pd(*l*-**B**)(1,3-diphenylpropenyl)](SbF_6) were dissolved at −40 °C, and equilibration was followed by NMR by raising the temperature, thus confirming the presence of the exo species as the major isomer in solution.

Very similar to the case of the mixed phosphorus/sulfur ligands **V** and **VI** (Figure 1) reported by Evans et al.,[22] we can assume from the X-ray structure along with the NMR spectroscopic data, that the enantioselectivity observed for the reaction is the result of a Curtin−Hammett condition in which alkylation trans to phosphorus is faster in the major exo palladium π-allyl diastereoisomer, while allyl isomerization is fast, affording the palladium−olefin complex *S* (Figure 4).

In fact, nucleophilic addition results in the release of strain, which was initially present in the exo π-allyl complex because of nonbonding interactions between the methyl group on the nitrogen and the proximal phenyl substituent on the π-allyl moiety (Figure 4). On the contrary, in the endo π-allyl complex a steric strain is likely developed upon nucleophilic addition to form the palladium−olefin complex *R* (Figure 4).

We were not able to grow crystals of suitable quality for the X-ray structure determination of the π-allyl complexes prepared from ligands **E**. However, the ^{1}H and ^{31}P NMR spectra of [Pd(*l*-**E**)(1,3-diphenylpropenyl)](SbF_6) in $CDCl_3$ showed a 1:0.4:1.6:2.6 mixture of diastereomeric complexes ($\delta^{31}P$ = 91.1, 96.7, 98.2 and 103.2 ppm, respectively) in rapid equilibrium, consistent with a nitrogen inversion taking place, in addition to the fast endo/exo isomerization of the π-allyl moiety for both of the resulting stereoisomers. Because of the complexity of the ^{1}H NMR data, we were not able to determine the relative ratio of the two exo diastereomers, for comparison with the 20% ee observed for ligands **E**.

In conclusion, new enantiomerically pure mixed P,N ligands were prepared from the *N*,*N*′-dimethyl-1,2-diphenylethane-1,2-diamine backbone. When the nitrogen coordination center is a secondary amine, the stereochemistry of the backbone (1*R*, 2*S*-**B** versus 1*R*, 2*R*-**E**) strongly influences the control of the nitrogen stereochemistry during the formation of palladium complexes, in contrast to the situation observed for the mixed phosphorus/sulfur ligands **V** and **VI** (Figure 1). Our experimental data confirmed that the stereogenic nitrogen center in the different chelates was effectively controlled in the case of **B** in contrast to **E**, leading to excellent yields and enantioselectivities in the catalytic allylic alkylation of 1, 3-diphenylpropenyl acetate with dimethyl malonate. To date, investigation of the potential benefit of the formation of stereogenic centers at nitrogen on binding to metals has mainly focused on 1,2-diamines containing systems,[17−20] while its vicinity to the metal center might strongly influence the stereoinduction. However, in the case of mixed phosphine/alkylamine ligands, the presence of configurationally stable asymmetric nitrogen upon coordination was assumed,[21,45] although not demonstrated, and its role was not investigated in any detail. In our present system, a significant asymmetric induction enhancement was observed when the prochiral amine was locked into an enantiopure *N*-chiral form by palladium coordination. Indeed, additional data will be necessary to assess the importance of the *N*-chirality contribution to asymmetric induction, in the case of mixed N,P ligands.

Experimental Section

All experiments were done under argon atmosphere. THF, diethyl ether, and toluene were distilled from sodium/benzophenone. Dichloromethane was distilled from CaH_2. Other solvents and reagents were purchased from Aldrich and used without further

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purification. All NMR spectra were recorded on a AC-300 or AC-400 Bruker spectrometer. Chemical shifts were reported in ppm using the residual solvent signal of $CDCl_3$ (^1H spectra, 7.28 ppm; ^{13}C spectra, 77.23 ppm) or C_6D_6 (^1H spectra, 7.15 ppm; ^{13}C spectra, 128.6 ppm). ^{31}P NMR were taken using an internal capillary of H_3PO_4 (85% in deuterated water, 0 ppm) as reference. In reporting spectral data, the following abbreviations were used: *s* = singlet, *d* = doublet, *t* = triplet, *q* = quadruplet, *m* = multiplet, dd = doublet of doublet, and br *s* = broad singlet. Constants (*J*) are given in Hertz (Hz). High resolution (HRMS) and low resolution (MS) mass spectra were taken on a ZabSpec-TOF micromass instrument under ESI mode and are reported in *m*/*z* units. The elemental analyses were performed by Service Central d'Analyse (Vernaison, France). Optical rotation values were taken on a Perkin-Elmer 341 polarimeter (using a 10 cm cell). Flash chromatographies were performed using Kieselgel-60 silica gel (230−400 mesh, Merck). Thin layer (TLC) analyses were done with Merck silica gel F-254 aluminum-backed plates.

