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Modular Furanoside Phosphite-Phosphoroamidites, a Readily Available Ligand Library for Asymmetric Palladium-Catalyzed Allylic Substitution Reactions. Origin of Enantioselectivity

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Abstract: A library of furanoside phosphite-phosphoroamidite ligands has been synthesized and screened in the palladium-catalyzed allylic substitution reactions of several substrate types. These series of ligands can be prepared efficiently from easily accessible D-xylose and D-glucose. Their modular nature enables the position of the phosphoroamidite group, configuration of C-3 of the furanoside backbone and the substituents/configurations in the biaryl phosphite/phosphoroamidite moieties to be easily and systematically varied. By carefully selecting the ligand components, therefore, high regio- and enantioselectivities (*ee*s up to 98%) and good activities have been achieved in a broad range of mono- and disubstituted hindered and unhindered linear and cyclic substrates. The NMR studies on the palladium-π-allyl intermediates provide a deeper understanding about the effect of the ligand parameters on the origin of enantioselectivity. They also indicate that the nucleophilic attack takes place predominantly at the allylic terminal carbon atom located *trans* to the phosphoroamidite moiety.

Keywords: C–C coupling; chiral pool; furanoside phosphite-phosphoroamidites; palladium; P ligands

Introduction

The palladium-catalyzed asymmetric allylic substitution is an important tool in organic synthesis, allowing the formation of enantioselective carbon-carbon and carbon-heteroatom bonds.[1] Many chiral ligands (mainly P and N ligands), which possess either C_2- or C_1-symmetry, have provided high enantiomeric excesses for several types of disubstituted substrate.[1] However, in general, there are still problems of substrate specificity (for example, *ee*s are high in disubstituted linear hindered substrates and low in unhindered substrates, and *vice versa*) and reaction rates. On the other hand, monosubstituted substrates still require more active and more regio- and enantioselective Pd catalysts.[1] Most chiral ligands developed for Pd-catalyzed asymmetric allylic substitution are mixed bidentate donor ligands (such as P-N, P-S, S-N and P-P′ types).[1,2,3] The efficiency of this type of heterodonor ligand has mainly been attributed to the electronic effects of the donor atoms. Recently, a group of less electron-rich heterodonor compounds – the phosphite-phosphoroamidite ligands – has also demonstrated their potential utility in this process, providing excellent enantioselectivities and activities.[3a,b] The presence of biaryl phosphite/phosphoroamidite moieties in the ligand design was beneficial because: (1) reaction rates increased thanks to the larger π-acceptor ability of these moieties,[3,4] and (2) the substrate specificity decreased because the chiral pocket created (the chiral cavity in which the allyl group is embedded) is flexible enough to enable perfect coordination of hindered and unhindered substrates.[5] Despite these advantages, only one series of phosphite-phosphoroamidite ligands possessing a 1,2-amino alcohol backbone has been extensively studied.[3b] However, these ligands proved to be effective in the allylic substitution of disubstituted substrates but for monosubstituted substrates their regio- and enantioselectivities were only moderate.[3b] On the other hand, the mechanistic aspects with these ligands are still not understood well enough for a prior prediction of the type of ligand needed for high selectivity. More research into the scope of the phosphite-

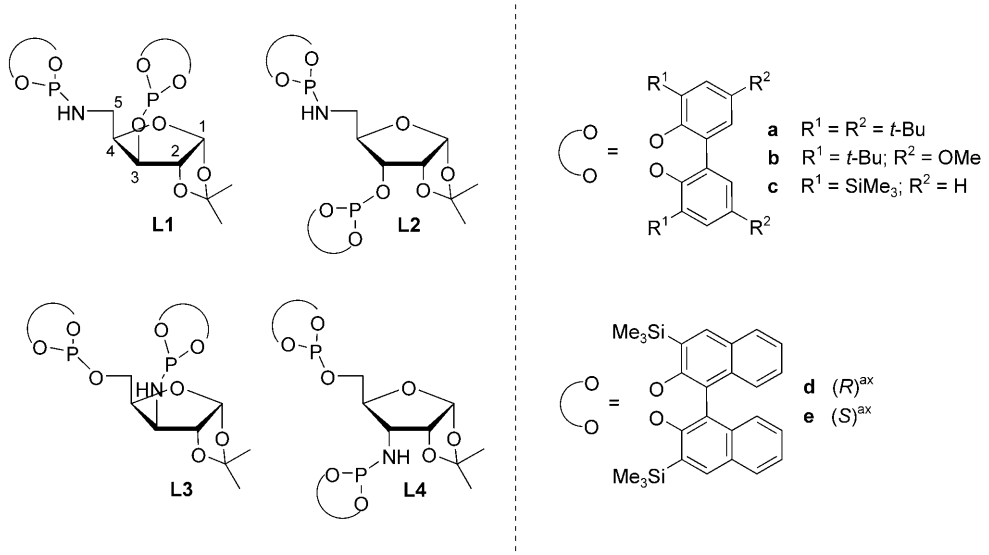


Figure 1. Library of phosphite-phosphoromidite ligands (**L1**–**L4a**–**e**) with furanoside backbone.

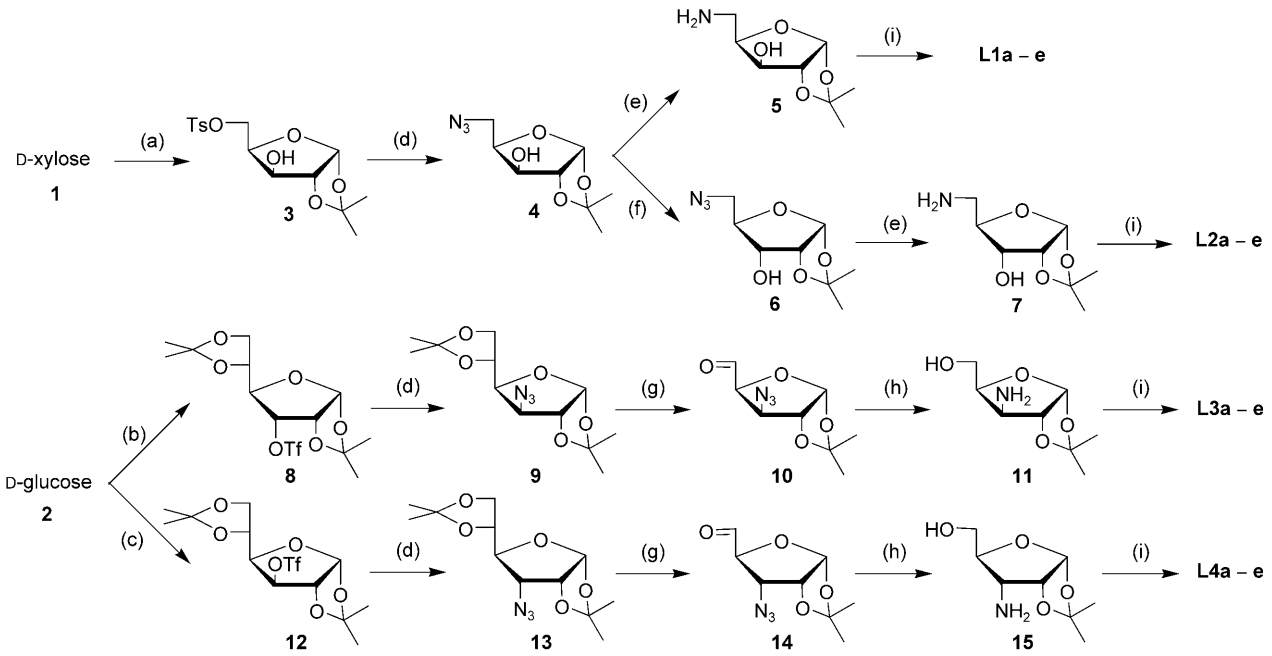
phosphoroamidite ligands in this process is therefore needed. For this purpose, carbohydrates are particularly advantageous thanks to their low price and easy modular constructions.[6] In this paper, we report the synthesis and application of a new chiral phosphite-phosphoroamidite ligand library (Figure 1, **L1**–**L4a**–**e**) for the Pd-catalyzed allylic substitution reactions of several substrate types.[7] We also discuss the synthesis and characterization of the Pd-π-allyl intermediates in order to provide greater insight into the origin of enantioselectivity with these catalytic systems. The library was synthesized and screened using a series of parallel reactors each equipped with 12 different positions. As well as biaryl phosphite/phosphoroamidite moieties being present in the ligand design, this ligand library also has the advantage of a flexible ligand scaffold that enables the ligands to be easily tuned in different ligand parameters and how the ligands affect catalytic performance to be explored. With this library in hand(Figure 1), we therefore investigated the effect of systematically varying the position of the phosphoroamidite group at either C-5 (ligands **L1** and **L2**) or C-3 (ligands **L3** and **L4**) of the furanoside backbone, the configuration at C-3 of the furanoside backbone and the substituents and configurations in the biaryl phosphite/phosphoroamidite moieties (**a**–**e**). By carefully selecting the ligand parameters, we achieved high selectivities (regio- and enantioselectivities) and activities in different substrate types.

Results and Discussion

Synthesis of Ligand Libraries

The sequence of ligand synthesis is illustrated in Scheme 1. Ligands **L1**–**L4a**–**e** were synthesized very efficiently from the corresponding easily accessible monotosylated or monotriflated sugar derivatives (**3**, **8** and **12**, Scheme 1). Compounds **3**, **8** and **12** are easily made in a few steps from the corresponding D-xylose or D-glucose.[8,9,10] These compounds (**3**, **8** and **12**) were chosen as intermediates for the preparation of ligands because they will easily allow incorporation of the various elements that will enable us to study the position of the phosphoroamidite (at either C-5 or C-3) as well as the configuration of C-3. Compounds **3**, **8** and **12** were treated with sodium azide to produce the desired azides **4**,[11] **9**[12] and **13**[10] [Scheme 1, step (d)]. Note that the azide formation follows an S_N2-like pathway, so for azides **9** and **13**, the absolute configuration of the stereogenic C-3 is inverted. At this point, the synthesis follows different pathways depending of the ligand to be prepared. Thus, amino alcohol **5** is easily obtained by reduction of the azide **4** using triphenylphosphine.[11] For the preparation of amino alcohol **7**, which differs from **5** in the configuration of C-3, the hydroxy group at C-3 was inverted following a two-step procedure that involves oxidation of the alcohol at C-3 using PCC and reduction of the ketone formed with $NaBH_4$ at low temperature.[13] Subsequent reduction of the azide **6** with triphenylphosphine, as for compound **5**, provides the corresponding amino alcohol **7**.[13]

Amino alcohols **11** and **15** have been synthesized following the same synthetic pathway. Therefore,



Scheme 1. Synthesis of phosphite-phosphoroamidite ligand library **L1**–**L4a**–**e**. (a) ref.[8] (b) ref.[9] (c) ref.[10] (d) DMF/NaN_3 (yields: 86–93%). (e) PPh_3/THF/H_2O (yields: 88–92%). (f) PCC/CH_2Cl_2/molecular sieves 4 Å (yields: 80–83%); then $NaBH_4$/EtOH/H_2O (yields: 79–82%). (g) AcOH/H_2O then $NaIO_4$/$NaHCO_3$/H_2O (yields: 85–91%). (h) $NaBH_4$/EtOH then PPh_3/THF/H_2O (yields: 51–82%). (i) $ClP(OR)_2$; $(OR)_2$ = **a**-**e**/Py/toluene (yields: 34–54%).

compounds **9** and **13** were converted to the corresponding aldehydes **10** and **14**. This transformation takes place *via* acid-catalyzed selective ring opening of the 5,6-di-*O*-acetal ring to produce the corresponding 5,6-diols and subsequent treatment of the latter compounds with sodium metaperiodate to afford the desired compounds **10**[14] and **14**[15] [Scheme 1, step (g)]. Compounds **10** and **14** were then converted to the corresponding amino alcohols **11** and **15** by sequential reduction of the aldehyde group and the azide group by $NaBH_4$ and triphenylphosphine, respectively [Scheme 1, step (h)].[16]

The last step of the ligand synthesis is common for all of them [Scheme 1, step (i)]. Therefore, treating the corresponding 1,3-amino alcohols (**5**, **7**, **11** and **15**) with 2 equivalents of the appropriate *in situ* formed phosphorochloridite [$ClP(OR)_2$; $(OR)_2$ = **a**–**e**] in the presence of pyridine provided easy access to the desired phosphite-phosphoroamidite ligands **L1**–**L4a**–**e**. All the ligands were stable during purification on neutral alumina under an atmosphere of argon and they were isolated as white solids. They were stable at room temperature and very stable to hydrolysis. Elemental analyses were in agreement with the structure assigned. The ^1H and ^{13}C NMR spectra were as expected for these C_1 symmetrical ligands. Two signals for each compound were observed in the ^{31}P NMR spectrum (see Experimental Section). Rapid ring inversions (atropoisomerization) in the biphenyl-phosphorus moieties (**a**–**c**) occurred on the NMR time scale since the expected diastereoisomers were not detected by low-temperature phosphorus NMR.[17]

Allylic Substitution of Acyclic Substrates

In this section we report the use of the chiral phosphite-phosphoroamidite (**L1**–**L4a**–**e**) ligands in the Pd-catalyzed allylic substitution (Figure 2) of linear disubstituted substrates with different steric properties: *rac*-1,3-diphenylprop-2-en-1-yl acetate **S1** (widely used as a model substrate) and *rac*-pent-3-en-2-yl acetate **S2**, and linear monosubstituted substrates: 1-(1-naphthyl)-2-propenyl acetate **S3** and 3-(1-naphthyl)-2-propenyl acetate **S4**. Two nucleophiles were tested. In all cases, the catalysts were generated *in situ* from π-allyl-palladium chloride dimer $[PdCl(\eta^3\text{-}C_3H_5)]_2$ and the corresponding ligand.[1]

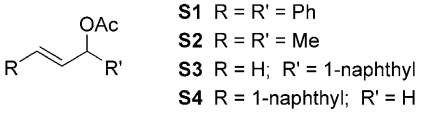
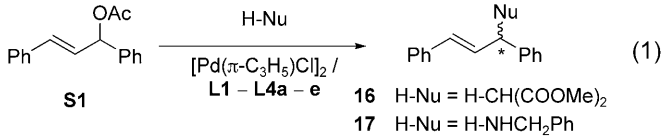


Figure 2. Acyclic substrates.

