Chiral 4-(Diphenylphosphanyl)-1-(dialkylamino)butane Ligands – Synthesis, Applications in Asymmetric Alkylation and Theoretical Study

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Various 4-(diphenylphosphanyl)-1-(dialkylamino)butane ligands were prepared from commercial (2*S*,3*S*)-2,3-*O*-isopropylidene-D-threitol. These ligands, associated with $Pd_2(dba)_3$, gave enantioselectivities of up to 75% in the alkylation of racemic 1,3-diphenylprop-2-enyl acetate with dimethyl malonate anion. A theoretical study shows the important role played by two factors in the alkylation reaction: steric control, leading to the formation of a unique diastereoisomer of the π-allylpalladium complex, and orbital control, which orients the attack of the nucleophile *trans* to the phosphorus atom.

Introduction

Asymmetric metal catalysis is one of the most powerful methods for the preparation of enantiomerically pure compounds.[1] An impressive number of chiral ligands have been prepared and used, among them P,P-, P,N- and N,N-based ligands. The phosphanyloxazolines, P,N-based ligands, induce high enantioselectivities, particularly in the palladium-catalyzed allylic substitution.[2] In comparison, P,N ligands with an sp^3 nitrogen atom have been used less in asymmetric catalysis. Hayashi et al. prepared chiral β-(aminoalkyl)phosphanes[3] and [(aminoalkyl)ferrocenyl]-phosphanes.[4] Chiral aminophosphanes, in which the chirality is on the substituents of the nitrogen atom through a pyrrolidine[5–6] or a naphthyl unit,[7] have also been described more recently. These ligands were successfully used in asymmetric hydrogenation, cross-coupling reactions and mainly allylic substitution.

We recently reported, in a preliminary communication, the synthesis of chiral aminophosphanes derived from tartaric acid and their use in asymmetric alkylation.[8] We describe in this paper a full account of the synthesis of these new chiral ligands and their use as ligands in asymmetric alkylation, as well as a theoretical study concerning the nucleophilic attack on π-allyl(palladium) complexes associated with these ligands.

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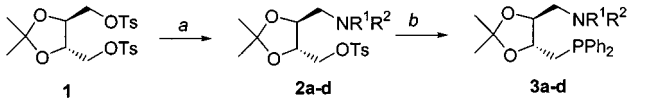
Results and Discussion

Synthesis of the P,N-Based Ligands

Ligands **3a**–**d**, bearing at least one aryl group at the nitrogen atom, were prepared from commercially readily available bis(tosylate) **1** (Scheme 1). Reaction of **1** at −17 °C in tetrahydrofuran with one equiv. of lithium diphenylamide, obtained by treating diphenylamine with *n*-butyllithium at −78 °C, gave diphenylamino tosylate **2a** in 26% yield. Subsequent treatment of compound **2a** with lithium diphenylphosphide in tetrahydrofuran led to the formation of the diphenylamino phosphane **3a** in 40% yield. Steric and electronic modifications of the substituents at the nitrogen atom were introduced with methyl(phenyl)-, *p*-methoxyphenyl(methyl)- and phenyl(α-naphthyl)amine instead of diphenylamine; the corresponding amino phosphanes **3b**, **3c**, and **3d** were obtained in 18%, 7%, and 21% yield, respectively, from compound **1**. All attempts to introduce the *p*-nitrophenyl(methyl)amino group failed, only the elimination product was observed.



a : $R^1 = R^2 = C_6H_5$; **b** : $R^1 = C_6H_5$, $R^2 = CH_3$; **c** : $R^1 = C_6H_4$-*p*-OCH_3, $R^2 = CH_3$
d : $R^1 = C_6H_5$, R^2 = α-naphtyl

Scheme 1. a: $LiNR^1R^2$, THF, −17 °C; b: $LiPPh_2$, THF, 25 °C

Reaction of monotosylate **4**[9] with sodium azide in DMF gave the azido alcohol **5** in 95% yield (Scheme 2). Reduction of compound **5** with molecular hydrogen in the presence of 20% Pd/C led quantitatively to the amino alcohol **6**. Condensation of this amino alcohol **6** with two equiv. of benzyl bromide, 2,4,6-trimethylbenzyl bromide, 2-naphtylmethyl bromide or 2,2′-bis(bromomethyl)biphenyl in acetonitrile in the presence of potassium carbonate gave the bis(alkylamino) alcohols **7a**–**d** in 58–85% yield. Tosylation of these

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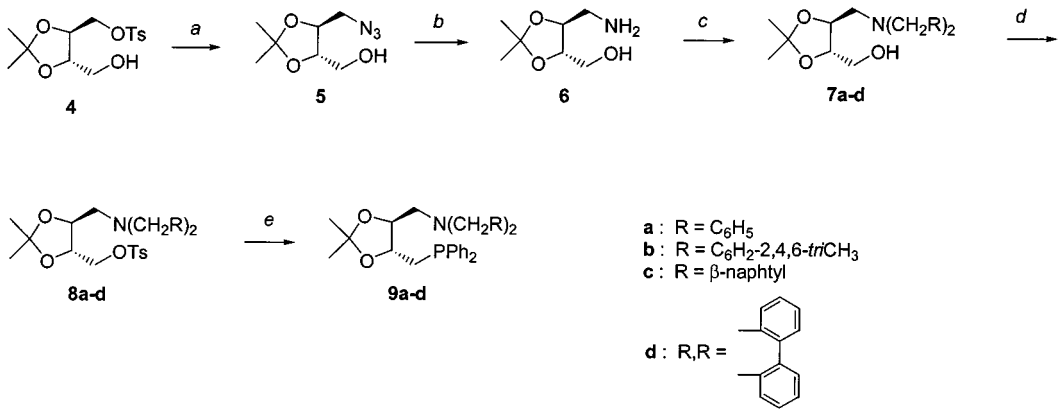
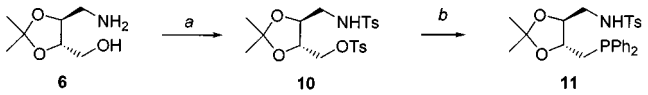


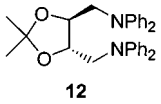
Scheme 2. a: NaN_3, DMF, 24 h, 95%; b: H_2, Pd/C, EtOH, 48 h, 100%; c: RCH_2Br (2 equiv.), K_2CO_3, CH_3CN, 30 min; d: $LiPPh_2$, THF, 25 °C

bis(alkylamino) alcohols **7** led to the bis(alkylamino) tosylates **8a**−**d**, whose treatment by lithium diphenylphosphide gave the desired bis(alkylamino) phosphanes **9a**−**d** in 40%, 45%, 20%, and 80% yield, respectively.

Reaction of amino alcohol **6** with two equiv. of tosyl chloride in pyridine gave the bis(tosylate) **10** in 65% yield (Scheme 3); tosylamino diphenylphosphane **11** was obtained in 73% yield by subsequent treatment of **10** with more than two equiv. of lithium diphenylphosphide. Finally, the bis(diphenyl)amino ligand **12** was obtained as a byproduct in the preparation of compound **2a**.

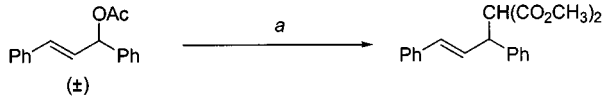


Scheme 3. a: TsCl, C_5H_5N, 25 °C, 65%; b: $LiPPh_2$, THF, 25 °C



Asymmetric Alkylation

The effectiveness of the above ligands in asymmetric allylic alkylation was tested in the reaction of racemic (*E*)-1,3-diphenylprop-2-enyl acetate with dimethyl malonate; an in situ catalyst prepared from $Pd_2(dba)_3$ and the chiral ligand in THF was used (Scheme 4).