***d*,*l*-1,2-Bis-(4-bromophenyl)-*N*,*N*′-dimethyl-*N*-(diphenylthiophosphinyl)-ethane-1,2-diamine (5).** The *meso*-diamine **4** (3 g, 7.54 mmol) was dissolved in degassed distilled toluene (60 mL) under nitrogen. To this solution was added distilled triethylamine (4.5 mL, 31 mmol) followed, after stirring for 5 min, by dropwise addition of freshly distilled chlorodiphenylphosphine (3 mL; 16.7 mmol). The resulting mixture was stirred at room temperature for 30 min, and a suspension of sublimed sulfur powder (510 mg, 15.94 mmol) in toluene (45 mL) was transferred to the above solution under nitrogen, which was stirred for an additional 10 min. The reaction was quenched by the addition of water (15 mL) and saturated sodium hydrogenocarbonate solution (30 mL). The aqueous layer was separated and extracted with toluene. The organic layer was washed with saturated brine and dried over sodium sulfate. Toluene was removed under reduced pressure to yield a yellow oil that was allowed to stand in air overnight. The residue was taken up in dichloromethane and after filtration was purified by column chromatography on neutral alumina, eluting with petroleum ether/dichloromethane (50/50), and then slowly increasing the proportion of dichloromethane; 3.5 g of product was obtained (76% yield). ^1H NMR (300.1 MHz, $CDCl_3$): δ 1.56 (1H, br s, NH); 2.10 (3H, s, N-CH_3); 2.35 (3H, d, $^3J_{H\text{-}P}$ = 10.8 Hz, P-N-CH_3); 4.10 (1H, d, ^3J = 11.1 Hz, CH-N); 5.77 (1H, dd,$^3J_{H\text{-}P}$ = 12.3 Hz, ^3J = 11.1 Hz, CH-N-P); 7.00 (2H, m, H from PPh_2 α to C-P); 7.20 (6H, m, H from PPh_2 α to C-P + H from PPh_2 β to C-P); 7.35 (4H, m, H from $(C_6H_4)_2$ α to C-CH-N); 7.45 (2H, m, H from PPh_2 en γ de C-P); 7.49 (4H, d, H from $(C_6H_4)_2$ α to C-Br).^{13}C NMR (75.5 MHz, $CDCl_3$): δ 30.7 (P-N-CH_3, $^2J_{C\text{-}P}$ = 3.7 Hz); 34.5 (N-CH_3); 60.4 (CH-N-P, $^2J_{C\text{-}P}$ = 6.2 Hz); 64.5 (N-CH, $^3J_{C\text{-}P}$ = 8.5 Hz); 121.7 (C-Br); 122.0 (C-Br); 128.0 (CH from PPh_2 β to C-P, $^3J_{C\text{-}P}$ = 3.7 Hz); 128.1 (CH from PPh_2 β to C-P, $^3J_{C\text{-}P}$ = 3.7 Hz); 130.6 (CH from (C_6H_4) α to C-CH-N); 130.7 (CH from (C_6H_4) α to C-CH-N); 131.1 (CH from (C_6H_4) α to C-Br); 131.5 (CH from PPh_2 α to C-P); 131.6 (CH from PPh_2 γ to C-P, $^4J_{C\text{-}P}$ = 2.0 Hz); 131.7 (CH from PPh_2 γ to C-P, $^4J_{C\text{-}P}$ = 2.1 Hz); 132.4 (C from PPh_2, α to P, $^1J_{C\text{-}P}$ = 49.0 Hz); 133.8 (C from PPh_2, α to P, $^1J_{C\text{-}P}$ = 48.4 Hz); 136.9 (C from C-CH-N); 139.6 (C from C-CH-N).^{31}P NMR (121.5 MHz, $CDCl_3$): δ 69.3. MS-CI+ = 615 [MH^+], 416, 200. Elemental analysis calculated for $C_{28}H_{27}Br_2N_2PS$: C 54.74%, H 4.43%, N 4.56%, P 5.04%; found: C 55.26%, H 4.45%, N 4.63%, P 5.18%.

Optical Resolution of 5. A mixture of *d*,*l*-**5** (2.84 g, 4.52 mmol) and 76 mL of 97% ethanol was refluxed until complete dissolution. Meanwhile D-tartaric acid (684 mg, 4.62 mmol) was dissolved in boiling water (76 mL) and added to the above solution, and the resulting mixture was refluxed for 45 min. The reaction mixture was then allowed to cool at room temperature and then stirred for 1 h, while precipitation of a salt was observed. This salt was collected by filtration and washed with cold 48% ethanol (3 × 50 mL). This salt was suspended in distilled water (25 mL), and aqueous 50% (w/w) sodium hydroxide (370 μL) was added, followed by dichloromethane (25 mL). After stirring for 1 h, the phases were separated, and the aqueous phase was extracted using dichloromethane (3 × 20 mL). The combined organic phases were washed with saturated brine (35 mL), dried over sodium sulfate, and evaporated. This treatment was repeated once to obtain the *l* form of compound **5** (1.07 g, ee >98% [HPLC], yield of the separation 75%) as a white powder. $[\alpha]_D^{20}$ = −71.3 (*c* = 1 in CH_2Cl_2); mp 83 °C. The two combined mother liquors obtained above were concentrated under vacuum, and the residue was stirred with distilled water (25 mL) and aqueous 50% (w/w) sodium hydroxide (370 μL), followed by dichloromethane (70 mL). After stirring for 1 h, the phases were separated, and the aqueous phase was extracted using dichloromethane (3 × 25 mL). The combined organic phases were washed with saturated brine (35 mL), dried over sodium sulfate, and evaporated. The resulting crude mixture was treated once with L-tartaric acid, using a procedure identical to that described for the preparation of *l*-**5**. *d*-**5** (1.29 g, ee >97%, yield of the separation 90%) was finally obtained as a white powder. $[\alpha]_D^{20}$ = 70.9 (*c* = 1 in CH_2Cl_2); mp 91 °C. HPLC (Chiracel AD-H column, flow, 0.5 mL min^{-1}; solvent, hexane/i-propanol [95/5]; detection, 254 nm) retention times: *d*-**5** [69 min], *l*-**5** [52 min].