Allylic Substitution of *rac*-1,3-Diphenylprop-2-en-1-yl Acetate S1 using Dimethyl malonate and Benzylamine as Nucleophiles

In the first set of experiments, we used the palladium-catalyzed asymmetric substitution reactions of **S1** [Eq. (1)], with dimethyl malonate and benzylamine as nucleophiles, to probe the potential of the phosphite-phosphoroamidite ligand library **L1**–**L4a**–**e. S1** was chosen as a substrate because this reaction has been performed with a wide range of ligands enabling the direct comparison of the efficiency of the various ligand systems.[1]



(1)

Initially, we determined the optimal reaction conditions by conducting a series of experiments in which the solvent and ligand-to-palladium ratio were varied. For this purpose we studied the effect of four solvents (tetrahydrofuran, toluene, dimethylformamide and dichloromethane) at three ligand-to-palladium ratios (L/Pd = 0.8, L/Pd = 1.1 and L/Pd = 2) with four ligands (**L1a**, **L2a**, **L3a** and **L4a**). Our results show that the efficiency of the process strongly depended on the nature of the solvent, whereas varying the ligand-to-palladium ratio has no effect (see Supporting Information). The best combination of activity and enantioselectivity was achieved with dichloromethane as solvent.

For the purpose of comparison, the rest of the ligands were tested under optimitzed conditions (i.e., a ligand-to-palladium ratio of 1.1 and dichloromethane as solvent). Table 1 shows the results when dimethyl malonate and benzylamine were used as nucleophiles. These results indicate that catalytic performance (activities and enantioselectivities) is highly affected by the position of the phosphoroamidite group at either C-5 or C-3 of the furanoside backbone, the configuration of C-3 and the substituents and configurations in the biaryl phosphite/phosphoroamidite moieties (**a**–**e**). Activities >2000 mol **S1** $\times$ (mol Pd $\times$ h)$^{-1}$ and enantioselectivities up to 98% were obtained. Catalytic performance in the Pd-catalyzed allylic amination of **S1** followed the same trend as for the allylic alkylation of **S1** (Table 1). Although, as expected, the activities were lower than in the alkylation reaction, they were higher than those obtained with other successful ligands.[1] The stereoselectivity of the amination was the same as for the alkylation reaction, though the CIP descriptor was inverted because of the change in the priority of the groups.

Table 1. Selected results for the Pd-catalyzed allylic substitution of **S1** using the phosphite-phosphoroamidite ligand library **L1**–**L4a**–**e**.[a]

		H-Nu = H-CH(COOMe)$_2$		H-Nu = H-NHCH$_2$Ph	
Entry	Ligand	% Conv. [*t*/min][b]	% *ee*[c]	% Conv. (*t*/h)[b]	% *ee*[c]
1	**L1a**	88 (15)	62 (*S*)	100 (6)	61 (*R*)
2[d]	**L1b**	100 (60)[e]	59 (*S*)[e]	100 (4)	56 (*R*)
3	**L1c**	72 (15)	69 (*S*)	86 (6)	67 (*R*)
4	**L1d**	71 (30)	6 (*S*)	69 (6)	12 (*R*)
5[d]	**L1e**	99 (120)[f]	98 (*S*)[f]	98 (6)	97 (*R*)
6	**L2a**	64 (15)	55 (*S*)	64 (6)	54 (*R*)
7[d]	**L2b**	83 (15)	52 (*S*)	100 (5)	51 (*R*)
8	**L2c**	13 (15)	33 (*S*)	41 (6)	25 (*R*)
9	**L2d**	12 (120)	80 (*S*)	21 (6)	75 (*R*)
10	**L2e**	15 (120)	12 (*S*)	27 (6)	11 (*R*)
11	**L3a**	41 (15)	42 (*R*)	52 (6)	43 (*S*)
12[d]	**L3b**	84 (15)	40 (*R*)	89 (6)	33 (*S*)
13	**L3c**	58 (15)	48 (*R*)	43 (6)	44 (*S*)
14	**L4a**	72 (15)	49 (*S*)	64 (6)	43 (*R*)
15[d]	**L4b**	93 (15)	42 (*S*)	100 (6)	41 (*R*)
16[d]	**L4c**	52 (15)	56 (*S*)	32 (6)	49 (*R*)

[a] All reactions were run at room temperature: 0.5 mol% [PdCl(η^3-C_3H_5)]$_2$, 1.1 mol% ligand, CH_2Cl_2 as solvent, **S1** (0.5 mmol), BSA (1.5 mmol), dimethyl malonate (1.5 mmol).
[b] Conversion percentage determined by ^{1}H NMR.
[c] Enantiomeric excesses determined by HPLC. Absolute configuration drawn in parentheses.
[d] Isolated yields of **16** and **17** were >93% based on recovered starting material.
[e] Reaction carried out using 0.05 mol% of catalyst. TOF = 2280 mol **S1** $\times$ (mol Pd $\times$ h)$^{-1}$ measured after 5 min.
[f] Reaction carried out using 0.05 mol% of catalyst. TOF = 960 mol **S1** $\times$ (mol Pd $\times$ h)$^{-1}$ measured after 5 min.

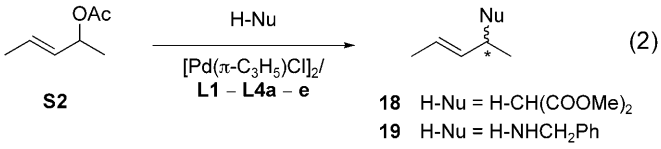
We first studied the effect of the position of the phosphoroamidite group at either C-5 (ligands **L1** and **L2**) or C-3 (ligands **L3** and **L4**) of the furanoside backbone and the configuration of C-3. Ligands **L1** and **L2**, that contain the phosphoroamidite group at the C-5 position, produced better activities and enantioselectivities than ligands **L3** and **L4**, with the phosphoroamidite group at the C-3 position. We also observed a cooperative effect between the position of the phosphoroamidite group and the configuration of carbon atom C-3 of the furanoside backbone. The results indicate that the matched combination is achieved with ligands **L1**, which has the phosphoroamidite moiety attached to C-5 and an *S* configuration of carbon atom C-3 of the tetrahydrofuran ring.

We next studied the effects of the biaryl phosphite/phosphoroamidite moieties using ligands **L1–L4a–e** (Table 1). It was observed that these moieties affected both activities and enantioselectivities of the reaction. The presence of methoxy groups in the *para* position of the biphenyl moieties has a positive effect on activity, but leads to lower enantioselectivities (Table 1, entries 2, 7, 12 and 15). We also observed a cooperative effect between the configuration of the biaryl moieties and the configuration of carbon atom C-3. The results indicated that the matched combination is achieved with ligand **L1e**, which has an *S* configuration at both carbon atom C-3 and in the biaryl phosphite/phosphoroamidite moieties (Table 1, entry 5).

In summary, the best result (in terms of activity and enantioselectivity) was obtained with ligand **L1e** (Table 1, entry 5, TOFs of 960 mol **S1** × (mol Pd × h)$^{-1}$ and *ee*s up to 98%), which contains the optimal combination of ligand parameters (position of the phosphoroamidite group, configuration at C-3 of the furanoside backbone and the substituents and configurations in the biaryl phosphite/phosphoroamidite moieties). These results clearly show the efficiency of using highly modular scaffolds in the ligand design.

Allylic Substitution of *rac*-Pent-3-en-2-yl Acetate S2 using Dimethyl malonate and Benzylamine as Nucleophiles

We also screened the phosphite-phosphoramidite ligand library **L1–L4a–e** in the allylic substitution of the linear substrate **S2** [Eq. (2)].



(2)

Substrate **S2** is less sterically demanding than substrate **S1**, which we used before. Enantioselectivity for **S2** is therefore more difficult to control than with hindered substrates such as **S1**. If *ee*s are to be high, the ligand must create a small chiral pocket (the chiral cavity in which the allyl is embedded) around the metal centre, mainly because of the presence of less sterically demanding methyl *syn* substituents.[1] There are therefore fewer successful catalyst systems for the Pd-catalyzed allylic substitution of this substrate than for the allylic substitution of hindered substrates such as **S1**.[3b,5,18] Due to the flexibility conferred by the biaryl phosphite/phosphoroamidite moieties, we expect to obtain also good enantioselectivities for this substrate.

Preliminary investigations into the solvent and ligand-to-palladium ratio revealed a different trend in solvent effect than with the previously tested substrate **S1**. Enantioselectivities and activities were best when THF was used and the ligand-to-palladium ratio was 1.1 (see Supporting Information).

The results of using the phosphite-phosphoroamidite ligand library **L1–L4a–e** in the optimized conditions are shown in Table 2 (see also Supporting Infor-

Table 2. Selected results for the Pd-catalyzed allylic substitution of **S2** using ligand library **L1–L4a–e.**[a]

Entry	Ligand	% Conv. (*t*/h)[b]0	% *ee*[c]
1	**L1a**	100 (0.5)	10 (*R*)
2[d]	**L1b**	100 (0.3)	8 (*R*)
3	**L1c**	100 (0.5)	34 (*R*)
4	**L1d**	100 (0.5)	58 (*S*)
5	**L1e**	100 (0.5)	39 (*R*)
6[d]	**L2a**	100 (0.5)	16 (*S*)
7[d]	**L2b**	100 (0.3)	9 (*S*)
8	**L2c**	48 (0.5)	36 (*S*)
9	**L2d**	43 (0.5)	21 (*S*)
10	**L2e**	42 (0.5)	74 (*S*)
11	**L3a**	100 (0.5)	10 (*S*)
12[d]	**L3b**	100 (0.3)	6 (*S*)
13	**L3c**	100 (0.5)	31 (*S*)
14	**L3d**	100 (0.5)	16 (*R*)
15[d]	**L4b**	100 (0.3)	12 (*R*)
16	**L4c**	100 (0.5)	43 (*R*)
17	**L4d**	51 (0.5)	72 (*R*)
18[d,e]	**L2e**	82 (4)	84 (*S*)
19[d,e]	**L4e**	68 (4)	83 (*R*)
20[f]	**L2e**	74 (20)	72 (*S*)
21[f]	**L4e**	65 (20)	71 (*R*)

[a] All reactions were run at room temperature: 0.5 mol% $[PdCl(\eta^3\text{-}C_3H_5)]_2$, THF as solvent, 1.1 mol% ligand, **S2** (0.5 mmol), BSA (1.5 mmol), dimethyl malonate (1.5 mmol).
[b] Conversion measured by GC. Reaction time shown in parentheses.
[c] Enantiomeric excesses measured by GC. The absolute configuration appears in parentheses.
[d] Isolated yields of **18** were >92% based on recovered **S2**.
[e] $T = 0\,^{\circ}C$.
[f] Using benzylamine as nucleophile.