Scheme 4. a: $CH_2(CO_2Me)_2$, base, cat. $Pd_2(dba)_3$, ligand

As a typical procedure, tris(dibenzylideneacetone)dipalladium and the amino phosphane were mixed in a solvent at room temperature under argon; *rac*-(*E*)-1,3-diphenylprop-2-enyl acetate was added, then the sodium salt of dimethyl malonate was added to the π-allylpalladium complex solution. The substituted product thus obtained was isolated by chromatography. The results are summarized in Table 1.

Table 1. Allylic alkylation of (±)-(*E*)-1,3-diphenylpropenyl acetate with dimethyl malonate, catalyzed by palladium complexes[a]

Entry	Ligand	Solvent	Conversion (%)[b]	ee (%)[b]
1	DIOP	THF	95	0
2	**12**	THF	90	0
3	**3a**	THF	97	50
4	**3b**	THF	94	68
5	**3c**	THF	96	63
6	**3d**	THF	93	69
7	**3d**	THF[c]	47	30
8	**3d**	CH_2Cl_2[d]	94	67
9	**3d**	CH_2Cl_2[c]	95	68
10	**3d**	Toluene[c]	4	8
11	**3d**	Toluene/CH_2Cl_2 (4:1)[d]	12	10
12	**9a**	THF	94	62
13	**9b**	THF	97	75
14	**9c**	THF	99	57
15	**9d**	THF	99	48
16	**11**	THF	49	39

[a] [acetate]/[malonate]/[NaH]/[$Pd_2(dba)_3$]/[ixgand] = 50:150:150:1:2; solvent: THF; 25 °C; 24 h. − [b] Determined by HPLC analysis with chiral stationary column Daicel Chiralcel OD−H (hexane/2-propanol 98:2); the configuration of the alkylated product was (*S*).[10] − [c] *N*,*O*-Bis(trimethylsilyl)acetamide (or BSA) and KOAc were used instead of NaH. − [d] *N*,*O*-Bis(trimethylsilyl)acetamide only was used instead of NaH.

It should first be noted that the use of ligands with C_2 symmetry, such as DIOP or ligand **12**, led to the formation of the racemic alkylated product (Entries 1−2). Ligands **3a**−**d** gave enantioselectivities up to 69% in THF as the solvent (Entries 3−6). Dissymmetrization at the nitrogen atom increased the enantioselectivity, although an enantioselectivity of 50% was observed with **3a** as the ligand; values of 68% and 69% were obtained in the presence of **3b** or **3d**, respectively. The presence of a methoxy group on the phenyl ring lowered the enantioselectivity (63% for **3c**). To increase the enantioselectivity, the alkylation was performed under various conditions, with **3d** as the ligand. While the use of BSA as the base in the presence of KOAc gave both lower yield and enantioselectivity (Entry 7), performing the reaction in CH_2Cl_2 gave almost the same e.e. (68%) in the

presence or absence of KOAc (Entries 8−9). The use of toluene (Entry 10) or a mixture of toluene/CH_2Cl_2 (Entry 11) as solvent again gave low yield and enantioselectivity. The use of ligands **9** in this alkylation reaction led to high chemical yields, with enantioselectivities depending on the nature of the aromatic ring. The highest enantioselectivity (75%) was obtained with ligand **9b**, which has 2,4,6-trimethylbenzyl substituents on the nitrogen atom. Finally, ligand **11** gave low yield (only 49%) and quite modest enantioselectivity (39%). To obtain more insight into the reasons behind the high enantioselectivities when these ligands are used, we undertook a theoretical study.

Theoretical Study

Some theoretical studies on η^3-allyl complexes of palladium have already been reported. In the past, semi-empirical methods have been used to study the nucleophilic attack on such complexes: Extended Hückel type (EHT) calculations were carried out to probe the effect of ligand asymmetry,[11] to distinguish between the central and the terminal carbon atoms,[12] to calculate the effect of the substituents on the regioselectivity,[13] and CNDO type calculations were carried out to determine the ligand effects.[14] The conclusions of these studies were that the nucleophilic attack on η^3-allylpalladium complexes is orbital-controlled rather than charge-controlled. More recently, studies using ab initio methods, both at the Hartree−Fock level and with the density functional theory (DFT), have begun to appear.[15−20]

In the present work we have used both types of methods, EHT and DFT. To determine the site of the nucleophilic attack, we have used the same method as in our previous work.[13] Since the reaction is frontier orbital controlled, we have focused first on the shape of the complex LUMO (Lowest Unoccupied Molecular Orbital) which interacts with the nucleophile HOMO (Highest Occupied Molecular Orbital). The larger the coefficient on one carbon atom in this orbital, the easier is the attack of the nucleophile on that carbon atom. Then we have put some nucleophiles at the same distance to both terminal carbon atoms and compared the overlap populations. These calculations are based on the EHT method. However, it is known from experiments that the presence of ligands of different natures on the palladium center induces a dissymmetry in the complex.[21−23] The EHT method does not allow the optimization of geometries. This is why we used a DFT method for these optimizations, to have reliable geometries for the EHT calculations.

Computational Methods

The parameters used for the EHT calculations are the usual ones[24][25] and the program is ICON version 8.0 from the group of R. Hoffmann at Cornell University.[26] The ab initio calculations are performed with Gaussian 94[27] with the DFT formalism. The chosen function is that of Perdew and Wang (BPW91). For palladium and phosphorus, the pseudopotentials of Hay and Wadt are used with the corresponding double ζ basis set of Dunning/Huzinaga (D95). A d polarization function is added to the palladium, nitrogen and carbon atoms. The ligands on the phosphorus center are modelled by PH_3 and NH_3 to save computational time. Since the allyl moiety is symmetrical with one phenyl group on each terminal carbon atom, we chose to model it in the first instance by the unsubstituted allyl group C_3H_5. By doing this, we obtained the electronic effects without taking into account the steric effects.

Results

The optimized geometry is shown in Figure 1. The most important information is that the Pd−$C_{trans\text{-}P}$ bond (2.23 Å) is longer than the Pd−$C_{trans\text{-}N}$ one (2.16 Å). This result can be explained by the *trans* effect of the phosphorus atom, which is greater than that of the nitrogen atom.[28] Experimentally, the same difference was observed,[15] although the nitrogen ligand was not of the same nature (sp^2 instead of sp^3). The C^1-C^2 and C^2-C^3 bond lengths are not equal either (1.417 and 1.432 Å, respectively). This means that the C^2-C^3 bond has a weaker double bond character. The carbon atoms C^1 and C^3 are 0.14−0.15 Å above the P−Pd−N plane, and the allyl plane makes an angle of 111° with the Pd−C^1−C^3 plane. Similar geometries were found experimentally.[22,23,29] The charge on carbon atoms C^1 and C^3 (0.55 e^-) is the same. As found in our previous EHT study, the LUMO is mainly the antibonding combination of the d_{xy} orbital of the metal center and the n-allyl orbital and the next unoccupied orbital is composed almost exclusively of the π*-allyl orbital.