***d* or *l*-1,2-Bis-(4-bromophenyl)-*N*-methyl-*N*-(diphenylthiophosphinyl)-*N*′,*N*′-dimethyl-ethane-1,2-diamine (6).** Compound **5** (802 mg, 1.31 mmol) was suspended in 99% formic acid (3 mL, 79.7 mmol). Then, 37% formaldehyde aqueous solution (1.38 mL, 49.9 mmol) was added, and the reaction mixture was heated at 80 °C for 4 h. The formic acid and formaldehyde were removed under reduced pressure, and the residue was taken up in dichloromethane (50 mL). The organic phase was stirred with 6 M aqueous potassium hydroxide (50 mL). After 15 min, the phases were separated, and the aqueous phase was extracted using dichloromethane (3 × 30 mL). The combined organic layers were washed with saturated brine (50 mL), dried over sodium sulfate, and evaporated under reduced pressure; 778 mg of product was obtained (95% yield). ^1H NMR (300.1 MHz, $CDCl_3$): δ 2.06 (6H, s, N-$(CH_3)_2$); 2.21 (3H, d, $^3J_{H\text{-}P}$ = 10.5 Hz, P-N-CH_3); 4.24 (1H, d, ^3J = 12 Hz, CH-N); 6.42 (1H, dd,$^3J_{H\text{-}P}$ = 12 Hz, ^3J = 12 Hz, CH-N-P); 6.91 (2H, dd, $^3J_{H\text{-}P}$ = 13.5 Hz, ^3J = 8.4 Hz, H from PPh_2 α to C-P); 7.17 (6H, m, H from PPh_2 β to C-P); 7.33 (4H, m, H from PPh_2); 7.42 (2H, d, ^3J = 8.4 Hz, H from $(C_6H_4)_2$ α to C-Br); 7.44 (2H, d, ^3J = 8.4 Hz, H from $(C_6H_4)_2$ α to C-Br); 7.55 (2H, d, ^3J = 8.4 Hz, H from $(C_6H_4)_2$ α to C-CH-N).^{13}C NMR (100.6 MHz, $CDCl_3$): δ 30.5 (P-N-CH_3); 40.6 (N-$(CH_3)_2$); 55.2 (CH-N-P, $^2J_{C\text{-}P}$ = 5.9 Hz); 67.0 (N-CH, $^3J_{C\text{-}P}$ = 7.6 Hz); 121.1 (C-Br); 121.6 (C-Br); 127.9 (CH from PPh_2 β to C-P, $^3J_{C\text{-}P}$ = 4.9 Hz); 128.0 (CH from PPh_2 β to C-P, $^3J_{C\text{-}P}$ = 3.6 Hz); 130.7 (CH from (C_6H_4) α to C-CH-N); 131.0 (CH from (C_6H_4) α to C-CH-N); 131.0 (CH from (C_6H_4) α to C-Br); 131.1 (aromatic); 131.2 (CH from PPh_2 α to C-P, $^2J_{C\text{-}P}$ = 14.7 Hz); 131,4 (CH from PPh_2 α to C-P, $^2J_{C\text{-}P}$ = 14.2 Hz); 131.8 (C from C-CH-N-P); 131.9 (CH from PPh_2 γ to C-P); 132.9 (C from PPh_2 α to P, $^1J_{C\text{-}P}$ = 39.1 Hz); 134.2 (C from PPh_2 α to P, $^1J_{C\text{-}P}$ = 26.6 Hz); 137.4 (C from C-CH-N).^{31}P NMR (121.5 MHz, $CDCl_3$): δ 69.8. Elemental analysis calculated for $C_{29}H_{29}Br_2N_2PS$: C 55.43%, H 4.65%, N 4.46%, P 4.93%; found: C 55.69%, H 4.71%, N 4.60%, P 5.03%. *d*-6 ee >97%, $[\alpha]_D^{20}$ = 74.9 (*c* = 1 in CH_2Cl_2); mp 207 °C. *l*-6 ee >98%, $[\alpha]_D^{20}$ = −73.6 (*c* = 1 in CH_2Cl_2); mp 206 °C. HPLC (Chiracel AD-H column, flow, 0.5 mL min^{-1}; solvent, hexane/*i*-propanol [95/5]; detection, 254 nm) retention times: *d*-**6** [17.4 min], *l*-**6** [18.5 min].

Monochlorhydrate Form of Compound 6 (7). Compound **6** (600 mg, 0.95 mmol) was dissolved in THF (18 mL), and *circa* 5 drops of 37% hydrochloric acid were added to this solution. After stirring at room temperature for 1 h, the white salt that formed was filtered off, then taken up in dichloromethane. The organic solution was dried over sodium sulfate and evaporated to dryness to yield **7** as a white powder (608 mg, 98% yield). ^1H NMR (300.1 MHz, $CDCl_3$): δ 2.33 (3H, d, $^3J_{H\text{-}P}$ = 10.5 Hz, P-N-CH_3); 2.40

(1H, m, NH); 2.73 (6H, s, N-$(CH_3)_2$); 6.10 (1H, m, CH-N); 6,71 (1H, dd,$^3J_{H\text{-}P}$ = 12 Hz, ^3J = 12 Hz, CH-N-P); 6.81 (2H, dd, $^3J_{H\text{-}P}$ = 13.5 Hz, s^3J = 7.3 Hz, H from PPh_2 α to C-P); 7.07 (2H, dd, $^3J_{H\text{-}P}$ = 13.5 Hz, ^3J = 7.3 Hz, H from PPh_2 α to C-P); 7.17−7.19 (4H, m, H from PPh_2 β to C-P); 7.32 and 7.40 (2H, 2dd, ^3J = 7.5 Hz, ^4J = 7.3 Hz, H from PPh_2 γ to C-P); 7.53 (4H, d, ^3J = 8.4 Hz, H from $(C_6H_4)_2$ α to C-CH-N); 7.88 (4H, 2d, ^3J = 8.4 Hz, H from $(C_6H_4)_2$ α to C-Br) ^{31}P NMR (121.5 MHz, $CDCl_3$): δ 71.1. The Br/P/S/Cl ratio measured by energy dispersive X-ray spectroscopy (EDXS) gave the 2/1/1/1 expected value.