mation for more results on the allylic amination reaction). Again, activities and enantioselectivities were affected by the position of the phosphoroamidite group at either C-5 or C-3 of the furanoside backbone, the configuration of C-3 and the substituents and configurations in the biaryl phosphite/phosphoroamidite moieties. However, the effect of these parameters was different from their effect on the substitution of hindered substrate **S1**. Thus, enantioselectivities were best with ligands **L2e** and **L4e** (*ee*s up to 84%; Table 2, entries 18–21). These results, which clearly show again the efficiency of using highly modular scaffolds in the ligand design, are among the best reported for this type of unhindered substrates.[3b,5,18]

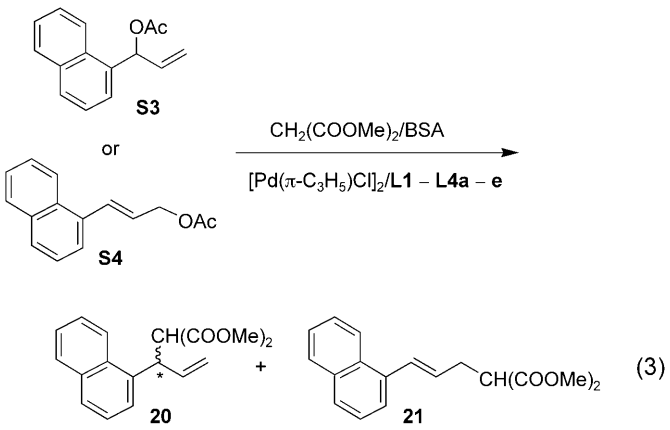
Regarding the effects of the position of the phosphoroamidite group at either C-5 (ligands **L1** and **L2**) or C-3 (ligands **L3** and **L4**) of the furanoside backbone and the configuration of C-3, in contrast to **S1**, the enantioselectivity is mainly affected by the configuration of C-3, while the effect of position of the phosphoroamidite is less pronounced. Therefore, ligands **L2** and **L4** that contain an *R*-configuration at C-3 provide higher enantioselectivities than ligands **L1** and **L3** with an opposite configuration at C-3. However, the sense of enantioselectivity is controlled by both the position of the phosphoroamidite group and the configuration of C-3. Therefore, ligands **L1** and **L4** gave *R*-substitution products, whereas ligands **L2** and **L3** gave *S*-substitution products.

The effect of the substituents of the biphenyl phosphite/phosphoroamidite moieties on catalytic performance is similar to the effect in the previous substitution of **S1**. However, the cooperative effect between the configuration of the biaryl phosphite/phosphoroamidite moieties and the configurations of the ligand backbone is different. This resulted in a matched combination for ligands **L2e** and **L4e**, which have an *R*-configuration at carbon atom C-3 and an *S*-configuration in the biaryl phosphite/phosphoroamidite moieties.

In summary, the results indicate that the size of the chiral pocket is mainly controlled by the configuration of carbon atom C-3 and the substituents/configuration of the biaryl moieties. Thus, ligands **L2** and **L4** lead to a smaller chiral pocket and therefore to higher enantioselectivities than ligands **L1** and **L3**. Moreover, both enantiomers of the substitution products **18** and **19** can be obtained in high enantioselectivity by simple changing the position of the phosphoroamidite in ligands **L2** and **L4**. Interestingly, comparing these excellent results with the poor enantioselectivity obtained with the related diphosphite ligands (*ee*s up to 59%),[4b] we can conclude that the introduction of a phosphoroamidite moiety has been highly advantageous.

Allylic Substitution of Monosubstituted Linear Substrates S3 and S4

To further study the potential of these readily available ligands, we also tested **L1**–**L4a**–**e** in the the regio- and stereoselective allylic alkylation of 1-(1-naphthyl)-2-propenyl acetate **S3** and 3-(1-naphthyl)-2-propenyl acetate **S4** with dimethyl malonate as nucleophile [Eq. (3)].



(3)

For these substrates, not only does the enantioselectivity of the process need to be controlled but regioselectivity is also a problem because a mixture of regioisomers can be obtained. Most Pd catalysts developed to date favour the formation of achiral linear product **21** rather than the desired branched isomer **20**.[19] The development of highly regio- and enantioselective Pd catalysts is therefore still a challenge.[5a,c,20]

The results obtained with the phosphite-phosphoroamidite ligand library **L1**–**L4a**–**e** are summarized in Table 3. High activities and enantioselectivities up to 90% combined with regioselectivities up to 75% in favour of the branched product **20** were obtained, under standard reaction conditions, with the Pd/**L2d** and Pd/**L4d** catalyst systems. The results indicated that the selectivity (regio- and enantioselectivity) is mainly affected by the configuration of C-3 and the substituents/configuration in the biaryl moieties, while the effect of position of the phosphoroamidite is less pronounced. The trade-off between regio- and enantioselectivities was therefore best for ligands that contain an *R*-configuration at C-3 (ligands **L2** and **L4**) and either bulky *tert*-butyl groups at both *ortho* and *para* positions of the biphenyl moieties or bulky *R*-binaphthyl phosphite-phosphoroamidite moieties.

These results are among the best reported for this type of substrates.[5a,c,20] Therefore, the replacement of a phosphite moiety by a phosphoroamidite group in related diphosphite ligands has lead again to higher regio- (up to 75% *vs.* up to 29%[4b]) and enantioselec-

Table 3. Selected results for the Pd-catalyzed allylic alkylation of monosubstituted substrate **S3** and **S4** using the ligand library **L1–L4a–e** under standard conditions.[a]

Entry	Ligand	Substrate	% Conv.[b] (min)	**20**/**21**[c]	% *ee*[d]
1	**L1a**	**S3**	100 (120)	20/80	21 (*S*)
2	**L1b**	**S3**	100 (120)	30/70	17 (*S*)
3	**L1c**	**S3**	100 (120)	35/65	51 (*S*)
4	**L1d**	**S3**	100 (120)	70/30	7 (*R*)
5	**L1e**	**S3**	100 (120)	65/35	66 (*S*)
6	**L2a**	**S3**	100 (120)	70/30	71 (*S*)
7	**L2b**	**S3**	100 (120)	70/30	9 (*S*)
8	**L2c**	**S3**	100 (120)	35/65	65 (*S*)
9[e]	**L2d**	**S3**	100 (180)	70/30	90 (*S*)
10	**L2e**	**S3**	100 (120)	60/40	61 (*S*)
11	**L3a**	**S3**	100 (120)	55/45	36 (*R*)
12	**L3b**	**S3**	100 (120)	40/60	5 (*R*)
13	**L3c**	**S3**	100(120)	45/65	30 (*R*)
14	**L4a**	**S3**	100 (120)	60/40	73 (*S*)
15	**L4b**	**S3**	100 (120)	60/40	6 (*S*)
16	**L4c**	**S3**	100 (120)	25/75	63 (*S*)
17	**L4d**	**S3**	68 (120)	75/25	89 (*S*)
18[e]	**L2d**	**S4**	100 (180)	70/30	90 (*S*)

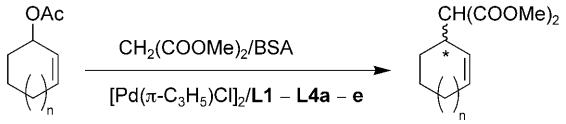
[a] All reactions were run at room temperature: 1 mol% $[PdCl((\eta^3\text{-}C_3H_5)]_2$, dichloromethane as solvent, 2.2 mol% ligand, substrate (0.5 mmol), BSA (1.5 mmol), dimethyl malonate (1.5 mmol).
[b] Reaction time in minutes shown in parentheses.
[c] Percentage of branched (**20**) and linear (**21**) isomers.
[d] Enantiomeric excesses of **20** determined by HPLC. The absolute configuration appears in parentheses.
[e] Isolated yields of **20** were 67%.

tivities (up to 90% *vs.* up to 33%[4b]). In addition, the efficiency of the ligand design is also corroborated by the fact that these Pd phosphite-phosphoroamidite catalysts provided higher combinations of regio- and enantioselectioselectivities than with previously published 1,2-amino alcohol-based phosphite-phosphoroamidite ligands.[3b]

Allylic Alkylation of Cyclic Substrates

Encouraged by the excellent results obtained for several di- and monosubstituted linear substrates, we examined the allylic alkylation of cyclic substrates **S5** and **S6**. The enantioselectivity with these substrates is difficult to control, mainly because of the presence of less sterically bulky *anti* substituents. These *anti* substituents are thought to play a crucial role in the enantioselection observed with cyclic substrates in the corresponding Pd-allyl intermediates.[1]

In this section we show that the chiral phosphite-phosphoroamidite ligand library **L1**–**L4a**–**e** applied above to the Pd-catalyzed allylic substitution of linear substrates (**S1**–**S4**) can also be used for cyclic substrates (*ee*s up to 91%). We tested two cyclic substrates [Eq. (4)]: *rac*-cyclohex-2-en-1-yl acetate **S5** (which is widely used as a model substrate) and *rac*-cyclohep-2-en-1-yl acetate **S6**.



S5 n = 1
S6 n = 2

22 n = 1
23 n = 2

(4)

Preliminary investigations into the solvent effect and ligand-to-palladium ratio showed the same trends as with the previously tested unhindered linear substrate **S2**. The trade-off between enantioselectivities and reaction rates was therefore optimum with THF and a ligand-to-palladium ratio of 1.1 (see Supporting Information).

The results of using the phosphite-phosphoroamidite ligand library **L1**–**L4a**–**e** under the optimized conditions are shown in Table 4. We also obtained high activities and enantioselectivities (up to 91%) in the allylic substitution of cyclic substrates **S5** and **S6** with Pd/**L2a** and Pd/**L3a**.

Activities followed the same trend as those observed in the alkylation of **S1** and **S2**. However, the effect of the ligand parameters on the enantioselectivity was different from the effect observed in the substitution of the linear substrates **S1** and **S2**. Although, we observed a cooperative effect between the position of the phosphoroamidite group and the configuration of carbon atom C-3, in contrast to the substitution of **S1** and **S2**, this resulted in a matched combination for ligands **L2** and **L3**. Ligands **L2** have the phosphoroamidite group at the C-5 position and an *R*-configuration at C-3, while ligands **L3** have the phosphoroamidite group at the C-3 position and an *S*-configuration at C-3 stereocentre. Moreover, unlike the substitution of **S1** and **S2**, the presence of bulky *tert*-butyl groups at both *ortho* and *para* positions of the biaryl moieties has an extremely positive effect on enantioselectivity.

Interestingly, the sense of enantioselectivity is mainly governed by the configuration of C-3. Thus, both enantiomers of the substitution products **22** and **23** can be accessed in high enantioselectivities by simple changing the configuration of C-3 (Table 4, entries 6 and 11).