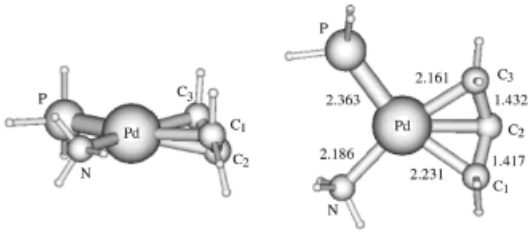


Figure 1. Optimized geometry for palladium complex Pd(NH_3)(PH_3)(η^3-allyl)

After this geometry optimization, we performed EHT calculations, following the method of our previous work.[13] We choose the same standard distances but we kept the difference between Pd−C^1 and Pd−C^3 bonds fixed (0.08 Å). The following geometry was used: Pd−P = 2.3 Å, Pd−N = 2.15 Å, Pd−C^1 = 2.20 Å, Pd−C^3 = 2.12 Å, $C^1-C^2 = C^2-C^3$ = 1.43 Å, P−Pd−N = 100°. For the sake of simplicity, the allyl plane was taken to be perpendicular to the P−Pd−N plane and to the bisector of the P−Pd−N angle. The hydrogen atoms on the carbon atoms C^1 and C^3 are bent away from the metal center by 15°. The projection on the *xy* plane is shown in Figure 2. The complex LUMO is also shown.

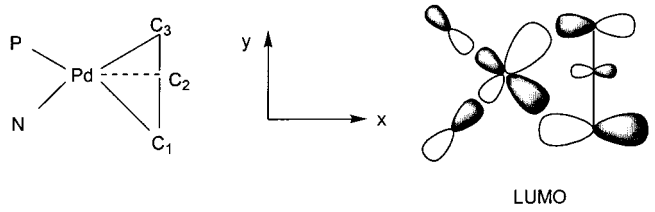


Figure 2. Projection of the model allyl−Pd complex on the *xy* plane and shape of its LUMO

We observe that the p_x coefficient is larger on the carbon atom C^1 than on C^3 (0.53 and 0.48, respectively). If the reaction is orbital-controlled, an incoming nucleophile will prefer to attack the carbon atom with the largest contribution in the LUMO. Hence it will preferentially attack C^1, *trans* to the phosphorus atom. Why is the LUMO dissymmetrical? The molecular orbital interaction diagram between the P−Pd−N and the allyl fragments shows that the LUMO, which is mainly antibonding between d_{xy} and the n-allyl orbital, also contains a small antibonding contribution of the π-allyl orbital and a small bonding contribution of the π*-allyl orbital, according to Equation 1.

$$\text{LUMO} = 0.80\ (\text{Pd}-\text{P}-\text{N LUMO}) - 0.69\ (\text{n}) - 0.04\ (\pi) + 0.08\ (\pi^*) \quad (1)$$

In fact, the LUMO of the P−Pd−N fragment is dissymmetric because the two ligands are different. This allows the mixing of the three allyl orbitals which are of different symmetry and they do not mix when the metal fragment is symmetrical (Figure 3).

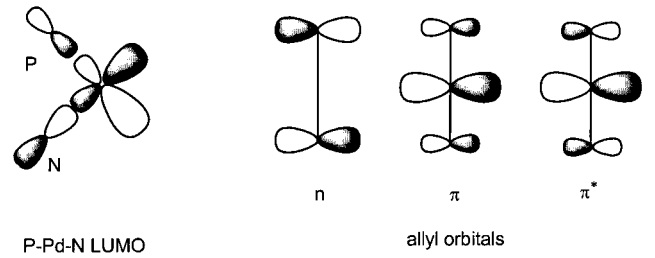


Figure 3. Shape of the LUMO of the P−Pd−N fragment and of the n, π and π* orbitals of the allyl fragment

However, we saw previously that other metal orbitals must be taken into account in the interaction with a nucleophile: for instance, the next LUMO and some occupied orbitals which have contributions to p_x of C^1 and p_x of C^3. Therefore, we tested the approach of some nucleophiles by putting them at the same distance to carbon atoms C^1 and C^3, and comparing the overlap population that represents the strength of the formed bond. To avoid too many steric repulsions, the allyl part is taken as being planar, this means that the hydrogen atoms are no longer bent away from the palladium center but are in the allyl plane (this looks like the transition state of an S_N2 reaction). We chose NH_3, $NHMe_2$ and the malonate anion $^-CH(CO_2Me)_2$ as nucleophiles, the latter of which is the nucleophile experimentally used in the present work. The amines and the malonate anion are put at 2 Å and 2.1 Å away from the carbon atoms, respectively. The best conformation of the nucleophile was searched for by rotating around the approach axis. The results are shown in Table 2. For all nucleophiles, the overlap population is larger with carbon atom C^1 than with C^3; this confirms that a nucleophile will preferentially attack at the carbon atom *trans* to the phosphorus atom, as long as only electronic interactions are taken into account. It is obvious that steric constraints, if for instance the carbon atoms are substituted, can reverse this trend.

Table 2. Overlap populations between a nucleophile and the terminal carbon atoms C^1 and C^3; energy in eV of the nucleophile HOMO

Nucleophile	HOMO	C^1	C^3
NH_3	−13.71	0.143	0.138
$NH(Me)_2$	−12.95	0.157	0.152
$^-HC(CO_2Me)_2$	−12.35	0.180	0.175

The interaction between the nucleophile and the allylic complex can be separated into terms of two-electron and four-electron interactions, by a simple perturbational treatment.[13][30] We consider the function f(x), which is the sum of the stabilizing interactions of the nucleophile HOMO with the vacant orbitals of the complex and the destabilizing interactions between the nucleophile HOMO and the occupied orbitals of the complex (Equation 2). The more positive f(x) is, the more the interaction is stabilizing.

$$f(x) = 0.75\Sigma(x + E_i)\ C_i^2 + \Sigma(0.875\ E_j - 0.125x)^2\ C_j^2/(E_j - x) \quad (2)$$

In Equation 2, x is the energy of the nucleophile HOMO, C_i and C_j are the coefficients of the p_x orbital of the attacked carbon atom in the occupied and vacant complex orbitals, respectively, and E_i and E_j are the energies of the corresponding complex orbitals; x was varied and f(x) was calculated for C_1 [$f_1(x)$] and C_3 [$f_3(x)$]. The difference $F(x) = f_1(x) - f_3(x)$ is drawn in Figure 4. If $F(x) < 0$, the nucleophile prefers carbon atom C^3, if $F(x) > 0$, the nucleophile prefers C^1. The attack preference depends on the HOMO of the nucleophile. For a high-lying HOMO (see Table 2), such as that of the malonate anion, carbon atom $C^{1\ trans}$ to the phosphorus atom is preferentially attacked; this agrees with the experimental results. The attractive two-electron interactions always favor the attack on $C_{trans\text{-}P}$ and, conversely, the repulsive four-electron interactions favor the attack on $C_{cis\text{-}P}$. Therefore, the site of attack depends on the balance between these two terms. The attractive term increases greatly with the HOMO energy. The repulsive term, being proportional to the sum of the interacting orbital energies (Equation 2), depends little on the HOMO position.