***d* or *l*-1,2-Bis-(4-bromophenyl)-*N*-methyl-*N*-(diphenylthiophosphinyl)-*N′*-isopropyl-*N′*-methyl-ethane-1,2-diamine (8).** Compound **5** (200 mg, 0.32 mmol) was dissolved in a mixture of methanol (6 mL). Then, acetone (2 mL), acetic acid (37 μL, 0.64 mmol), sodium cyanoborohydride (80 mg, 1.28 mmol), and KSF (200 mg) were added under argon. The reaction medium was stirred at room temperature for 72 h. A white precipitate formed, and acetone (2 mL), acetic acid (37 μL), sodium cyanoborohydride (80 mg), and KSF (200 mg) were again added, and the mixture was stirred for an additional day. Then dichloromethane (15 mL) and distilled water (15 mL) were added. The aqueous phase was then extracted using dichloromethane (3 × 15 mL). The combined organic phases were then washed with saturated brine, dried over sodium sulfate, filtrated, and concentrated under reduced pressure. The residue was then purified by column chromatography on silica, eluting with ethyl acetate/dichloromethane (2/98) to yield **8** in 65% yield (138 mg). ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 0.55 (3H, d, $^3J_{H\text{-}H}$ = 6.5 Hz, CH_3-C), 0.73 (3H, d,$^3J_{H\text{-}H}$ = 6,5 Hz, CH_3-C), 2.05 (3H, s, N-CH_3), 2.24 (3H, d, $^3J_{H\text{-}P}$ = 10.4 Hz, P-N-CH_3), 2.98 (1H, sept, $^3J_{H-H}$= 6.5 Hz, C<u>H</u>$(CH_3)_2$), 4.39 (1H, d, $^3J_{H\text{-}H}$ = 11,9 Hz, CH-N), 6.42 (1H, dd,$^3J_{H\text{-}P}$ = 12.4 Hz, ^3J = 12.4 Hz, CH-N-P), 6.9 (2H, m, aromatic), 7.2 (6H, m, aromatic), 7.32(2H, m, aromatic), 7.4 (6H, m, aromatic), 7.52 ((2H, m, aromatic).^{13}C NMR (100.6 MHz, $CDCl_3$): δ 19.1 (CH_3-C-N), 20.6 (CH_3-C-N), 29.5 (CH_3-N), 30.4 (P-N-CH_3,$^2J_{C\text{-}P}$ = 3.7 Hz), 53.0 (N-<u>C</u>HMe$_2$), 55.8 (CH-N-P, $^2J_{C\text{-}P}$ = 6 Hz), 66.2 (CH-N-*i*Pr, $^3J_{C\text{-}P}$ = 8 Hz), 120.7 (C-Br), 121.2 (C-Br), 127.8 ($^3J_{C\text{-}P}$ = 5 Hz), 127.9 ($^3J_{C\text{-}P}$ = 4 Hz), 130.6, 130.9, 131.1, 131.2 ($^2J_{C\text{-}P}$ = 15.7 Hz), 131.2, 131.4 ($^2J_{C\text{-}P}$ = 14.7 Hz), 132.8 (C-P, $^1J_{C\text{-}P}$ = 41.6 Hz,), 134.1 (C-P, $^1J_{C\text{-}P}$ = 29.2 Hz,), 136.2 (<u>C</u>-CH-N), 137.8 (<u>C</u>-CH-N). ^{31}P NMR (121.5 MHz, $CDCl_3$): δ 70.0. HRMS (CI+) calculated for $C_{31}H_{34}Br_2N_2PS$ (MH^+): m/z = 655.0547, found m/z = 655.0544. *d*-8 ee >96%, $[\alpha]_D^{20}$ = 62.8 (c = 1 in CH_2Cl_2); mp 202 °C. *l*-8 ee >96%, $[\alpha]_D^{20}$ = −62.8 (c = 1 in CH_2Cl_2); mp 205 °C. HPLC (Chiracel AD-H column, flow, 0.5 mL min^{-1}; solvent, hexane/i-propanol [98/2]; detection, 254 nm) retention times: *d*-**8** [15.0 min], *l*-**8** [13.6 min].