To sum up, the best enantioselectivities were therefore obtained with ligands **L2a** and **L3a**, which have bulky substituents at the *ortho* and *para* positions of the biaryl moieties and the appropriate combination of the position of the phosphoroamidite group and the configuration at C-3. These results are among the best reported for this type of unhindered substra-

Table 4. Selected results for the Pd-catalyzed allylic alkylation of **S5** and **S6** using the phosphite-phosphoroamidite ligand library **L1**–**L4a**–**e**.[a]

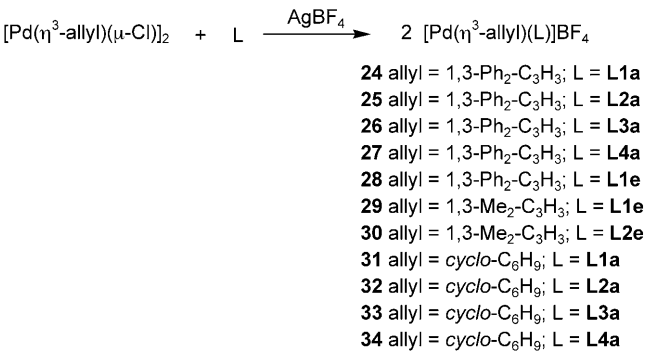
Entry	Ligand	**S5**		**S6**	
		% Conv. (*t*/min)[b]	% *ee*[c]	% Conv. (*t*/h)[b]	% *ee*[c]
1[d]	**L1a**	100 (120)	12 (*R*)	63 (6)	17 (*R*)
2	**L1b**	100 (120)	4 (*R*)	75 (6)	8 (*R*)
3	**L1c**	72 (120)	40 (*R*)	45 (6)	49 (*R*)
4	**L1d**	20 (120)	19 (*R*)	13 (6)	17 (*R*)
5	**L1e**	26 (120)	67 (*S*)	11 (6)	64 (*S*)
6[d]	**L2a**	100 (120)	85 (*S*)	52 (6)	91 (*S*)
7	**L2b**	100 (120)	65 (*S*)	69 (6)	66 (*R*)
8	**L2c**	33 (120)	32 (*S*)	39 (6)	35 (*R*)
9	**L2d**	11 (120)	52 (*R*)	9 (6)	43 (*R*)
10	**L2e**	10 (120)	78 (*S*)	10 (6)	78 (*S*)
11[d]	**L3a**	100 (120)	80 (*R*)	46 (6)	81 (*R*)
12	**L3b**	100 (120)	53 (*R*)	65 (6)	49 (*R*)
13	**L3c**	62 (120)	27 (*R*)	45 (6)	32 (*R*)
14[d]	**L4a**	100 (120)	57 (*S*)	65 (6)	55 (*S*)
15	**L4b**	100 (120)	50 (*S*)	77 (6)	54 (*S*)
16	**L4c**	42 (120)	24 (*S*)	32 (6)	26 (*S*)

[a] All reactions were run at room temperature: 0.5 mol% $[PdCl(\eta^3\text{-}C_3H_5)]_2$, THF as solvent, 1.1 mol% ligand, substrate (0.5 mmol), BSA (1.5 mmol), dimethyl malonate (1.5 mmol).
[b] Conversion measured by GC. Reaction time shown in parentheses.
[c] Enantiomeric excesses measured by GC. The absolute configuration appears in parentheses.
[d] Isolated yields of **22** and **23** > 93% based on recovered starting material.

tes.[1f,5a,c,18,21] Again the replacement of a phosphite moiety by a phosphoroamidite group in the ligand design leads to higher enantioselectivities than when the corresponding diphosphite ligands are used (*ee*s up to 34%).[4b]

Origin of Enantioselectivity: Study of the Pd-π-Allyl Intermediates

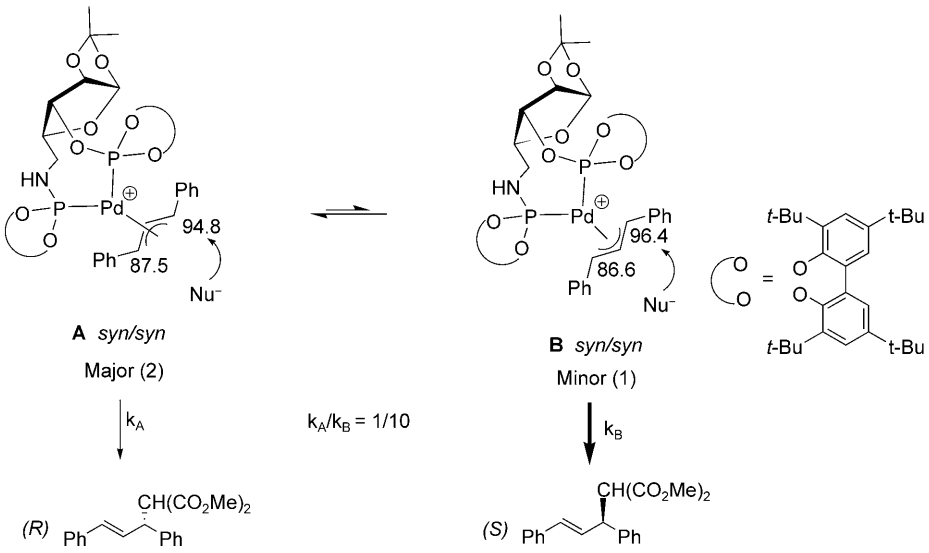
To provide further insight into how ligand parameters affect catalytic performance, we studied the Pd-π-allyl compounds **24**–**34**, $[Pd(\eta^3\text{-allyl})(L)]BF_4$ (L = phosphite-phosphoroamidite ligands), since they are key intermediates in the allylic substitution reactions studied.[1] These ionic palladium complexes, which contain 1,3-diphenyl, 1,3-dimethyl or cyclohexenyl allyl groups, were prepared using the previously described method from the corresponding Pd-allyl dimer and the appropriate ligand in the presence of silver tetrafluoroborate (Scheme 2).[22] The complexes were characterized by elemental analysis and by ^1H, ^{13}C and ^{31}P NMR spectroscopy. The spectral assignments (see Experimental Section) were based on information from ^1H-^1H, ^{31}P-^1H and ^{13}C-^1H correlation measurements in combination with ^1H-^1H NOESY experiments. Unfortunately, we were unable to obtain any crystal of sufficient quality to perform X-ray diffraction measurements.



Scheme 2. Preparation of $[Pd(\eta^3\text{-allyl})(L)]BF_4$ complexes **24**–**34**.

Palladium 1,3-Diphenylallyl Complexes

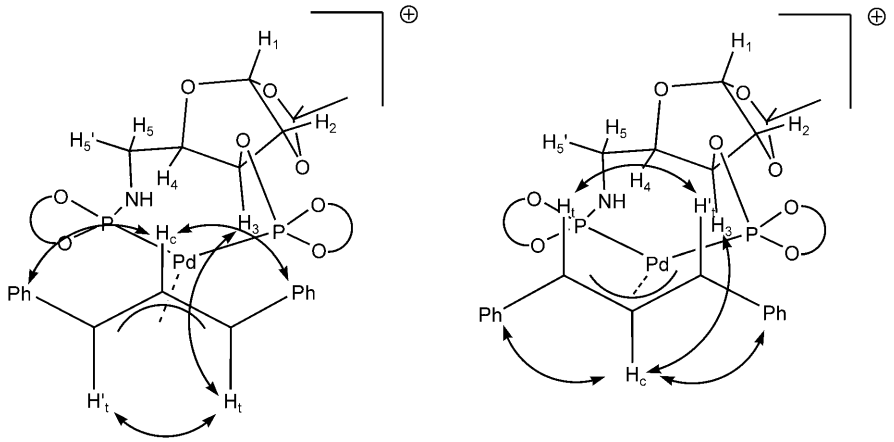
When the phosphite-phosphoroamidite ligand library **L1**–**L4a**–**e** was used in the allylic substitution of substrate **S1**, the catalytic results indicated that enantioselectivity is highly affected by the ligand parameters. A phosphoroamidite group attached at C-5 of the furanoside backbone, an *S*-configuration at C-3 of the tetrahydrofuran ring and *S*-binaphthyl phosphite/phosphoroamidite moieties are therefore required if enantioselectivity is to be high. To understand this catalytic behaviour, we studied Pd-π-allyl complexes **24**–**28**, which contain ligands **L1a, L2a**, **L3a**, **L4a** and **L1e**, respectively. With complexes **24**–**27**, we contemplated the four possible combinations of varying the



Scheme 3. Diastereoisomer Pd-allyl intermediates for **S1** with ligand **L1a**. The relative amounts of each isomer are drawn in parenthesis. The chemical shifts (in ppm) of the allylic terminal carbons are shown.

position of the phosphoroamidite group and the configuration of carbon atom C-3 and their study will allow us to understand the effect of these parameters. Finally with complex **28**, we studied the matched combination of the observed cooperative effect between the configuration at C-3 and the configuration of the biaryl phosphite/phosphoroamidite moieties.

The VT-NMR (30 °C to −80 °C) study of Pd-allyl intermediate **24**, which contains ligand **L1a**, had a mixture of two isomers in equilibrium in a ratio of 2:1 (see Experimental Section).[23] Both isomers were unambiguously assigned by NMR (^{1}H, ^{31}P, ^{13}C, ^{1}H-^{1}H, ^{1}H-^{13}C and ^{1}H-^{31}P correlation and NOESY experiments) to the two *syn*/*syn endo* **A** and *exo* **B** isomers (Scheme 3). In both isomers, the NOE indicates interactions between both terminal protons of the allyl group and also between the central allyl proton with *ortho* hydrogens of both phenyl groups of the allyl ligand, which clearly indicates a *syn*/*syn* disposition (Figure 3). Moreover, hydrogen H-3 of the sugar backbone shows a NOE interaction with one of the terminal allyl protons of the major isomer **A**, while in **B** isomer this interaction appears with the central allyl proton. Such interactions can be explained by assuming a *syn*/*syn endo* disposition for isomer **A** and a *syn*/*syn exo* disposition for isomer **B** (Figure 3). For both isomers, the carbon NMR chemical shifts indicate that the more electrophilic allyl carbon terminus is *trans* to the phosphoroamidite moiety. Assuming that the nucleophilic attack takes place at the more electrophilic allyl carbon terminus[1] and on the basis of the observed stereochemical outcome of the reac-



syn/*syn* **24A** *syn*/*syn* **24B**

Figure 3. Relevant NOE contacts from NOESY experiment of [Pd(η^3-1,3-diphenylallyl)(**L1a**)]BF_4 (**24**) isomers.

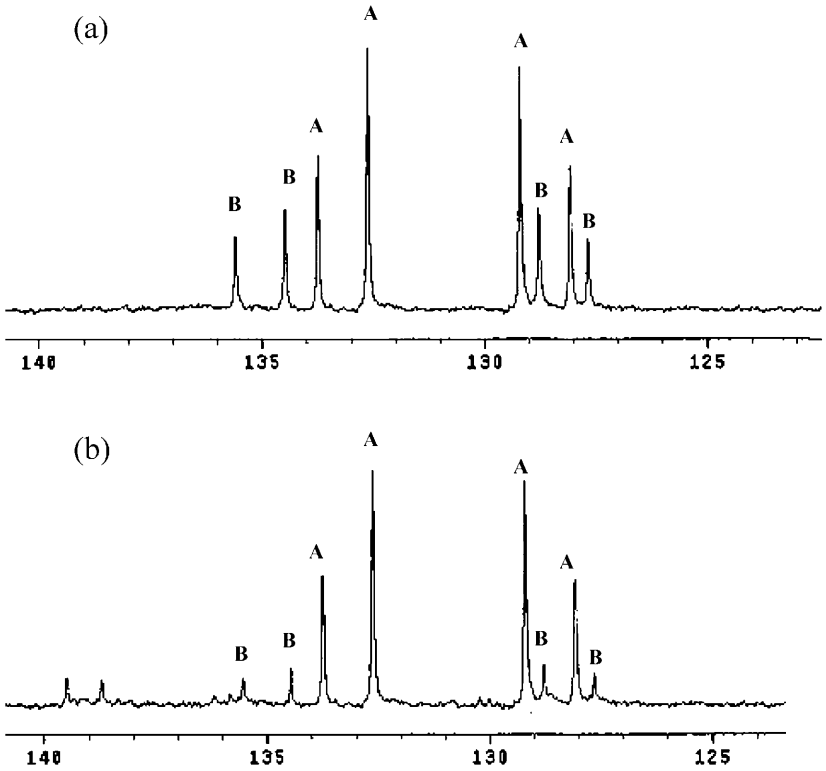


Figure 4. $^{31}P\{^{1}H\}$ NMR spectra of [Pd(η^3-1,3-diphenylallyl)(**L1a**)]BF_4 (**24**) in CD_2Cl_2 at −60 °C (a) before the addition of sodium malonate and (b) after the addition of sodium malonate.

tion [62% (*S*) in product **16**], and as the enantiomeric excess of alkylation product **16** differs from the diastereoisomeric excess [*de* = 33% (*R*)] of the Pd intermediates, the **B** isomer must react faster than the **A** isomer. To prove this we also studied the reactivity of the Pd intermediates with sodium malonate at low temperature by *in situ* NMR (Figure 4). Our results show that the minor isomer **B** reacts around 10 times faster than isomer **A**. If we take into account the relative reaction rates and the abundance of both isomers, the calculated *ee* should be 66% (*S*), which matches the *ee* obtained experimentally.[24] We can therefore conclude that the nucleophilic attack takes place predominantly at the allyl terminus *trans* to the phosphoroamidite moiety of the minor **B** Pd intermediate. This is also consistent with the fact that, for both isomers, the most electrophilic allylic terminal carbon atom is the one *trans* to the phosphoroamidite in the minor **B** isomer.