We therefore explained why the electronic interactions favor attack on carbon atom $C_{trans\text{-}P}$. We can predict that the use of a nucleophile with a higher HOMO than malonate, such as $^-C(CH_3)(CO_2Me)_2$, for example, would enhance the regioselectivity. How can the enantioselectivity be

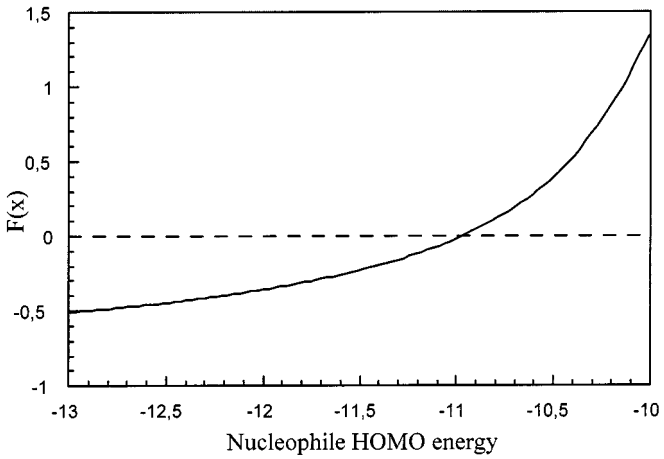


Figure 4. Plot of f(x) versus energy of the nucleophile HOMO

explained? For the π-allylpalladium complexes, two diastereoisomers are possible, *exo* and *endo* (Figure 5).

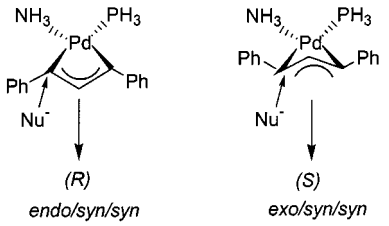


Figure 5. Most stable diastereoisomers of the model $(PH_3)(NH_3)$-(1,3-diphenylallyl)Pd complex

The phenyl rings may be positioned *syn* or *anti*, therefore eight diastereoisomers are possible. Using the EHT method, we calculated all of them and optimized the angle of the phenyl rings with the allyl plane. When the phenyl group is *syn*, it prefers to be in the allyl plane, when it is *anti*, it prefers to be perpendicular to this plane. This is in agreement with previous calculations.[5] The most stable isomers (by 13 kcal mol^{-1}) are those depicted in Figure 5 (*exo*/*syn*/*syn* and *endo*/*syn*/*syn*). With our model ligands PH_3 and NH_3, they are quasi isoenergetic, which cannot explain the enantioselectivity, since, by attack *trans* to the phosphorus atom, they each lead to one of the enantiomers (*S*) and (*R*). We therefore modeled the real catalyst by substituting the phosphorus and nitrogen atoms with phenyl and methyl groups, as shown in Figure 6. This corresponds to real catalysts [Pd/**3a**] and [Pd/**3b**], obtained by association of the palladium center with ligands **3a** and **3b**.

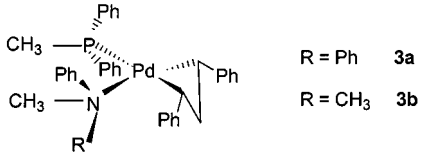


Figure 6. Modeling of the catalyst $Pd(CH_3PPh_2)(CH_3NPhR)(\eta^3$-1,3-diphenylallyl)

The substituents on the phosphorus and nitrogen atoms are disposed in a geometry that reproduced the X-ray structure of DIOP.[31] We calculated the *exo* and *endo* isomers for both [Pd/**3a**] and [Pd/**3b**]. For [Pd/**3b**] there are two *exo* and two *endo* isomers depending on the relative position (pseudo-axial or pseudo-equatorial) of the C_6H_5 and CH_3 substituents on the nitrogen atom. For [Pd/**3a**] the *exo* form is more stable by 30 kcal mol^{-1}. For [Pd/**3b**], the *exo* form is more stable by 18 kcal mol^{-1} when the methyl group is pseudo-axial and the *endo* form is more stable by 67 kcal mol^{-1} when the methyl group is pseudo-equatorial. However, the structure with the pseudo-equatorial methyl group is far less stable than that with the pseudo-axial one (47 kcal mol^{-1}). Therefore, of the four diastereoisomers of [Pd/**3b**], the most stable also has the *exo* geometry. The *exo* form of [Pd/**3a**] and [Pd/**3b**], attacked *trans* to the phosphorus atom, gives the (*S*) enantiomer, which is the one experimentally obtained. Despite the fact that the EHT method only gives qualitative results, the energy differences are large enough to be reliable. Hence, the enantioselectivity is explained by the existence of only one diastereoisomer of the complexes [Pd/**3a**] and [Pd/**3b**], regioselectively attacked *trans* to the phosphorus atom.

Conclusion

In conclusion, the new chiral amino phosphane ligands, easily obtained from tartaric acid, give enantioselectivities of up to 75% in the palladium-catalyzed alkylation of racemic 1,3-diphenylprop-2-enyl acetate with malonate anion. The calculations summarized in this paper allow the origin of the enantioselectivity in this asymmetric allylic alkylation to be understood. Two factors play an important role. The first one is steric control, which leads to the formation of a unique diastereoisomer (*exo*) of the η^3-allylpalladium complex. The second one is orbital control, which orients the nucleophile attack *trans* to the phosphorus atom; this is due to the dissymmetrical ligand. This is not the case for DIOP or ligand **12**. Our calculations also allow some predictions: To enhance the enantioselectivity, the HOMO of the nucleophile must be as high as possible. This means that the anion of $CH(CH_3)(CO_2Me)_2$ or of cyclopentanedione should be more efficient than the malonate anion $CH(CO_2Me)_2^-$

Experimental Section

General Remarks: ^{1}H NMR (200 or 300 MHz), ^{13}C NMR (50 or 75 MHz), and ^{31}P NMR (80 MHz) spectra were obtained with a Brüker AM 200 or AM 300 spectrometer. − Optical rotations were determined with a Perkin−Elmer 241 polarimeter. − GC analyses were recorded with a Shimadzu capillary gas chromatograph, equipped with a Chiraldex™ type B−PH (30 m × 0.32 mm) capillary column. − Reactions involving organometallic catalysis were carried out in Schlenk tubes under an inert gas. Tetrahydrofuran was distilled from sodium/benzophenone. (2*S*,3*S*)-2,3-*O*-Isopropylidene-1-*O*-*p*-toluenesulfonyl-D-threitol (**4**) was prepared according to a literature procedure.[9]

General Procedure for Preparation of Amino Tosylates 2: A solution of the lithium derivative of the secondary amine, obtained by mixing the amine (5 mmol) and butyllithium in hexane (5 mmol) in

THF (5 mL), was slowly added to a solution of ditosylate **1** (2.35 g, 5 mmol) in THF (5 mL) at −17°C. The solution was stirred for 1 h at −17°C, then 12 h at room temperature, and was finally treated with H_2O (50 mL). The organic compound was extracted with CH_2Cl_2 (3 × 50 mL). Evaporation of the solvent, followed by flash chromatography gave the amino tosylate **2**.

(2*S*,3*S*)-4-Diphenylamino-2,3-*O*-isopropylidene-1-*O*-tosylbutane-1,2,3-triol (2a): 26% yield; R_f = 0.5 (eluent: hexane/ethyl acetate, 4:1); $[\alpha]_D^{20}$ = +8.5 (*c* = 1.1, $CHCl_3$). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.29 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 2.43 (s, 3 H, CH_3), 3.90−4.05 (m, 5 H, CH_2N, CH_2O, CHO), 4.05−4.20 (m, 1 H, CHO), 6.90−7.10 (m, 6 H, H_{arom}), 7.15−7.30 (m, 6 H, H_{arom}), 7.71 (d, *J* = 8.3 Hz, 2 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.6 (CH_3), 26.8 (CH_3), 27.2 (CH_3), 55.0 (d, CH_2N), 69.2 (CH_2O), 76.0 (CHO), 76.9 (CHO), 110.2 (CMe_2), 121.2, 121.9, 128.0, 129.4, 129.8, 132.5, 145.0 and 148.0 (C_{arom}). − $C_{26}H_{29}NO_5S$ (467.58): calcd. C 66.79, H 6.86; found C 66.65, H 6.57.