***d* or *l*-1,2-Bis-(4-bromophenyl)-*N*-methyl-*N*-(diphenylthiophosphinyl)-*N′*-benzyl-*N′*-methyl-ethane-1,2-diamine (9).** Compound **5** (200 mg, 0.32 mmol) was dissolved in a mixture of methanol (8 mL), acetic acid (78.5 μL, 1.31 mmol), and benzaldehyde (200 μL, 1.96 mmol), under argon. The reaction medium was stirred at room temperature for 1 h and sodium cyanoborohydride (82 mg, 1.30 mmol) was added. A white precipitate formed while the mixture was stirred for two additional hours. The precipitate was filtered, rinsed with methanol, and dissolved in dichloromethane. The organic phase was then dried over sodium sulfate, filtrated, and concentrated under reduced pressure to yield **9** in 85% yield (205 mg). ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 1.94 (3H, s, N-CH_3); 2.15 (3H, d, $^3J_{H\text{-}P}$ = 10.2 Hz, P-N-CH_3); 3.12 and 3.46 (2H, d,^3J = 13.2 Hz, CH_2−N); 4.29 (1H, d,^3J = 12 Hz, CH-N); 6.47 (1H, dd,$^3J_{H\text{-}P}$ = 12 Hz, ^3J = 12 Hz, CH-N-P); 6.77−7.45 (23H, m, aromatic). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 30.5 (P-N-CH_3), 37.2 (CH_3-N), 55.5 (CH-N-P, $^2J_{C\text{-}P}$ = 7 Hz), 57.9 (N-<u>C</u>H_2Ph), 66.0 (CH-N-Bn, $^3J_{C\text{-}P}$ = 8.6 Hz), 121.1 (C-Br), 121.7 (C-Br), 126.9, 127.9 ($^3J_{C\text{-}P}$ = 3.7 Hz), 128.1, 128.1 ($^3J_{C\text{-}P}$ = 2.8 Hz), 128.7, 130.9, 131.0, 131.1 ($^2J_{C\text{-}P}$ = 17.5 Hz), 131.2, 131.3, 131.4 ($^2J_{C\text{-}P}$ = 15.3 Hz), 131.8, 132.8 (C-P, $^1J_{C\text{-}P}$ = 42.3 Hz), 132.85, 134.1 (C-P, $^1J_{H\text{-}P}$ = 30.1 Hz,), 137.3 (<u>C</u>-CH-N), 138.9 (<u>C</u>-CH-N).^{31}P NMR (121.5 MHz, $CDCl_3$): δ 70.2. HRMS (CI+) calculated for $C_{35}H_{34}Br_2N_2PS$ (MH^+): m/z = 703.0547, found m/z = 703.0546. *d*-9 ee >98%, $[\alpha]_D^{20}$ = 41.5 (c = 1 in CH_2Cl_2); mp 188 °C. *l*-9 ee >99%, $[\alpha]_D^{20}$ = −41.3 (c = 1 in CH_2Cl_2); mp 186 °C. HPLC (Chiracel AD-H column, flow, 0.5 mL min^{-1}; solvent, hexane/i-propanol [95/5]; detection, 254 nm) retention times: *d*-**9** [20.2 min], *l*-**9** [12.6 min].

***d* or *l*-1,2-Bis-(4-bromophenyl)-*N*-methyl-*N*-(diphenylphosphino)-*N′*,*N′*-dimethyl-ethane-1,2-diamine (A).** Compound **7** (613 mg, 0.92 mmol) was dissolved in dry dichloromethane (60 mL) under an inert atmosphere, and the solution was warmed at 40 °C and then brought back to room temperature. To this reaction mixture, methyl triflate (209 μL, 1.85 mmol) was added in one portion, and the resulting solution was stirred at room temperature for 24 h. Then the solvent was removed under reduced pressure, and the residue was dissolved in degassed dichloromethane (20 mL) under inert atmosphere. Then HMPT was added (324 μL, 1.85 mmol), and the reaction medium was stirred at room temperature for 1 h. The solvent was removed under reduced pressure to yield a semisolid that was purified by column chromatography on silica gel eluting with dichloromethane; 492 mg of aminophosphine **A** was obtained (89% yield). ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 2.03 (6H, s, N-$(CH_3)_2$); 2.13 (3H, d, $^3J_{H\text{-}P}$ = 2.70 Hz, P-N-CH_3); 4.36 (1H, dd, ^3J = 12 Hz, $^4J_{H\text{-}P}$ = 0.9 Hz, CH-N); 4.74 (1H, dd,$^3J_{H\text{-}P}$ = 12 Hz, ^3J = 12 Hz, CH-N-P); 6.53 (2H, dd, $^3J_{H\text{-}P}$ = 7.2 Hz, ^3J = 7.2 Hz, H from PPh_2 α to C-P); 6.75 (2H, dd,$^3J_{H\text{-}P}$ = 7.2 Hz, ^3J = 7.2 Hz, H from PPh_2 α to C-P); 7.07−7.11 (6H, m, 4H from PPh_2 β to C-P + 2H from $(C_6H_4)_2$); 7.19 (2H, H from PPh_2 γ to C-P); 7.34 (2H, d, ^3J = 8.4 Hz, H from $(C_6H_4)_2$ α to C-Br); 7.46 (4H, m, H from $(C_6H_4)_2$ α to C-Br).^{13}C NMR (100.6 MHz, $CDCl_3$): δ 32.8 (P-N-CH_3, $^2J_{C-P}$ = 12.6 Hz); 40.6 (N-$(CH_3)_2$); 67,8 (N-CH, $^3J_{C\text{-}P}$ = 16 Hz); 68.5 (CH-N-P, $^3J_{C\text{-}P}$ = 47 Hz); 121.0 (C-Br); 121.3 (C-Br); 127.7 (CH from PPh_2); 128.1 (CH from PPh_2, $^2J_{C\text{-}P}$ = 7.6 Hz); 129.9; 131.0; 131.1; 131.4; 131.6; 131.8; 133.1; 138.2; 138.3; 138.4; 139.0.^{31}P NMR (121.5 MHz, $CDCl_3$): δ 62.9. Elemental analysis calculated for $C_{29}H_{29}Br_2N_2P$: C 58.41%, H 4.90%, N 4.70%, P 5.19%, Br 26.80%; found: C 57.72%, H 4.76%, N 4.72%, P 5.34%, Br 26.89%. *d*-A ee >97%, $[\alpha]_D^{20}$ = 45.7 (c = 1 in CH_2Cl_2); mp 62 °C. *l*-A ee >98%, $[\alpha]_D^{20}$ = −49.3 (c = 1 in CH_2Cl_2); mp 63 °C. HPLC (Chiracel AD-H column, flow, 0.5 mL min^{-1}; solvent, hexane/i-propanol [95/5]; detection, 254 nm) retention times: *d*-**A** [8.5 min], *l*-**A** [9.1 min].