The VT-NMR study of Pd-allyl intermediate **25**, which contains ligand **L2a**, also revealed a mixture of two *syn*/*syn endo* (**A**) and *exo* (**B**) isomers but in a ratio of 1:1 (see Experimental Section). In both isomers, the NOE indicates interactions between both terminal protons of the allyl group and also between the central allyl proton with *ortho* hydrogens of both phenyl groups of the allyl ligand, which clearly indicates a *syn*/*syn* disposition (Figure 5). Moreover, hydrogen H-3 of the sugar backbone shows an NOE interaction with the central allyl proton of the major isomer **A**, while in **B** isomer this interaction appears with one of the terminal allyl protons. Such interactions can be explained by assuming a *syn*/*syn endo* disposition for isomer **A** and a *syn*/*syn exo* disposition for isomer **B** (Figure 5). Also, the more electrophilic allyl carbon terminus was *trans* to the phosphoroamidite moiety (Scheme 4). However, an important difference between complexes **24** and **25** is the lower electronic differentiation between the more electrophilic allylic terminus carbon atoms of both isomers (**A** and **B**) in complex **25** [$\Delta(\delta^{13}C) \approx 0.8$ ppm] than in complex **24** 8 [$\Delta(\delta^{13}C) \approx 1.6$ ppm]. This low electronic differentiation can explain the lower enantioselectivity obtained with Pd/**L2a** in respect to Pd/**L1a**. In accordance, the reactivity of the Pd intermediates with sodium malonate at low temperature by *in situ* NMR indicates that isomer **B** in complex **25** reacts only 3 times faster than isomer **A**.

The VT-NMR study of Pd-allyl intermediate **26**, which contains ligand **L3a**, revealed also a mixture of two *syn*/*syn endo* (**A**) and *exo* (**B**) isomers in a ratio of 1:2 (Scheme 5). Again, the more electrophilic allyl carbon terminus was *trans* to the phosphoroamidite moiety. Unlike complex **24**, the effect of changing the position of the phosphoroamidite moiety produces a lower electronic differentiation between the more

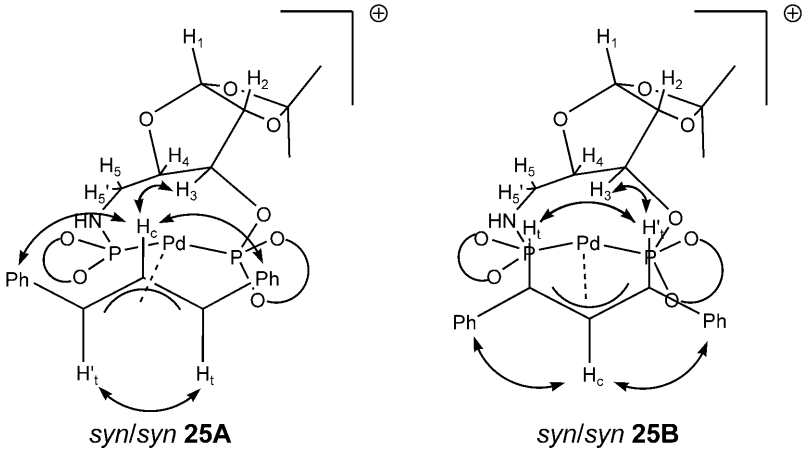
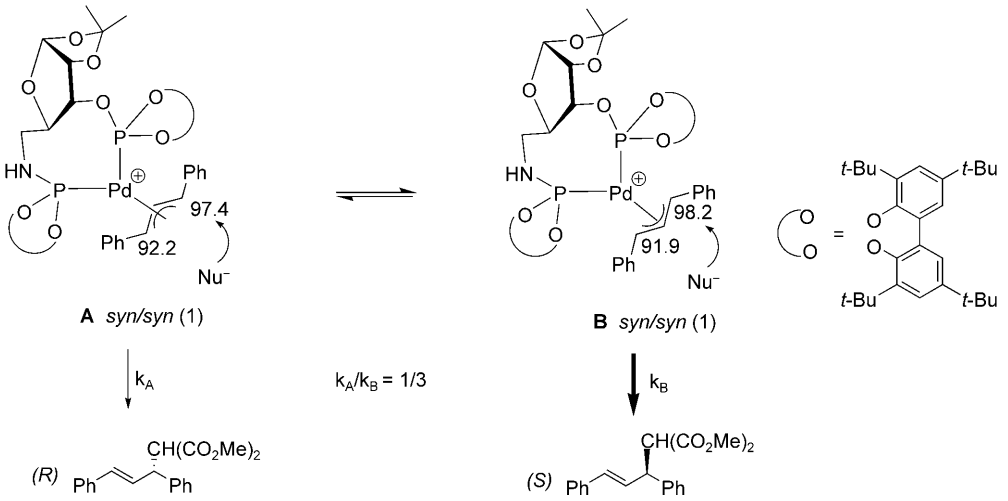
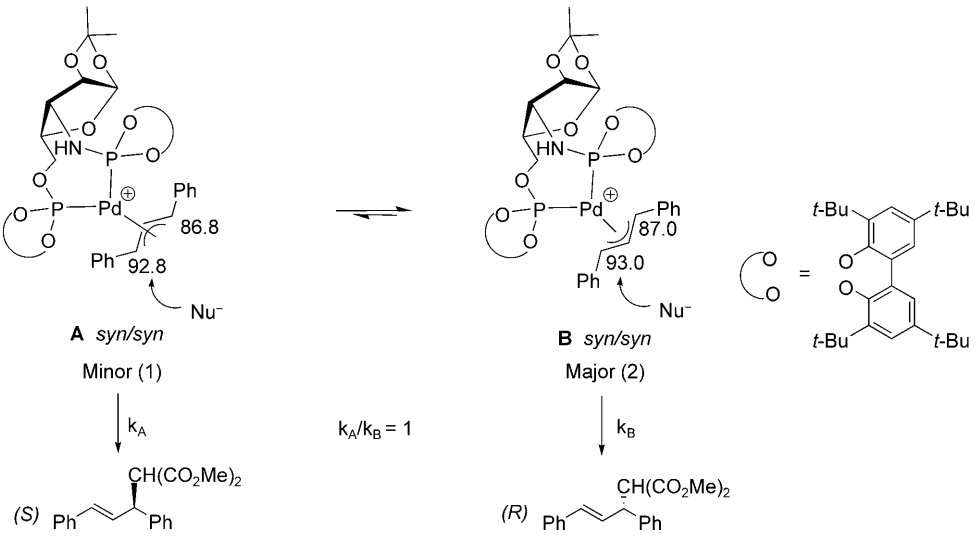


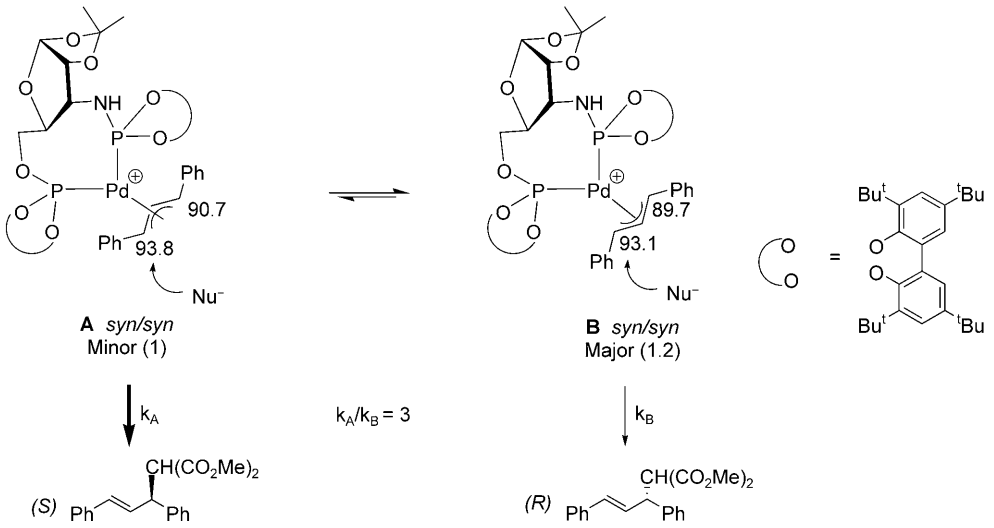
Figure 5. Relevant NOE contacts from NOESY experiment of [Pd(η^3-1,3-diphenylallyl)(**L2a**)]BF_4 (**25**) isomers.



Scheme 4. Diastereoisomer Pd-allyl intermediates for **S1** with ligand **L2a**. The relative amounts of each isomer are drawn in parenthesis. The chemical shifts (in ppm) of the allylic terminal carbons are shown.



Scheme 5. Diastereoisomer Pd-allyl intermediates for **S1** with ligand **L3a**. The relative amounts of each isomer are drawn in parenthesis. The chemical shifts (in ppm) of the allylic terminal carbons are shown.



Scheme 6. Diastereoisomer Pd-allyl intermediates for **S1** with ligand **L4a**. The relative amounts of each isomer are drawn in parenthesis. The chemical shifts (in ppm) of the allylic terminal carbons are shown.

electrophilic allylic terminus carbon atoms of both isomers (**A** and **B**) of complex **26** [$\Delta(\delta^{13}C) \approx 0.2$ ppm] than in complex **24** [$\Delta(\delta^{13}C) \approx 1.6$ ppm]. This low electronic differentiation suggests that the nucleophile can attack both isomers at a similar rate and fully accounts for the enantioselectivity observed.[25]

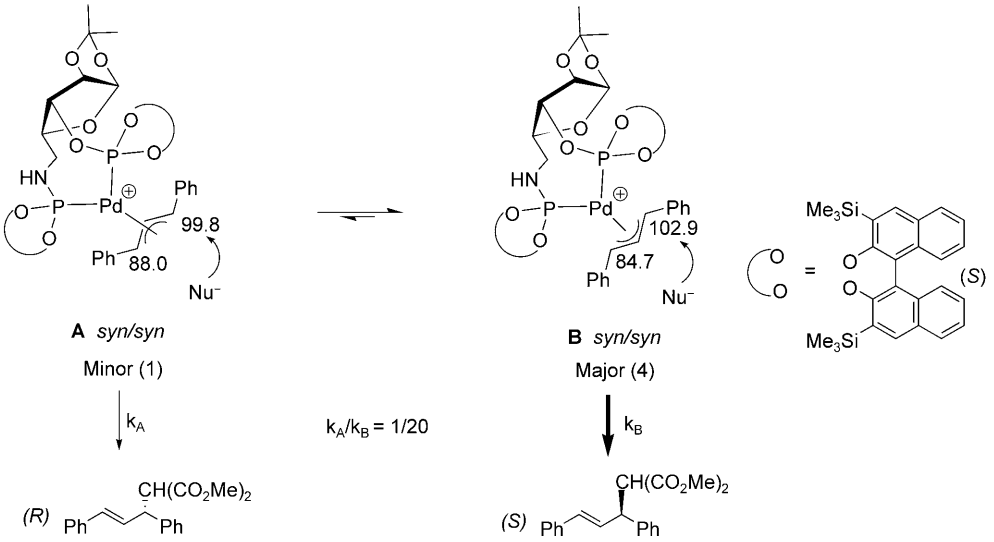
The VT-NMR study of Pd-1,3-diphenylallyl intermediate **27**, which contains ligand **L4a**, indicated the presence of a mixture of two *syn*/*syn endo* (**A**) and *exo* (**B**) isomers in a ratio of 1:1.2 (Scheme 6). In comparison with complex **26**, which contains ligand **L3a**, we found that the relative amount of isomer **A** with respect to **B** increased as well as the electronic differentiation between the more electrophilic allylic terminus carbon atoms of both isomers (**A** and **B**). These findings indicate that the nucleophilic attack takes place preferentially at the allyl terminus *trans* to the phosphoroamidite moiety of the **A** Pd intermediate.[26] These facts explain the higher enantioselectivity obtained with Pd/**L4a** than with Pd/**L3a**.

Finally, we studied the palladium intermediate [Pd(η^3-1,3-diphenylallyl)(**L1e**)]BF_4 (**28**), which contains enantiopure *S*-binaphthyl ligand **L1e**. This ligand provides the highest enantioselectivity and therefore contemplates the correct combination of ligand parameters (position of the phosphoroamidite moiety, configuration of C-3 at the ligand backbone and the substituents/configuration at the biaryl moieties). The VT-NMR study performed showed a mixture of the two *syn*/*syn endo* (**A**) and *exo* (**B**) isomers in a ratio of 1:4 (Scheme 7). Again, for both isomers, the carbon NMR chemical shifts indicate that the most electrophilic allyl carbon terminus is *trans* to the phosphoroamidite moiety. Comparing with the other Pd-1,3-diphenylallyl intermediates studied **24**–**27**, this presents the highest electronic differentiation between the more electrophilic allylic terminus carbon atoms of both isomers (**A** and **B**) [$\Delta(\delta^{13}C) \approx 3.1$ ppm] and also the highest population of the fast reacting isomer **B**.[27] These facts are in agreement with the high enantioselectivity observed using this ligand.