(2*S*,3*S*)-2,3-*O*-Isopropylidene-4-methyl(phenyl)amino-1-*O*-tosylbutane-1,2,3-triol (2b): 32% yield; R_f = 0.4 (eluent: hexane/ethyl acetate, 4:1); $[\alpha]_D^{20}$ = +24.6 (*c* = 1.1, $CHCl_3$). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.31 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 2.45 (s, 3 H, CH_3), 2.95 (s, 3 H, CH_3), 3.46 (dd, *J* = 15.0, 5.7 Hz, 1 H, CH_2N), 3.55 (dd, *J* = 15.0, 4.5 Hz, 1 H, CH_2N), 3.90−4.05 (m, 1 H, CHO), 4.05−4.20 (m, 3 H, CH_2O, CHO), 6.70 (m, 3 H, H_{arom}), 7.25 (m, 2 H, H_{arom}), 7.38 (d, *J* = 8.5 Hz, 2 H, H_{arom}), 7.76 (d, *J* = 8.5 Hz, 2 H, H_{arom}). − $C_{21}H_{27}NO_5S$ (405.51): calcd. C 62.20, H 6.71; found C 62.65, H 7.11.

(2*S*,3*S*)-2,3-*O*-Isopropylidene-4-*p*-methoxyphenyl(methyl)amino-1-*O*-tosylbutane-1,2,3-triol (2c): 25% yield; R_f = 0.55 (eluent: hexane/ethyl acetate, 3:1); $[\alpha]_D^{20}$ = +6.3 (*c* = 0.7, $CHCl_3$). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3), 2.88 (s, 3 H, CH_3), 2.89 (s, 3 H, CH_3), 3.40 (d, *J* = 5.2 Hz, 2 H, CH_2N), 3.78 (s, 3 H, CH_3), 3.90−4.05 (m, 1 H, CHO), 4.05−4.20 (m, 3 H, CH_2O, CHO), 6.60−7.00 (m, 4 H, H_{arom}), 7.20−7.40 (m, 2 H, H_{arom}). − $C_{22}H_{29}NO_6S$ (435.54): calcd. C 60.67, H 6.71; found C 61.82, H 6.40.

(2*S*,3*S*)-2,3-*O*-Isopropylidene-4-α-naphthyl(phenyl)amino-1-*O*-tosylbutane-1,2,3-triol (2d): 25% yield; R_f = 0.42 (eluent: hexane/ethyl acetate, 5:1); $[\alpha]_D^{20}$ = +21.6 (*c* = 0.8, $CHCl_3$). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 2.38 (s, 3 H, CH_3), 3.95−4.10 (m, 5 H, CH_2N, CH_2O, CHO), 4.15−4.25 (m, 1 H, CHO), 7.00−7.50 (m, 11 H, H_{arom}), 7.60−7.80 (m, 4 H, H_{arom}). − $C_{30}H_{31}NO_5S$ (517.64): calcd. C 69.61, H 6.04; found C 69.18, H 6.17.

(2*S*,3*S*)-4-Azido-2,3-*O*-isopropylidenebutane-1,2,3-triol (5): A mixture of (2*S*,3*S*)-2,3-*O*-isopropylidene-1-*O*-*p*-toluenesulfonyl-D-threitol (**4**)[9] (11.8 g, 37.5 mmol) and NaN_3 (3.5 g, 58 mmol) in DMF (95 mL) was heated at reflux for 24 h. After being cooled to room temperature, the solution was treated with H_2O (50 mL) and was then extracted with CH_2Cl_2 (3 × 50 mL). Evaporation of the solvent, followed by column chromatography (eluent: petroleum ether/ethyl acetate, 2:1) gave 6.6 g of compound **5** as an oil (95%); R_f = 0.3; $[\alpha]_D^{20}$ = −65.7 (*c* = 2.5, $CHCl_3$). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.36 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 2.84 (s, 1 H, OH), 3.34 (dd, *J* = 13.1, 4.6 Hz, 1 H, CH_2N), 3.55 (dd, *J* = 13.1, 3.7 Hz, 1 H, CH_2N), 3.74 (dd, *J* = 13.8, 3.9 Hz, 1 H, CH_2O), 3.86 (dd, *J* = 13.8, 4.0 Hz, 1 H, CH_2O), 4.02 (ddd, *J* = 11.4, 4.6, 3.7 Hz, 1 H, CHO), 4.07 (ddd, *J* = 11.4, 4.0, 3.9 Hz, 1 H, CHO). − $C_7H_{13}N_3O_3$ (187.20): calcd. C 44.91, H 6.00; found C 44.96, H 7.28.

(2*S*,3*S*)-4-Amino-2,3-*O*-isopropylidenebutane-1,2,3-triol (6): A solution of azido alcohol **5** (3 g, 16 mmol) in ethanol (20 mL) was hydrogenated at room temperature and atmospheric pressure in the presence of 20% Pd/C (300 mg). After 48 h, the solution was filtered and the solvent was evaporated to give 2.57 g of amino alcohol **6** as an oil (100%); $[\alpha]_D^{20}$ = −47.3 (*c* = 1.0, $CHCl_3$). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.32 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 2.20−2.50 (br. s, 3 H, NH_2, OH), 2.76 (dd, *J* = 12.6, 8.0 Hz, 1 H, CH_2N), 3.18 (dd, *J* = 12.6, 4.3 Hz, 1 H, CH_2N), 3.70−3.92 (m, 4 H, CH_2O, CHO). $C_7H_{15}NO_3$ (161.20): calcd. C 52.16, H 9.38; found C 51.76, H 9.16.

General Procedure for the Preparation of Amino Alcohols 7: The bromide (12.4 mmol) was slowly added to a mixture of amino alcohol **6** (1 g, 6.2 mmol) and K_2CO_3 (2,57 g, 18.6 mmol) in CH_3CN (6 mL), heated at reflux for 30 min. The reaction mixture was refluxed for 24 h, then cooled at room temperature, and treated with H_2O (10 mL). The solution was extracted with CH_2Cl_2 (3 × 30 mL). Evaporation of the solvent, followed by flash chromatography gave the corresponding dialkylated amino alcohol **7**.

(2*S*,3*S*)-4-Dibenzylamino-2,3-*O*-isopropylidenebutane-1,2,3-triol (7a): 85% yield; R_f = 0.3 (eluent: petroleum ether/ethyl acetate, 4:1); $[\alpha]_D^{20}$ = +32.1 (*c* = 0.8, $CHCl_3$). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.35 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3), 2.63 (s, 1 H, OH), 2.72 (d, *J* = 5.5 Hz, 2 H, CH_2N), 3.60−3.90 (m, 8 H, CH_2O, CHO, CH_2N), 7.30−7.50 (m, 10 H, H_{arom}). − $C_{21}H_{27}NO_3$ (341.45): calcd. C 73.87, H 7.97, N 4.10; found C 73.73, H 8.12, N 4.04.