***d* or *l*-1,2-Bis-(4-bromophenyl)-*N*-methyl-*N*-(diphenylphosphino)-*N′*-methyl-ethane-1,2-diamine (B).** Treatment of compound *d*-**5** or *l*-**5**, as described for the preparation of **A**, afforded ligand **B** as a white powder with a 83% yield. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 2.05 (3H, s, N-CH_3); 2.12 (3H, d, $^3J_{H\text{-}P}$ = 6.9 Hz, P-N-CH_3); 4.11 (1H, d, ^3J = 10.8 Hz, CH-N); 4.43 (1H, dd,$^3J_{H\text{-}P}$ = 10.8 Hz, ^3J = 10.8 Hz, CH-N-P); 6.52 (2H, m, aromatic); 6.69 (2H, m, aromatic); 7.00−7.20 (6H, m, aromatic); 7.26 (4H, m, aromatic); 7.35 (2H, m, aromatic), 7.42 (2H, m, aromatic).^{13}C NMR (100.6 MHz, $CDCl_3$): δ 32.9 (P-N-CH_3, $^2J_{C\text{-}P}$ = 12.9 Hz); 34.5 (N-CH_3); 65.3 (CH-NH, $^3J_{C\text{-}P}$ = 13.8 Hz), 73.8 (CH-N-P, $^2J_{C\text{-}P}$ = 47.6 Hz); 121.3 (C-Br); 121.7 (C-Br); 127.7 (CH, $^3J_{C\text{-}P}$ = 8 Hz); 127.8 (CH, $^3J_{C\text{-}P}$ = 8 Hz); 128.0, 128.25, 130.0, 130.4, 131.5 ($^2J_{C\text{-}P}$ = 26.5 Hz), 131.65, 131.7, 132.0 ($^2J_{C\text{-}P}$ = 26.5 Hz), 138.25 (C-P, $^1J_{C\text{-}P}$ = 63 Hz); 138.35 (C-P, $^1J_{C\text{-}P}$ = 63 Hz); 138.5 (<u>C</u>-CH-N); 140.5 (<u>C</u>-CH-N).^{31}P NMR (121.5 MHz, $CDCl_3$): δ 64.4. HRMS (CI+) calculated for $C_{28}H_{28}Br_2N_2P$ (MH^+): m/z = 581.0357, found m/z = 581.0356. *d*-B ee >99%, $[\alpha]_D^{20}$ = 10.0 (c = 1 in CH_2Cl_2); mp 132 °C. *l*-B ee >99%, $[\alpha]_D^{20}$ = −10.0 (c = 1 in CH_2Cl_2); mp 132 °C. HPLC (Chiracel AD-H column, flow, 0.5 mL min^{-1}; solvent, hexane/i-propanol [85/15]; detection, 254 nm) retention times: *d*-**B** [19.5 min], *l*-**B** [12.5 min].

***d* or *l*-1,2-Bis-(4-bromophenyl)-*N*-methyl-*N*-(diphenylphosphino)-*N′*-isopropyl-*N′*-methyl-ethane-1,2-diamine (C).** Treatment of compound *d*-**8** or *l*-**8**, as described for the preparation of

A, afforded ligand **C** as a white powder with a 83% yield. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 0.5 (3H, d, $^3J_{H\text{-}H}$ = 6.5 Hz, CH_3-C), 0.65 (3H, d, $^3J_{H\text{-}H}$ = 6,5 Hz, CH_3-C), 1.93 (3H, s, N-CH_3), 2.08 (3H, d, $^3J_{H\text{-}P}$ = 2.4 Hz, P-N-CH_3), 2.86 (1H, sept, $^3J_{H\text{-}H}$ = 6.5 Hz, C$\underline{H}$(CH_3)$_2$), 4.45 (1H, d, $^3J_{H\text{-}H}$ = 11,7 Hz, CH-N), 4.76 (1H, dd, $^3J_{H\text{-}P}$ = 12 Hz, ^3J = 12 Hz, CH-N-P), 6.47 (2H, m, aromatic), 6.68 (2H, m, aromatic), 7.04 (6H, m, aromatic), 7.18 (2H, m, aromatic), 7.23 (2H, m, aromatic), 7.35 (4H, m, aromatic). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 19.3 (CH_3-C-N), 20.7 (CH_3-C-N), 29.6 (CH_3-N), 33.0 (P-N-CH_3), 53.0 (N-C$\underline{H}$$Me_2$), 66.8 (CH-N-*i*Pr, $^3J_{C\text{-}P}$ = 16 Hz), 69.2 (CH-N-P, $^2J_{C\text{-}P}$ = 46 Hz), 120.5 (C-Br), 120.9 (C-Br), 127.6 ($^3J_{C\text{-}P}$ = 5 Hz), 127.8 ($^3J_{C\text{-}P}$ = 5 Hz), 128.0 ($J_{C\text{-}P}$ = 2 Hz), 130.3, 130.7, 130.9, 131.3, 131.5 ($^2J_{C\text{-}P}$ = 26 Hz), 131.7 ($^2J_{C\text{-}P}$ = 26 Hz), 137.9 (C-P, $^1J_{C\text{-}P}$ = 81.7 Hz,), 138.3 (C-CH-N), 139.1 (C-P, $^1J_{C\text{-}P}$ = 88.5 Hz,), 139. Five (C-CH-N).^{31}P NMR (121.5 MHz, $CDCl_3$): δ 63.0. HRMS (CI+) calculated for $C_{31}H_{34}Br_2N_2P$ (MH^+): *m*/*z* = 623.0827, found *m*/*z* = 623.0825. *d*-C ee >98%, $[\alpha]_D^{20}$ = 30.3 (*c* = 1 in CH_2Cl_2); mp 158 °C. *l*-C ee >99%, $[\alpha]_D^{20}$ = −29.1 (*c* = 1 in CH_2Cl_2); mp 157 °C. HPLC (Chiracel AD-H column, flow, 0.5 mL min $^{-1}$; solvent, hexane/i-propanol [98/2]; detection, 254 nm) retention times: *d*-**C** [8.1 min], *l*-**C** [8.9 min].