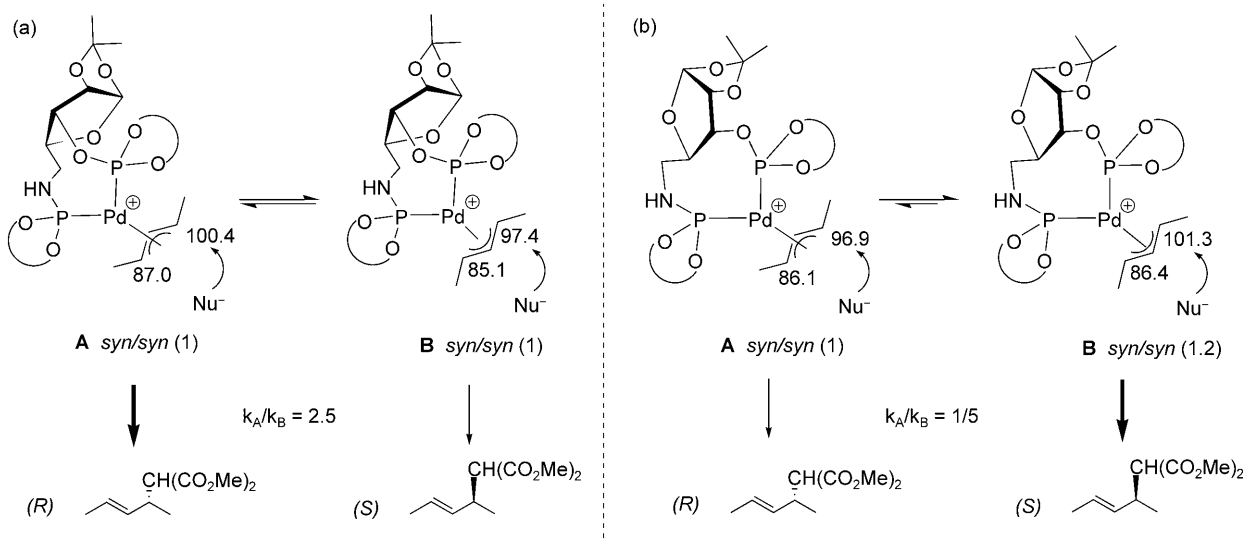
Palladium 1,3-Dimethylallyl Complexes

When the phosphite-phosphoroamidite ligand library **L1**–**L4a**–**e** was used in the allylic substitution of substrate **S2**, the catalytic results revealed a different trend regarding the effect of the ligand parameters than with the previously hindered substrates **S1**. The enantioselectivity is mainly therefore affected by the configuration of C-3, while the effect of position of the phosphoroamidite is less pronounced. Therefore, ligands **L2** and **L4** that contains an *R*-configuration at C-3 provide higher enantioselectivities than ligands **L1** and **L3** with an opposite configuration at C-3. To understand this catalytic behaviour, we studied Pd-π-allyl complexes **29** and **30**, which contain ligands **L1e** and **L2e**, respectively. While ligand **L2e**, which has an *R*-configuration at C-3, provided high enantioselectivities (Table 2, entries 18 and 19, *ee*s up to 84%), ligand **L1e**, with an opposite configuration at C-3, was less enantioselective (Table 2, entry 5, *ee*s up to 39%).

For both Pd-1,3-dimethylallyl intermediates **29** (**L1e**) and **30** (**L2e**), the study of the VT-NMR (35 °C to −80 °C) indicated the presence of a mixture of two isomers (**A** and **B**) at a ratio of 1:1 for complex **29** and at a ratio of 1:1.2 for complex **30** (Scheme 8). All species were assigned by NOE to the *syn*/*syn endo* **A** and *exo* **B** isomers (Scheme 8). For both complexes,



Scheme 7. Diastereoisomer Pd-allyl intermediates for **S1** with ligand **L1e**. The relative amounts of each isomer are drawn in parenthesis. The chemical shifts (in ppm) of the allylic terminal carbons are shown.



Scheme 8. Diastereoisomer Pd-allyl intermediates (a) **29** for **S2** with ligand **L1e** and (b) **30** for **S2** with ligand **L2e**. The relative amounts of each isomer are drawn in parenthesis. The chemical shifts (in ppm) of the allylic terminal carbons are shown.

the NOE indicates interactions between both terminal protons of the allyl group and also between the central allyl proton with methyl protons of the allyl ligand, which clearly indicates a *syn*/*syn* disposition for all the isomers (Figure 6). For isomers **29A** and **30B**, hydrogen H-3 of the sugar backbone shows an NOE interaction with one of the terminal allyl protons, while in **29B** and **30A** isomers this interaction appears with the central allyl proton. Such interactions can be explained by assuming a *syn*/*syn endo* disposition for isomers **A** and a *syn*/*syn exo* disposition for isomers **B** (Figure 6). As for the previous 1,3-diphenylallyl intermediates, the NMR data indicate that the more electrophilic allyl terminal carbon is *trans* to the phosphoroamidite moiety. However, for complex **29** the most electophilic allyl terminal carbon is located in isomer **A**, while for complex **30** it is located at isomer **B**. This together with the facts that for complex **30** both the population of the faster reacting isomer and the relative reaction rates are higher[28] than for complex **29** explains the difference in enantioselectivities observed for both catalytic systems.

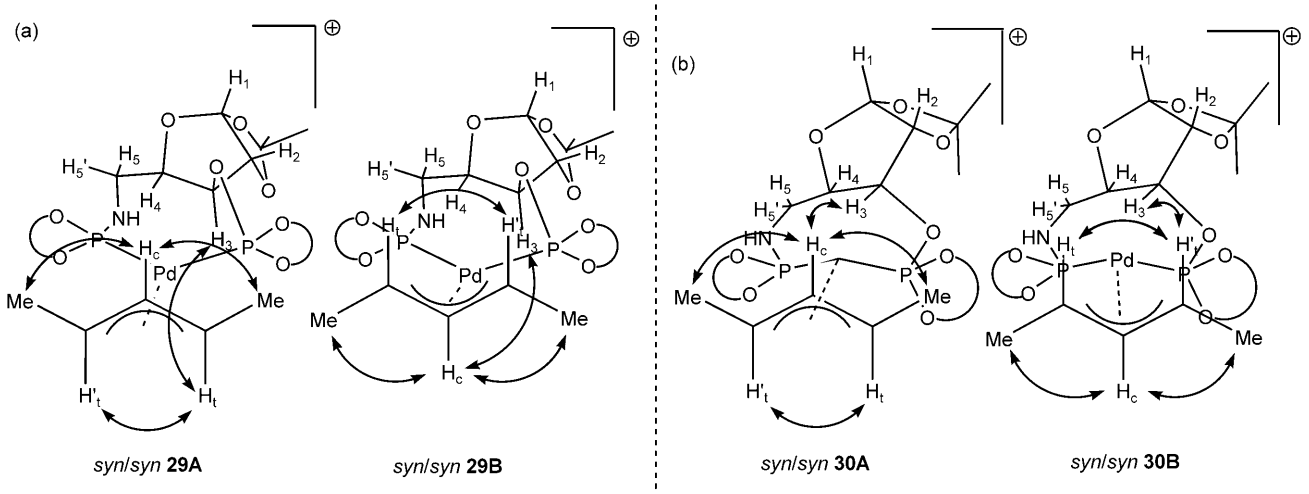
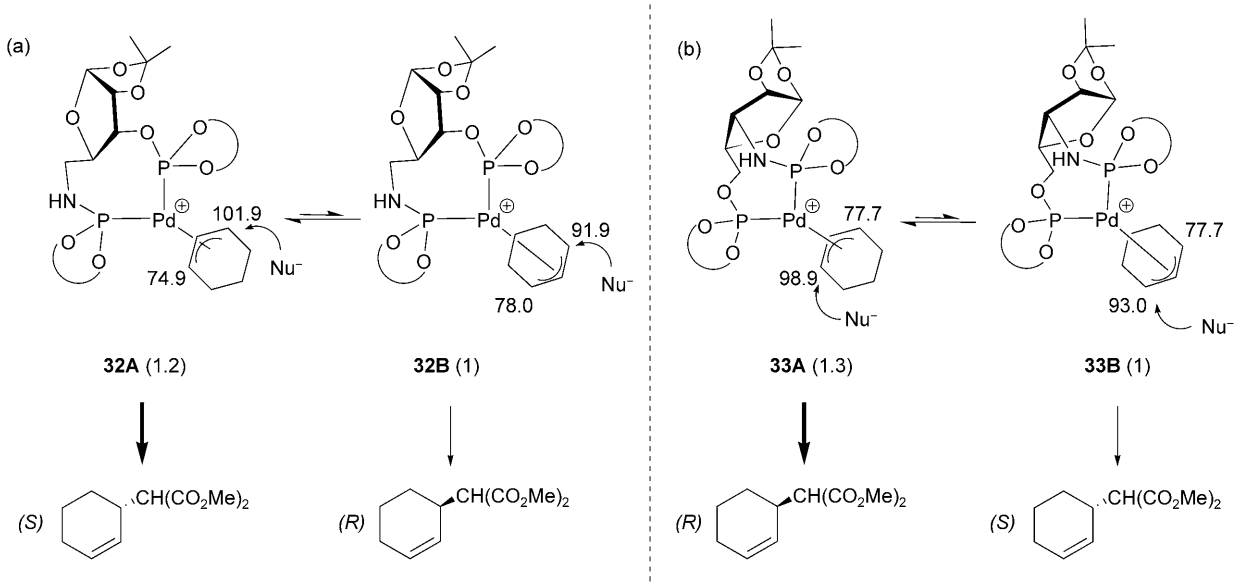


Figure 6. Relevant NOE contacts from NOESY experiments of: (a) [Pd(η^3-1,3-dimethylallyl)(**L1e**)]BF_4 (**29**) isomers and (b) [Pd(η^3-1,3-dimethylallyl)(**L2e**)]BF_4 (**30**) isomers.

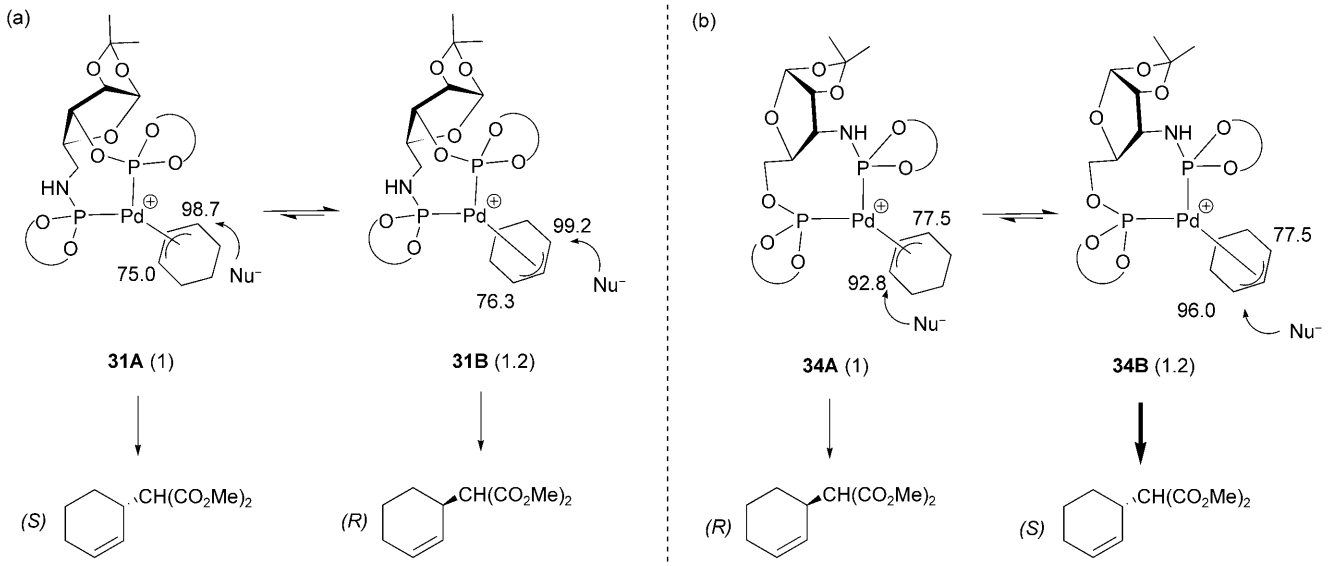
Palladium 1,3-Cyclohexenylallyl Complexes

When the phosphite-phosphoroamidite ligand library **L1**–**L4a**–**e** was used in the allylic substitution of cyclic substrates **S5** and **S6**, the catalytic results showed that the effect of the ligand parameters on the enantioselectivity was different from the effect observed in the substitution of the linear substrates **S1** and **S2**. The best results were obtained with ligands **L2** and **L3**, which have either the phosphoroamidite group at C-5 position and an *R*-configuration at C-3 or the phosphoroamidite group at C-3 position and an *S*-configuration at C-3 stereocenter, while the other combinations provided lower enantioselectivity. To understand this catalytic behavior, we studied Pd-π-allyl complexes **31**–**34**, which contain ligands **L1a**, **L2a**, **L3a** and **L4a**.