(2*S*,3*S*)-4-Bis(2,4,6-trimethylbenzyl)amino-2,3-*O*-isopropylidenebutane-1,2,3-triol (7b): 76% yield; R_f = 0.4 (eluent: petroleum ether/ethyl acetate, 4:1); $[\alpha]_D^{20}$ = +10.2 (*c* = 1, $CHCl_3$). − ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.35 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 1.65 (s, 1 H, OH), 2.23 (s, 6 H, CH_3), 2.26 (s, 12 H, CH_3), 2.58 (m, 2 H, CH_2N), 3.40−3.50 (m, 4 H, CH_2O), 3.49 (d, *J* = 12.5 Hz, 2 H, CH_2N), 3.69 (d, *J* = 12.5 Hz, 2 H, CH_2N), 3.80−4.00 (m, 2 H, CHO), 6.75 (s, 4 H, H_{arom}). − $C_{27}H_{39}NO_3$ (425.62): calcd. C 76.24, H 9.17; found C 76.21, H 9.34.

(2*S*,3*S*)-4-Bis(2-naphtylmethyl)amino-2,3-*O*-isopropylidenebutane-1,2,3-triol (7c): 82% yield; R_f = 0.34 (eluent: petroleum ether/ethyl acetate, 4:1); $[\alpha]_D^{20}$ = +14.0 (*c* = 0.65, $CHCl_3$). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.32 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.61 (s, 1 H, OH), 2.81 (d, *J* = 5.7 Hz, 2 H, CH_2N), 3.73 (d, *J* = 13.3 Hz, 2 H, CH_2N), 3.98 (d, *J* = 13.3 Hz, 2 H, CH_2N), 3.50−3.70 (m, 4 H, CH_2O), 4.00−4.20 (m, 2 H, CHO), 7.64 (m, 6 H, H_{arom}), 7.80−7.90 (m, 8 H, H_{arom}). − $C_{29}H_{31}NO_3$ (441.57): calcd. C 78.91, H 7.01; found C 80.15, H 7.06.

(2*S*,3*S*)-4-(6,7-Dihydro-5*H*-dibenzo[*c*,*e*]azepin-6-yl)-2,3-*O*-isopropylidenebutane-1,2,3-triol (7d): 58% yield; R_f = 0.20 (eluent: petroleum ether/ethyl acetate, 1:2). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.27 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3), 2.61 (dd, *J* = 12.7, 5.7 Hz, 1 H, CH_2N), 2.87 (s, 1 H, OH), 3.11 (dd, *J* = 12.7, 3.7 Hz, 1 H, CH_2N), 3.38 (d, *J* = 12.5 Hz, 2 H, CH_2N), 3.47 (d, *J* = 12.5 Hz, 2 H, CH_2N), 3.69 (dd, *J* = 9.4, 1.9 Hz, 1 H, CH_2O),), 3.87 (dd, *J* = 9.4, 3.4 Hz, 1 H, CH_2O), 3.90−4.15 (m, 2 H, CHO), 7.30−7.50 (m, 8 H, H_{arom}). − $C_{21}H_{25}NO_3$ (339.44): calcd. C 74.31, H 7.42; found C 74.24, H 7.27.

General Procedure for Preparation of Aminotosylates 8: p-Toluenesulfonyl chloride (1.13 g, 5.9 mmol, 1.1 equiv.) was added at 0°C to a solution of amino alcohol **7** (5.3 mmol) in pyridine (10 mL). After being stirred for 12 h, the solution was treated with cold H_2O (20 mL), and the organic product was extracted with CH_2Cl_2 (3 × 10 mL). Evaporation of the solvent gave a residue which was purified by flash chromatography to give the amino tosylate **8**.

(2*R*,3*S*)-4-Dibenzylamino-2,3-*O*-isopropylidene-1-*O*-tosylbutane-1,2,3-triol (8a): 91% yield; R_f = 0.35 (eluent: petroleum ether/ethyl

acetate, 4:1); $[\alpha]_D^{20} = -7.0$ ($c = 1.0$, $CHCl_3$). – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.18 (s, 6 H, CH_3), 2.36 (s, 3 H, CH_3), 2.56 (d, $J = 5.5$ Hz, 2 H, CH_2N), 3.45 (d, $J = 13.5$, 2 H, CH_2N), 3.59 (d, $J = 13.5$ Hz, 2 H, CH_2N), 3.60−3.80 (m, 2 H, CH_2O), 3.85 (m, 1 H, CHO), 4.05 (m, 1 H, CHO), 7.10−7.30 (m, 12 H, H_{arom}), 7.66 (d, $J = 8.1$ Hz, 2 H, H_{arom}). – $C_{28}H_{33}NO_5S$ (495.64): calcd. C 67.85, H 6.71; found C 67.80, H 6.70.

(2*R*,3*S*)-4-Bis(2,4,6-trimethylbenzyl)amino-2,3-*O*-isopropylidene-1-*O*-tosylbutane-1,2,3-triol (8b): 65% yield; $R_f = 0.60$ (eluent: petroleum ether/ethyl acetate, 4:1); $[\alpha]_D^{20} = -10.2$ ($c = 1.1$, $CHCl_3$). – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.19 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3), 2.23 (s, 6 H, CH_3), 2.24 (s, 12 H, CH_3), 2.45 (s, 3 H, CH_3), 2.56 (d, $J = 5.0$ Hz, 2 H, CH_2N), 3.50 (d, $J = 13.1$, 2 H, CH_2N), 3.58 (d, $J = 13.1$ Hz, 2 H, CH_2N), 3.60−3.71 (m, 4 H, CH_2O, CHO), 6.78 (s, 4 H, H_{arom}), 7.31 (d, $J = 8.1$ Hz, 2 H, H_{arom}), 7.70 (d, $J = 8.1$ Hz, 2 H, H_{arom}). – $C_{34}H_{45}NO_5S$ (579.80): calcd. C 70.43, H 7.82; found C 70.25, H 8.04.

(2*R*,3*S*)-4-Bis(2-naphtylmethyl)amino-2,3-*O*-isopropylidene-1-*O*-tosylbutane-1,2,3-triol (8c): 70% yield; $R_f = 0.40$ (eluent: petroleum ether/ethyl acetate, 4:1); $[\alpha]_D^{20} = -6.2$ ($c = 1.2$, $CHCl_3$). – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.25 (s, 3 H, CH_3), 1.27 (s, 3 H, CH_3), 2.37 (s, 3 H, CH_3), 2.75 (d, $J = 5.9$ Hz, 2 H, CH_2N), 3.73 (d, $J = 13.1$, 2 H, CH_2N), 3.88 (d, $J = 13.1$ Hz, 2 H, CH_2N), 3.70−3.90 (m, 2 H, CHO), 4.00−4.20 (m, 2 H, CH_2O), 7.20 (d, $J = 8.1$ Hz, 2 H, H_{arom}), 7.50−7.70 (m, 6 H, H_{arom}), 7.62 (d, $J = 8.1$ Hz, 2 H, H_{arom}), 7.70−7.90 (m, 8 H, H_{arom}). – $C_{36}H_{37}NO_5S$ (595.76): calcd. C 72.58, H 6.26; found C 72.60, H 6.21.

(2*R*,3*S*)-4-(6,7-Dihydro-5*H*-dibenzo[*c*,*e*]azepin-6-yl)-2,3-*O*-isopropylidene-1-*O*-tosylbutane-1,2,3-triol (8d): Yield: 63%; $R_f = 0.65$ (eluent: petroleum ether/ethyl acetate, 1:1). – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.38 (s, 3 H, CH_3), 1.44 (s, 3 H, CH_3), 2.42 (s, 3 H, CH_3), 2.66 (dd, $J = 13.1$, 4.8 Hz, 1 H, CH_2N), 2.85 (dd, $J = 13.1$, 6.5 Hz, 1 H, CH_2N), 3.34 (d, $J = 12.4$ Hz, 2 H, CH_2N), 3.46 (d, $J = 12.4$ Hz, 2 H, CH_2N), 3.96 (ddd, $J = 8.3$, 4.7, 3.9 Hz, 1 H, CHO), 4.10−4.30 (m, 12 H, CHO), 4.19 (dd, $J = 10.6$, 4.7 Hz, 1 H, CH_2O), 4.30 (dd, $J = 10.6$, 3.9 Hz, 1 H, CH_2O), 7.30−7.60 (m, 10 H, H_{arom}), 7.82 (d, $J = 8.2$ Hz, 2 H, H_{arom}). – $C_{28}H_{31}NO_5S$ (493.62): calcd. C 68.13, H 6.33; found C 68.47, H 6.90.