***d* or *l*-1,2-Bis-(4-bromophenyl)-*N*-methyl-*N*-(diphenylphosphino)-*N′*-benzyl-*N′*-methyl-ethane-1,2-diamine (D).** Treatment of compound *d*-**9** or *l*-**9**, as described for the preparation of **A**, afforded ligand **D** as a white powder with an 89% yield. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 1.87 (3H, s, N-CH_3); 2.08 (3H, d, $^3J_{H\text{-}P}$ = 2.4 Hz, P-N-CH_3); 3.14 and 3.38 (2H, d,^3J = 13.2 Hz, CH_2-N); 4.43 (1H, d,^3J = 12 Hz, CH-N); 4.85 (1H, dd,$^3J_{H\text{-}P}$ = 12 Hz, ^3J = 12 Hz, CH-N-P); 6.50 (2H, m, aromatic), 6.71 (4H, m, aromatic), 6.96- 7.28 (13H, m, aromatic), 7.42 (4H, m, aromatic). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 30.3 (P-N-CH_3), 37.0 (CH_3-N), 58.0 (N-C$\underline{H}_2$Ph), 67.0 (CH-N-P, $^2J_{C\text{-}P}$ = 16.9 Hz), 68.9 (CH-N-Bn, $^3J_{C\text{-}P}$ = 47.8 Hz), 120.9 (C-Br), 121.3 (C-Br), 126.9, 127.65, 127.7, 127.8, 128.05, 128.1, 128.6, 130.5, 130.9, 131.3, 131.35, 131.6 ($^2J_{C\text{-}P}$ = 26 Hz), 131.7 ($^2J_{C\text{-}P}$ = 26 Hz), 134.1, 138.2, 138.3, 138.7 (C-P, $^1J_{C\text{-}P}$ = 67.3 Hz), 138.8 (C-P, $^1J_{C\text{-}P}$ = 54.1 Hz,), 139.0.^{31}P NMR (121.5 MHz, $CDCl_3$): δ 63.0. HRMS (ESI+) calculated for $C_{35}H_{34}Br_2N_2P$ (MH^+): *m*/*z* = 671.0826, found *m*/*z* = 671.0822. *d*-D ee >98%, $[\alpha]_D^{20}$ = 16.3 (*c* = 1 in CH_2Cl_2); mp 159 °C. *l*-D ee >99%, $[\alpha]_D^{20}$ = −15.5 (*c* = 1 in CH_2Cl_2); mp 161 °C. HPLC (Chiracel AD-H column, flow, 0.5 mL min $^{-1}$; solvent, hexane/i-propanol [98/2]; detection, 254 nm) retention times: *d*-**D** [13.7 min], *l*-**D** [30.2 min].

[*l*-1,2-Bis-(4-bromophenyl)-*N*-methyl-*N*-(diphenylphosphino)-*N′*-methyl-ethane-1,2-diamine] palladium(II) dichloride. Compound *l*-(**B**) (23 mg, 0.023 mmol) was dissolved in CH_2Cl_2 (1 mL), and $(MeCN)_2PdCl_2$ (5.75 mg, 0.0220 mmol) was added. After stirring at room temperature for 1 h, the solution was concentrated under vacuum and diluted in CH_2Cl_2 (0.5 mL), and then Et_2O (5 mL) was added rapidly while stirring to precipitate (*l*-**B**)$PdCl_2$ as a yellow powder, which was filtrated and dried under vacuum overnight; 16.8 mg of product were obtained (97% yield). ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 2.48 (3H, d, $^3J_{H\text{-}P}$ = 6.4 Hz, P-N-CH_3); 2.65 (3H, d, *J* = 5.55 Hz, N-CH_3); 3.78 (1H, m, N-H); 4.18−4.25 (2H, m, CH-N, CH-N-P); 6.66 (2H, d, *J* = 8.30 Hz aromatic); 7.34−7.44 (7H, m, aromatic); 7.66 (2H, d, *J* = 8.30 Hz, aromatic); 7.73 (3H, m, aromatic); 7.94 (2H, d, *J* = 8.20 Hz, aromatic), 8.10−8.17 (2H, m, aromatic). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 40.9; 41.7; 70.4; 72.3; 128.4 (2C); 128,6(2C); 129.0(2C); 129.8(2C); 129.9(2C); 131.1(2C); 131.9 (2C); 132.1(2C); 132.3 (2C); 132.4 (2C); 132.8; 133.2; 133.3 134.9; ^{31}P NMR (121.5 MHz, $CDCl_3$): δ 71.6. $[\alpha]_D^{20}$ = −32.2 (*c* = 0.33 in $CHCl_3$); mp (decomposition): 245 C HRMS (ESI+) calculated for $C_{28}H_{27}Br_2Cl_2N_2PdPNa$ (MNa^+): *m*/*z* = 782.8563, found *m*/*z* = 782.8505. X-ray quality crystals were grown by slow vapor diffusion of Et_2O into a solution of *l*-(**B**)$PdCl_2$ in CH_2Cl_2 to yield yellow prisms.