The VT NMR (35 °C to −80 °C) of Pd intermediates **31**–**34**, which contains ligands **L1a**, **L2a**, **L3a** and **L4a**, showed a mixture of the two possible isomers in a ratio of 1:1.2, 1:1.2, 1:1.3 and 1.2:1, respectively (Scheme 9 and Scheme 10). All the isomers were unambiguously assigned by NOE to the *endo* **A** and *exo* **B** isomers (Figure 7). Therefore, for isomers **32A** and **34A**, the NOE indicates interactions between the H-3 of the furanoside backbone and the central allyl



Scheme 9. Diastereoisomer Pd-allyl intermediates: (a) **32** for **S5** with ligand **L2a** and (b) **33** for **S5** with ligand **L3a**. The relative amounts of each isomer are drawn in parenthesis. The chemical shifts (in ppm) of the allylic terminal carbons are shown.



Scheme 10. Diastereoisomer Pd-allyl intermediates: (a) **31** for **S5** with ligand **L1a** and (b) **34** for **S5** with ligand **L4a**. The relative amounts of each isomer are drawn in parenthesis. The chemical shifts (in ppm) of the allylic terminal carbons are shown.

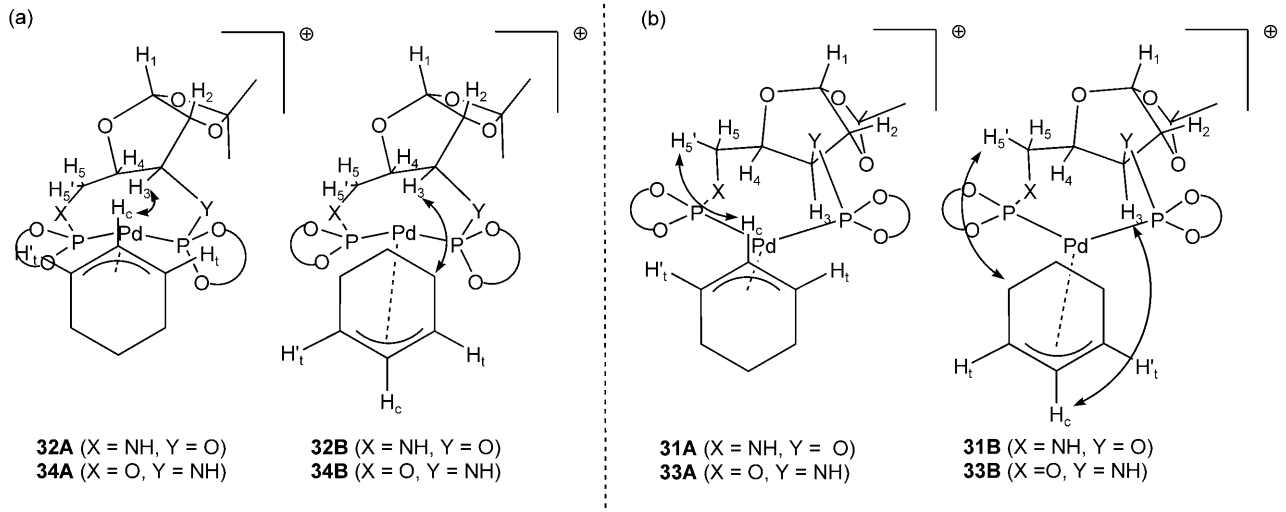


Figure 7. Relevant NOE contacts from NOESY experiment for: (a) complexes **32** and **34** and (b) complexes **31** and **33**.

proton, while for isomers **32B** and **34B** this interaction appears with one of the methylene hydrogens of the allyl ligand (Figure 7a). However, for isomers **31B** and **33B**, the NOE indicates interactions between H-3 and the central allyl proton and also between H-5 and one of the methylene hydrogens of the allyl ligand (Figure 7b). For all isomers, the carbon NMR chemical shifts indicated that the most electrophilic allylic terminus carbon is *trans* to the phosphoroamidite moiety. The *in situ* NMR study of the reactivity of the Pd intermediates with sodium malonate at low temperature showed that: (a) for complexes **32** and **33**, the most reacting isomer correspond to the major isomers **A** ($k_A/k_B > 8$); (b) for complex **34**, the most reacting isomer is **B** ($k_A/k_B \approx 1/3$) and (c) for complex **31**, both isomers reacts at a similar rate ($k_A/k_B \approx 1$). In addition, for complexes **32** and **33**, the electronic differentiation between the more electrophilic allylic terminus carbon atoms of both isomers (**A** and **B**) [$\Delta(\delta^{13}C) \approx 10$ and 5.9 ppm, respectively] are higher than in complexes **34** and **31** [$\Delta(\delta^{13}C) \approx 3.2$ and 0.5 ppm, respectively]. All these facts explain the highest enantioselectivity observed with complexes **32** and **33**.

Conclusions

A library of furanoside phosphite-phosphoroamidite ligands **L1**–**L4a**–**e** has been synthesized for the Pd-catalyzed allylic substitution reactions of several substrates with different electronic and steric properties. These ligands have the advantage that they are prepared efficiently from commercial D-xylose and D-glucose, inexpensive natural chiral feedstocks. In addition, the π-acceptor character and flexibility of the phosphite/phosphoroamidites moieties increases reaction rates and versatility. Moreover, the modular nature of the ligand library enables the position of the phosphoroamidite group, the configuration of C-3 of the furanoside backbone and the substituents/configurations in the biaryl phosphite/phosphoroamidite moieties to be easily and systematically varied, so that activities and enantioselectivities can be maximized for each substrate as required. By carefully selecting the ligand components, therefore, high regio- and enantioselectivities (*ee*s up to 98%) and good activities [TOFs > 2000 mol substrate × (mol Pd × h)$^{-1}$], have been achieved in a broad range of mono- and disubstituted linear hindered and unhindered substrates and cyclic substrates. It should be noted that for substrates **S2**, **S5** and **S6**, both enantiomers of substitution products can be obtained with high enantioselectivities by simply changing either the absolute configuration of C-3 or the position of the phosphoroamidite group. In addition, the efficiency of this ligand design is also corroborated by the fact that these Pd-phosphite-phosphoroamidite catalysts provided higher enantioselectivity than their diphosphite analogues in several substrate types.[4b] Moreover, this ligand design allows us to overcome the drawback of moderate regioselectivities in Pd-catalyzed allylic substitution of monosubsituted substrates **S3** and **S4** using 1,2-amino alcohol-based phosphite-phosphoroamidite ligands, which has recently emerged as a one of the most successful catalyst type developed for this process.[3b] These results open up the allylic substitution of a wide range of substrates to the potential effective use of readily available and highly modular sugar-based phosphite-phosphoroamidite ligands.

Study of the Pd-1,3-diphenyl-, 1,3-dimethyl- and 1,3-cyclohexenylallyl intermediates by NMR spectroscopy makes it possible to understand the catalytic behaviour observed. Therefore, for enantioselectivities to be high, the position of the phosphoroamidite group, the absolute configuration of C-3 and the substituents/configurations of the biaryl moieties need to be correctly combined in order to increase the electronic differentiation between the most electrophilic allylic terminus carbon atoms of the isomers formed and/or also form predominantly the isomer that reacts faster with the nucleophile. It also indicates that the nucleophilic attack takes place predominantly at the allylic terminal carbon atom located *trans* to the phosphoroamidite moiety.

Experimental Section

General Considerations

All reactions were carried out using standard Schlenk techniques under an atmosphere of argon. Solvents were purified and dried by standard procedures. Phosphorochloridites are easily prepared in one step from the corresponding biaryls.[29] Phosphite-phosphoroamidite ligands **L1**–**L2a**–**e** were prepared as previously described.[7,30] Compounds **3**,[8] **4**–**5**,[11] **6**–**7**,[13] **8**,[9] **9**,[12] **10**,[14] **12**–**13**[10] and **14**[15] have been previously prepared. Racemic substrates **S1**–**S6** were prepared as previously reported.[31,32,33,34] $[Pd(\eta^3\text{-}1,3\text{-}Ph_2\text{-}C_3H_3)(\mu\text{-}Cl)]_2$,[35] $[Pd(\eta^3\text{-}1,3\text{-}Me_2\text{-}C_3H_3)(\mu\text{-}Cl)]_2$[36] and $[Pd(\eta^3\text{-cyclohexenyl})(\mu\text{-}Cl)]_2$[37] were prepared as previously described. ^{1}H, ^{13}C{^{1}H}, and ^{31}P{^{1}H} NMR spectra were recorded using a 400 MHz spectrometer. Chemical shifts are relative to that of $SiMe_4$ (^{1}H and ^{13}C) as internal standard or H_3PO_4 (^{31}P) as external standard. ^{1}H, ^{13}C and ^{31}P assignments were done based on ^{1}H-^{1}H gCOSY, ^{1}H-^{13}C gHSQC and ^{1}H-^{31}P gHMBC experiments.

General Synthesis of Amino Alcohols 11 and 15

The corresponding crude aldehyde (3 g, 14 mmol) was taken up in 200 mL of water. Sodium borohydride (3.6 g, 95 mmol) was added in several portions and the mixture was stirred at 25 °C for 16 h. The mixture was extracted with dichloromethane (3 × 25 mL). The dried extract was evaporated and purified by flash chromatography (dichloromethane:acetone, 9:2) to give the corresponding azido-alcohols as white solids.

*3-Azido-3-deoxy-5-O-acetyl-1,2-O-isopropylidene-α-*D*-xylofuranose*; yield: 2.8 g (93%). ^{1}H NMR: δ = 1.36 (s, 3H, CH_3), 1.57 (s, 3H, CH_3), 1.98 (s, 1H), 3.61 (m, 1H), 3.70 (m, 1H), 3.98 (m, 1H), 4.14 (m, 1H), 4.75 (m, 1H), 5.81 (d, 1H, J = 4.2 Hz).

*3-Azido-3-deoxy-5-O-acetyl-1,2-O-isopropylidene-α-*D*-ribofuranose*; yield: 1.7 g (58%). ^{1}H NMR: δ = 1.52 (s, 3H, CH_3), 1.75 (s, 3H, CH_3), 2.1 (s, 1H), 3.84 (m, 1H), 3.93 (m, 1H), 4.03 (d, 1H), 4.36 (m, 1H), 4.68 (d, 1H), 5.93 (d, 1H, J = 4.2 Hz).

The corresponding azido alcohol (2 g, 9 mmol) was dissolved in a mixture of tetrahydrofuran:water (50 mL, 4:1). Triphenylphosphine (5.4 g, 19 mmol) was then added and the mixture was stirred at room temperature overnight. Then, tetrahydrofuran was removed by evaporation under vacuum and the residue extracted twice with diethyl ether. The aqueous phase was concentrated under vacuum to give the corresponding amino alcohols as white solids.

11: yield: 1.5 g (88%). ^{1}H NMR: δ = 1.29 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.98 (s, 3H), 3.14 (m, 1H), 3.77 (m, 1H), 3.83 (m, 2H), 4.41 (m, 1H), 5.73 (d, 1H, J = 3.6 Hz).

15: yield: 1.5 g (88%). ^{1}H NMR: δ = 1.29 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 2.02 (s, 3H), 3.50 (m, 1H), 3.92 (m, 2H), 4.24 (m, 1H), 4.41 (m, 1H), 5.95 (d, 1H, J = 4.0 Hz).

General Procedure for the Preparation of Phosphite-Phosphoroamidite Ligands L1–L4a–e

The phosphorochloridite (2.2 mmol) produced *in situ* was dissolved in toluene (5 mL) and pyridine (0.36 mL, 4.6 mmol) was added. Amino alcohol (1 mmol) was azeotropically dried with toluene (3×1 mL) and then dissolved in toluene (10 mL), to which pyridine (0.36 mL, 4.6 mmol) was added. The amino alcohol solution was transferred slowly at 0 °C to the solution of phosphorochloridite. The reaction mixture was warmed up to 80 °C and stirred overnight, and the pyridine salts were removed by filtration. Evaporation of the solvent gave a white foam, which was purified by flash chromatography (toluene/NEt_3 = 100/1) to produce the corresponding ligand as white powder.