(2*S*,3*S*)-2,3-*O*-Isopropylidene-1-*O*-tosyl-4-tosylaminobutane-1,2,3-triol (10): 65% yield; $R_f = 0.7$ (eluent: petroleum ether/ethyl acetate, 1:1); $[\alpha]_D^{20} = +5.6$ ($c = 1.1$, $CHCl_3$). – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.22 (s, 3 H, CH_3), 1.26 (s, 3 H, CH_3), 2.37 (s, 3 H, CH_3), 2.39 (s, 3 H, CH_3), 2.90−3.20 (m, 2 H, CH_2N), 3.80−4.10 (m, 6 H, CH_2O, CHO), 4.64 (t, $J = 6.5$ Hz, 1 H, NH), 710−7.30 (m, 5 H, H_{arom}), 7.60−7.80 (m, 5 H, H_{arom}), 7.71 (d, $J = 8.3$ Hz, 2 H, H_{arom}). – $C_{21}H_{27}NO_7S_2$ (469.57): calcd; C 53.72, H 5.80; found C 53.20, H 5.84.

General Procedure for Preparation of Amino Phosphanes 3 and 9: A solution of PPh_2Li, prepared under argon in THF (80 mL) at 0°C from $ClPPh_2$ (8.5 g, 38.5 mmol) and Li (10 equiv.), was slowly added to amino tosylate **2** or **8** (12.6 mmol), dissolved in THF (20 mL), until the red color of the solution remained. The solution was stirred for 2 h and was then hydrolyzed with H_2O (50 mL). The solvent was evaporated and the residue was treated with H_2O (50 mL) and CH_2Cl_2 (3 × 50 mL). Evaporation of the solvent, followed by flash chromatography gave the amino phosphane **3** or **9**.

(2*R*,3*S*)-1-Diphenylamino-4-diphenylphosphanyl-2,3-*O*-isopropylidenebutane-2,3-diol (3a): 40% yield; $R_f = 0.70$ (eluent: petroleum ether/ethyl acetate, 6:1); $[\alpha]_D^{20} = -11.3$ ($c = 1.0$, $CHCl_3$). – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.33 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 2.35−2.45 (m, 2 H, CH_2P), 3.88 (dd, $J = 13.6$, 6.7 Hz, 1 H, CH_2N), 4.01 (d, $J = 13.6$, 4.4 Hz, 1 H, CH_2N), 4.00−4.20 (m, 2 H, CHO), 7.05−7.70 (m, 20 H, H_{arom}). – ^{31}P (80 MHz, $CDCl_3$): δ = −22.1. – $C_{31}H_{32}NO_2P$ (481.58): calcd. C 77.32, H 6.70; found C 76.90, H 6.76.

(2*R*,3*S*)-1-Diphenylphosphanyl-2,3-*O*-isopropylidene-4-methyl(phenyl)aminobutane-2,3-diol (3b): 55% yield; $R_f = 0.50$ (eluent: petroleum ether/ethyl acetate, 6:1)): $[\alpha]_D^{20} = -12.3$ ($c = 0.9$, $CHCl_3$). – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.38 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 2.33 (dd, $J = 13.8$, 6.0 Hz, 1 H, CH_2P), 2.45 (dd, $J = 13.8$, 6.8 Hz, 1 H, CH_2P), 2.88 (s, 3 H, CH_3), 3.32 (dd, $J = 15.1$, 6.8 Hz, 1 H, CH_2N), 3.62 (d, $J = 15.1$, 4.2 Hz, 1 H, CH_2N), 3.86 (ddd, $J = 11.8$, 6.8, 6.0 Hz, 1 H, CHO), 4.11 (ddd, $J = 11.8$, 6.8, 4.2 Hz, 1 H, CHO), 6.70−6.85 (m, 3 H, H_{arom}), 7.20−7.40 (m, 12 H, H_{arom}). – ^{31}P (80 MHz, $CDCl_3$): δ = −23.8. – $C_{26}H_{30}NO_2P$ (419.51): calcd. C 74.44, H 7.21; found C 74.55, H 7.31.

(2*R*,3*S*)-1-Diphenylphosphanyl-2,3-*O*-isopropylidene-4-*p*-methoxyphenyl(methyl)aminobutane-2,3-diol (3c): 27% yield; $R_f = 0.34$ (eluent: petroleum ether/ethyl acetate, 10:1); $[\alpha]_D^{20} = -6.6$ ($c = 0.9$, $CHCl_3$). – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.31 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 2.27 (dd, $J = 13.8$, 6.0 Hz, 1 H, CH_2P), 2.37 (dd, $J = 13.8$, 6.5 Hz, 1 H, CH_2P), 2.74 (s, 3 H, CH_3), 3.19 (dd, $J = 14.8$, 6.7 Hz, 1 H, CH_2N), 3.40 (d, $J = 14.8$, 4.2 Hz, 1 H, CH_2N), 3.71 (s, 3 H, CH_3), 3.82 (ddd, $J = 11.2$, 6.5, 6.0 Hz, 1 H, CHO), 4.01 (ddd, $J = 11.2$, 6.7, 4.2 Hz, 1 H, CHO), 6.74 (m, 4 H, H_{arom}), 7.50 (m, 10 H, H_{arom}). – ^{31}P (80 MHz, $CDCl_3$): δ = −23.7. $-C_{27}H_{32}NO_3P$ (449.53): calcd. C 72.14, H 7.18; found: C 72.16, H 6.23.

(2*R*,3*S*)-1-Diphenylphosphanyl-2,3-*O*-isopropylidene-4-α-naphthyl-(phenyl)aminobutane-2,3-diol (3d): 82% yield; $R_f = 0.5$ (eluent: petroleum ether/ethyl acetate, 6:1); $[\alpha]_D^{20} = -35.2$ ($c = 0.9$, $CHCl_3$). – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.39 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 2.28 (dd, $J = 13.8$, 6.0 Hz, 1 H, CH_2P), 2.38 (dd, $J = 13.8$, 7.0 Hz, 1 H, CH_2P), 3.80−4.00 (m, 2 H, CH_2N), 4.00−4.20 (m, 2 H, CHO), 6.90−7.60 (m, 22 H, H_{arom}). – ^{31}P (80 MHz, $CDCl_3$): δ = −23.9. – $C_{35}H_{34}NO_2P$ (531.64): calcd. C 78.51, H 6.38; found C 78.54, H 6.50.