[*l*-1,2-Bis-(4-bromophenyl)-*N*-methyl-*N*-(diphenylphosphino)-*N′*-methyl-ethane-1,2-diamine] palladium (1,3-diphenylpropenyl)hexafluoroantimonate. Compound *l*-(**B**) (46 mg, 0.046 mmol) was dissolved in CH_2Cl_2 (1 mL), and [(1,3-diphenylpropenyl)$PdCl]_2$ (14.8 mg, 0.022 mmol) was added. After stirring at room temperature for 1 h, the solution was transferred by cannula into a flask containing $AgSbF_6$ (15.9 mg, 0.046 mmol) and stirred for one more hour in the dark. The reaction was transferred and filtered by cannula into a flask and concentrated under reduced pressure to yield a 1:0.7 mixture of diastereomeric π-allyl complexes, as an orange powder; 46.2 mg of product were obtained (90% yield). Major isomer. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 1.54 (3H, d, *J* = 4.8 Hz, C−N−CH_3); 1.91 (1H, m, C−N−H); 2.47 (3H, d, *J* = 6.1 Hz, P-N-CH_3); 4.18−4.25 (2H, m, CH-N, CH-N-P); 4.49 (1H, d, *J* = 11.1 Hz, P-CH-Pd); 5.99 (1H, dd, *J* = 9.3, 3.9 Hz, N-CH-Pd); 6.35 (2H, d, *J* = 8.1 Hz, aromatic); 6.67 (1H, t, *J* = 12.9 Hz, N−C−CH−C-P); 6.28−7.99 (26H, m, aromatic). ^{31}P NMR (121.5 MHz, $CDCl_3$): δ 73.1 (s). Minor isomer. ^{1}H NMR (300.1 MHz, $CDCl_3$) δ 1.30 (1H, m, C−N−H); 2.27 (3H, d, *J* = 5.54 Hz, C−N−CH_3); 2.55 (3H, d, *J* = 5.4 Hz, P-N-CH_3); 4.18−4.25 (2H, m, CH-N, CH-N-P); 5.25 (1H, d, *J* = 12 Hz, P-CH-Pd); 5.32 (1H, t, *J* = 10.8 Hz, N-CH-Pd); 6.23 (2H, d, *J* = 8.1 Hz, aromatic); 6.50 (2H, m, N−C−CH−C-P, aromatic); 6.28−7.99 (26H, m, aromatic).^{31}P NMR (121.5 MHz, $CDCl_3$): δ 80.9 (s). HRMS (ESI+) calculated for $C_{43}H_{40}Br_2N_2PdP$ (M^+): *m*/*z* = 881.0326, found *m*/*z* = 881.0323. $[\alpha]_D^{20}$ = 35.0 (*c* = 0.08 in $CHCl_3$); mp (decomposition), 237 °C. X-ray quality crystals were grown by slow vapor diffusion of Et_2O into a solution of the mixture of diastereomers in CH_2Cl_2 to yield orange prisms.

Asymmetric Allylic Alkylation of rac-(E)-1,3-Diphenyl-3-acetoxyprop-1-ene with Dimethyl Malonate: (*S*,*E*)-Methyl 2-carbomethoxy-3,5-diphenylpent-4-enoate. The desired ligand (0.019 mmol) was dissolved in degassed distilled CH_2Cl_2 (2 mL) under argon. To this solution, $[Pd(\pi\text{-}C_3H_5)Cl]_2$ (3.7 mg, 0.010 mmol) was added, and the mixture was stirred at room temperature for 30 min. Then, *rac*-1,3-diphenyl-3-acetoxyprop-1-ene (160 mg, 0.63 mmol) was added, followed by dimethyl malonate (210 μL, 1.84 mmol), *N*,*O*-Bis(trimethylsilyl)acetamide (444 μL, 1.82 mmol) and lithium acetate (5 mg, 0.075 mmol). After 12 h, the solution was washed with diluted HCl (0.1 M) and brine. The combined aqueous solutions were extracted with CH_2Cl_2. The combined organic solutions were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The yellow oil was purified by flash chromatography (petroleum ether/AcOEt, 85/15) to yield the desired compound as an oil (194 mg, 96%). ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 7.4−7.1 (m, 10H), 6.48 (d, 1H, *J* = 15.9 Hz), 6.33 (dd, 1H, *J* = 15.9, 8.5 Hz), 4.27 (dd, 1H, *J* = 10.9, 8.6 Hz), 3.95 (d, 1H, *J* = 10.9 Hz), 3.70 (s, 3H), 3.52 (s, 3H). HPLC (Chiracel OD-H column, flow, 0.5 mL min^{-1}; solvent, hexane/i-propanol [98/2]; detection, 254 nm) retention times: [10.2 min], [10.8 min]. Absolute stereochemistry of (*E*)-methyl 2-carbomethoxy-3,5-diphenylpent-4-enoate was determined by comparison of the optical rotation to literature values.[46]

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Supporting Information Available: Crystallographic data for *d*-**5**: L-(HO_2C-CHOH-CHOH-CO_2H): 3 H_2O, (*l*-**B**)$PdCl_2$, and [Pd(*l*-**B**)(1,3-diphenylpropenyl)](SbF_6) as a CIF file. This material is available free of charge via the Internet at http://pubs.acs.org.

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