(2*R*,3*S*)-4-Dibenzylamino-1-diphenylphosphanyl-2,3-*O*-isopropylidenebutane-2,3-triol (9a): 40% yield; $R_f = 0.22$ (eluent: petroleum ether/ethyl acetate, 19:1); $[\alpha]_D^{20} = -21.8$ ($c = 0.9$, $CHCl_3$). – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.19 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3), 2.16 (ddd, $J = 13.9$, 7.7, 1.4 Hz, 1 H, CH_2P), 2.22 (ddd, $J = 13.9$, 4.5, 1.9 Hz, 1 H, CH_2P), 2.47 (dd, $J = 13.7$, 5.5 Hz, 1 H, CH_2N), 2.60 (dd, $J = 13.7$, 4.3 Hz, 1 H, CH_2N), 3.46 (d, $J = 13.6$ Hz, 2 H, CH_2N), 3.61 (d, $J = 13.6$ Hz, 2 H, CH_2N), 3.60−3.75 (m, 1 H, CHO), 3.90−4.00 (m, 1 H, CHO), 7.10−7.30 (m, 20 H, H_{arom}). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 27.2 (CH_3), 27.3 (CH_3), 32.4 (d, $J = 15.0$ Hz, CH_2P), 54.8 (CH_2N), 59.0 (2 × CH_2N), 77.3 (d, $J = 13.1$ Hz, CHO), 80.7 (d, $J = 9.0$ Hz, CHO), 108.8 (CMe_2), 127.0−139.3 (C_{arom}). – ^{31}P (80 MHz, $CDCl_3$): δ = −23.1. – $C_{33}H_{36}NO_2P$ (509.63): calcd. C 77.78, H 7.12, N 2.75, P 6.08; found C 77.34, H 7.12, N 2.90, P 6.84.

(2*R*,3*S*)-4-Bis(2,4,6-trimethylbenzyl)amino-1-diphenylphosphanyl-2,3-*O*-isopropylidenebutane-2,3-triol (9b): 45% yield; $R_f = 0.6$ (eluent: petroleum ether/ethyl acetate, 9:1); $[\alpha]_D^{20} = -1.6$ ($c = 1.3$, $CHCl_3$). – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.19 (s, 3 H, CH_3), 1.31 (s, 3 H, CH_3), 2.00−2.30 (m, 2 H, CH_2P), 2.23 (s, 6 H, CH_3), 2.25 (s, 12 H, CH_3), 2.45−2.60 (m, 2 H, CH_2N), 3.42 (d, $J = 12.4$ Hz, 2 H, CH_2N), 3.63 (d, $J = 12.4$ Hz, 2 H, CH_2N), 3.72−3.90 (m, 2 H, CHO), 7.30−7.70 (m, 10 H, H_{arom}). – ^{31}P (80 MHz, $CDCl_3$): δ = −23.6. – $C_{39}H_{48}NO_2P$ (593.79): calcd. C 78.89, H 8.15; found C 78.25, H 8.03.

(2*R*,3*S*)-4-Bis(2-naphtylmethyl)amino-1-diphenylphosphanyl-2,3-*O*-isopropylidenebutane-2,3-triol (9c): 20% yield; R_f = 0.22 (eluent: petroleum ether/ethyl acetate, 7:1); $[\alpha]_D^{20}$ = −28.6 (*c* = 0.6, $CHCl_3$). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.29 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 2.10−2.30 (m, 2 H, CH_2P), 2.71−2.80 (m, 2 H, CH_2N), 3.62 (d, *J* = 12.0 Hz, 2 H, CH_2N), 3.73 (d, *J* = 12.0 Hz, 2 H, CH_2N), 4.05−4.20 (m, 2 H, CHO), 7.20−7.80 (m, 24 H, H_{arom}). − ^{31}P (80 MHz, $CDCl_3$): δ = −23.5. − $C_{41}H_{40}NO_2P$ (609.75): calcd. C 80.76, H 6.61; found C 80.25, H 6.03.

(2*R*,3*S*)-4-(6,7-Dihydro-5*H*-dibenzo[*c*,*e*]azepin-6-yl)-1-diphenylphosphanyl-2,3-*O*-isopropylidenebutane-2,3-triol (9d): 80% yield, R_f = 0.32 (eluent: petroleum ether/ethyl acetate, 5:1). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 2.31 (m, 2 H, CH_2P), 2.72 (m, 2 H, CH_2N), 3.32 (d, *J* = 12.3 Hz, 2 H, CH_2N), 3.38 (d, *J* = 12.3 Hz, 2 H, CH_2N), 4.00−4.20 (m, 2 H, CHO), 7.20−7.60 (m, 18 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 27.4 (CH_3), 27.5 (CH_3), 32.8 (d, *J* = 16.3 Hz, CH_2P), 55.9 (2 × CH_2N), 57.4 (CH_2N), 77.6 (d, *J* = 14.8 Hz, CHO), 80.7 (d, *J* = 7.8 Hz, CHO), 109.3 (CMe_2), 127.6−141.3 (C_{arom}). − ^{31}P (80 MHz, $CDCl_3$): δ = −23.8. − $C_{33}H_{34}NO_2P$ (507.62): calcd. C 78.08, H 6.75; found C 79.10, H 6.59.

(2*R*,3*S*)-1-Diphenylphosphanyl-2,3-*O*-isopropylidene-4-tosylaminobutane-2,3-diol (11): 73% yield; R_f = 0.25 (eluent: petroleum ether/ethyl acetate, 4:1); $[\alpha]_D^{20}$ = −4.2 (*c* = 0.3, $CHCl_3$). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.28 (s, 3 H, CH_3), 1.34 (s, 3 H, CH_3), 2.42 (s, 3 H, CH_3), 2.30−2.50 (m, 2 H, CH_2P), 3.00−4.20 (m, 2 H, CH_2N), 4.79 (t, *J* = 6.1 Hz, 1 H, NH), 3.80−4.20 (m, 2 H, CHO), 7.20−7.40 (m, 10 H, H_{arom}), 7.42 (d, *J* = 8.2 Hz, 2 H, H_{arom}), 7.83 (d, *J* = 8.2 Hz, 2 H, H_{arom}). − ^{31}P (80 MHz, $CDCl_3$): δ = −24.6. − $C_{26}H_{30}NSO_4P$ (483.57): calcd. C 64.58, H 6.25, N 2.89; found C 63.96, H 6.09, N 2.87.

(2*S*,3*S*)-1,4-Bis(diphenylamino)-2,3-*O*-isopropylidenebutane-2,3-diol (12): $[\alpha]_D^{20}$ = −5.2 (*c* = 0.8, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40 (s, 6 H, CH_3), 3.85 (d, *J* = 4.8 Hz, 4 H, CH_2), 4.20 (m, 2 H, CH), 6.90−7.02 (m, 12 H, H_{arom}), 7.18−7.32 (m, 8 H, H_{arom}). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.5 (CH_3), 55.7 (CH_2), 77.8 (s, CH), 109.7 (CMe_2), 121.5, 121.8, 129.4 and 148.2 (C_6H_5). − $C_{31}H_{32}N_2O_2$ (464.61): calcd. C 80.14, H 6.94, N 6.03; found C 80.08, H 6.85, N 6.15.

Asymmetric Alkylation. − Typical Procedure: A solution of the sodium salt of dimethyl malonate, prepared from dimethyl malonate (118.9 mg, 0.900 mmol) and sodium hydride in THF (2 mL) at room temperature, was added to a mixture of $Pd_2(dba)_3$ (55 mg, 6.10^{-3} mmol), ligand (12.10^{-3} mmol) and *rac*-(*E*)-1,3-diphenylprop-2-enyl acetate (75.7 mg, 0.300 mmol) in THF (2 mL). The solution was stirred for 24 h and was then quenched with a small amount of water. Evaporation of the solvent, followed by column chromatography gave the alkylated product. The conversion and enantiomeric purity was determined by HPLC with a chiral stationary phase column Chiraldex OD−H (hexane/2-propanol = 98:2). The absolute configuration was determined by polarimetry.[10]

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