L3a: yield: 0.54 g (51%). ^{31}P NMR (C_6D_6): δ = 142.9 (s), 147.5 (s); ^{1}H NMR (C_6D_6): δ = 1.09 (s, 3H, CH_3), 1.27 (s, 9H, CH_3, *t*-Bu), 1.28 (s, 9H, CH_3, *t*-Bu), 1.29 (s, 9H, CH_3, *t*-Bu), 1.30 (s, 9H, CH_3, *t*-Bu), 1.32 (s, 3H, CH_3), 1.53 (s, 9H, CH_3, *t*-Bu), 1.57 (s, 9H, CH_3, *t*-Bu), 1.60 (s, 9H, CH_3, *t*-Bu), 1.64 (s, 9H, CH_3, *t*-Bu), 2.96 (m, 1H, NH), 3.90 (m, 1H, H-3), 4.19 (m, 1H, H-5), 4.24 (m, 1H, H-5′), 4.32 (m, 1H, H-4), 4.35 (d, 1H, H-2, $^3J_{2,1}$ = 3.2 Hz), 5.67 (d, 1H, H-1, $^3J_{1,2}$ = 3.2 Hz), 7.0–7.7 (m, 8H, CH=); ^{13}C NMR (C_6D_6): δ = 26.9 (CH_3), 27.3 (CH_3), 31.7 (CH_3, *t*-Bu), 31.8 (CH_3, *t*-Bu), 31.9 (CH_3, *t*-Bu), 32.0 (CH_3, *t*-Bu), 32.1 (CH_3, *t*-Bu), 32.2 (CH_3, *t*-Bu), 35.0 (C, *t*-Bu), 35.1 (C, *t*-Bu), 36.0 (C, *t*-Bu), 36.1 (C, *t*-Bu), 58.0 (d, C-3, $J_{C,P}$ = 7.5 Hz), 64.3 (d, C-5, $J_{C,P}$ = 9.9 Hz), 79.5(C-4), 86.6 (d, C-2, $J_{C,P}$ = 5.3 Hz), 104.9 (C-1), 111.9 (CMe_2), 124.5 (CH=), 124.7 (CH=), 124.8 (CH=), 127.5 (CH=), 128.9 (CH=), 129.6 (CH=),134.0 (C), 134.1 (C), 134.3 (C), 140.5 (C), 140.9 (C), 141.0 (C), 141.1 (C), 146.9 (C), 147.1 (C), 147.4 (C); anal. calcd. (%) for $C_{64}H_{93}NO_8P_2$: C 72.08, H 8.79, N 1.31; found: C 72.45, H 8.83, N 1.29.

L3b: yield: 0.44 g (45%). ^{31}P NMR (C_6D_6): δ = 140.3 (s), 148.0 (s); ^{1}H NMR (C_6D_6): δ = 1.12 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.46 (s, 9H, CH_3, *t*-Bu), 1.49 (s, 9H, CH_3, *t*-Bu), 1.51 (s, 9H, CH_3, *t*-Bu), 1.54 (s, 9H, CH_3, *t*-Bu), 3.18 (m, 1H, NH), 3.32 (s, 3H, CH_3O), 3.34 (s, 6H, CH_3O), 3.37 (s, 3H, CH_3O), 4.00 (m, 1H, H-3), 4.27 (m, 2H, H-5 and H-5′), 4.34 (d, 1H, H-2, $^3J_{2,1}$ = 3.6 Hz), 4.42 (m, 1H, H-4), 5.80 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 6.6–7.2 (m, 8H, CH=); ^{13}C NMR (C_6D_6): δ = 26.7 (CH_3), 27.3 (CH_3), 31.4 (CH_3, *t*-Bu), 31.5 (CH_3, *t*-Bu), 31.6 (CH_3, *t*-Bu), 31.7 (CH_3, *t*-Bu), 35.7 (C, *t*-Bu), 35.8 (C, *t*-Bu), 35.9 (C, *t*-Bu), 36.0 (C, *t*-Bu), 55.4 (CH_3O), 55.5 (CH_3O), 58.4 (d, C-3, $J_{C,P}$ = 6.0 Hz), 63.9 (d, C-5, $J_{C,P}$ = 6.1 Hz), 79.6 (C-4), 86.6 (d, C-2, $J_{C,P}$ = 6.1 Hz), 105.1 (C-1), 112.0 (CMe_2), 113.3 (CH=), 113.6 (CH=), 113.8 (CH=), 114.9 (CH=), 115.2 (CH=), 126.0 (CH=), 128.0 (CH=), 128.8 (CH=), 134.6 (C), 134.7 (C), 134.8 (C), 142.7 (C), 142.9 (C), 143.0 (C), 156.6 (C), 156.7 (C), 156.8 (C); anal. calcd. (%) for $C_{52}H_{69}NO_{12}P_2$: C 64.92, H 7.23, N 1.46; found: C 65.02, H 7.33, N 1.52.

L3c: yield: 0.49 g (54%). ^{31}P NMR (C_6D_6): δ = 138.5 (s), 149.7 (s); ^{1}H NMR (C_6D_6): δ = 0.33 (s, 9H, CH_3Si), 0.35 (s, 9H, CH_3Si), 0.38 (s, 9H, CH_3Si), 0.40 (s, 9H, CH_3Si), 1.06 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 3.21 (m, 1H, NH), 3.95 (m, 1H, H-3), 4.18 (m, 2H, H-5 and H-5′), 4.35 (m, 1H, H-4), 4.41 (d, 1H, H-2, $^3J_{2,1}$ = 3.6 Hz), 5.87 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 6.9–7.4 (m, 12H, CH=); ^{13}C NMR (C_6D_6): δ = 0.45 (CH_3Si), 0.63 (CH_3Si), 0.67 (CH_3Si), 0.73 (CH_3Si), 26.8 (CH_3), 27.2 (CH_3), 58.5 (d, C-3, $J_{C,P}$ = 3.1 Hz), 63.7 (C-5), 79.2 (C-4), 86.4 (d, C-2, $J_{C,P}$ = 8.7 Hz), 105.1 (C-1), 112.1 (CMe_2), 125.1 (CH=), 125.5 (CH=), 128.8 (CH=), 131.7 (C), 131.8 (C), 132.0 (C), 132.5 (CH=), 132.9 (CH=), 133.0 (CH=), 135.7 (CH=), 135.9 (CH=), 155.1 (C), 155.2 (C), 156.0 (C), 156.1 (C); anal. calcd. (%) for $C_{44}H_{61}NO_8P_2Si_4$: C 58.31, H 6.78, N 1.55; found: C 58.55, H 6.81, N 1.59.

L4a: yield: 0.37 g (34%). ^{31}P NMR (C_6D_6): δ = 145.3 (s), 149.9 (s); ^{1}H NMR (C_6D_6): δ = 1.10 (s, 3H, CH_3), 1.25 (s, 9H, CH_3, *t*-Bu), 1.27 (s, 18H, CH_3, *t*-Bu), 1.28 (s, 12H, CH_3 and CH_3, *t*-Bu), 1.56 (s, 9H, CH_3, *t*-Bu), 1.57 (s, 9H, CH_3, *t*-Bu), 1.61 (s, 9H, CH_3, *t*-Bu), 1.68 (s, 9H, CH_3, *t*-Bu), 3.09 (m, 1H, NH), 3.49 (m, 1H, H-2), 3.56 (m, 1H, H-3), 3.77 (m, 1H, H-4), 4.00 (m, 1H, H-5), 4.41 (m, 1H, H-5′), 5.53 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 7.0–7.6 (m, 8H, CH=); ^{13}C NMR (C_6D_6): δ = 26.3 (CH_3), 26.7 (CH_3), 31.3 (CH_3, *t*-Bu), 31.5 (CH_3, *t*-Bu), 31.6 (CH_3, *t*-Bu), 31.7 (CH_3, *t*-Bu), 34.5 (C, *t*-Bu), 35.4 (C, *t*-Bu), 35.5 (C, *t*-Bu), 35.6 (C, *t*-Bu), 53.8 (d, C-3, $J_{C,P}$ = 9.8 Hz), 64.5 (d, C-5, $J_{C,P}$ = 10.6 Hz), 79.8 (C-4), 80.5 (m, C-2), 104.0 (C-1), 111.8 (CMe_2), 123.9 (CH=), 124.1 CH=), 124.4 (CH=), 126.3 (CH=), 126.8 (CH=), 126.9 (CH=), 127.3 (CH=), 128.4 (CH=), 133.6 (C), 133.8 (C), 133.9 (C), 140.4 (C), 140.7 (C), 140.8 (C), 146.3 (C),146.4 (C), 146.5 (C); anal. calcd. (%) for $C_{64}H_{93}NO_8P_2$: C 72.08, H 8.79, N 1.31; found: C 72.66, H 8.92, N 1.33.

L4b: yield: 0.37 g (38%). ^{31}P NMR (C_6D_6): δ = 144.7 (s), 149.2 (s); ^{1}H NMR (C_6D_6): δ = 1.07 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.51 (s, 9H, CH_3, *t*-Bu), 1.52 (s, 9H, CH_3, *t*-Bu), 1.55 (s, 9H, CH_3, *t*-Bu), 1.58 (s, 9H, CH_3, *t*-Bu), 3.28 (m, 1H, NH), 3.31 (s, 9H, CH_3O), 3.34 (s, 9H, CH_3O), 3.68 (m, 1H, H-3), 3.82 (m, 2H, H-2 and H-3), 4.12 (m, 1H, H-5), 4.49 (m, 1H, H-5′), 5.57 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 6.6–7.2 (m, 8H, CH=); ^{13}C NMR (C_6D_6); δ = 26.7 (CH_3), 27.1 (CH_3), 31.5 (CH_3, *t*-Bu), 31.6 (CH_3, *t*-Bu), 31.7 (CH_3, *t*-Bu), 31.8 (CH_3, *t*-Bu), 35.7 (C, *t*-Bu), 35.8 (C, *t*-Bu), 35.9 (C, *t*-Bu), 36.0 (C, *t*-Bu), 54.3 (d, C-3, $J_{C,P}$ = 15.1 Hz), 55.4 (CH_3O), 55.5 (CH_3O), 64.2 (d, C-5, $J_{C,P}$ = 10.6 Hz), 80.4 (C-4), 81.2 (m, C-2), 104.6 (C-1), 112.3 (CMe_2), 113.2 (CH=), 113.6 (CH=), 113.7 (CH=), 113.9 (CH=), 114.9 CH=), 115.0 (CH=), 115.1 (CH=), 126.0 (CH=), 128.0 (CH=), 128.9 (CH=), 134.6 (C), 134.7 (C), 134.8 (C), 135.0 (C), 143.1 (C), 143.2 (C), 143.3 (C), 156.6 (C), 156.7 (C); anal. calcd. (%) for $C_{52}H_{69}NO_{12}P_2$: C 64.92, H 7.23, N 1.46; found: C 65.11, H 7.29, N 1.42.

L4c: yield: 0.39 g (43%). ^{31}P NMR (C_6D_6): δ = 143.7 (s), 149.8 (s); ^{1}H NMR (C_6D_6): δ = 0.31 (s, 9H, CH_3Si), 0.32 (s, 9H, CH_3Si), 0.37 (s, 9H, CH_3Si), 0.40 (s, 9H, CH_3Si), 1.03 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 3.15 (m, 1H, NH), 3.24 (m, 1H, H-3), 3.50 (m, 1H, H-2), 3.79 (m, 2H, H-4 and H-5), 4.32 (m, 1H, H-5′), 5.41 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 6.9–7.4 (m, 12H, CH=); ^{13}C NMR (C_6D_6): δ = 0.5 (CH_3Si), 0.6 (CH_3Si), 0. 7 (CH_3Si), 26.8 (CH_3), 27.1 (CH_3), 54.0 (d, C-3, $J_{C,P}$ = 2.7 Hz), 65.3 (d, C-5, $J_{C,P}$ = 4.9 Hz), 80.4 (C-4), 80.9 (m, C-2), 104.5 (C-1), 112.3 (CMe_2), 125.0 (CH=), 125.1 (CH=), 125.3 (CH=), 125.7 (CH=), 132.0 (C), 132.1 (C), 132.4 (C), 132.5 (CH=), 132.8 (CH=), 132.9 (CH=), 133.1 (CH=), 135.3 (CH=), 135.7 (CH=), 135.9 (CH=), 155.6 (C), 155.7 (C); anal. calcd. (%) for $C_{44}H_{61}NO_8P_2Si_4$: C 58.31, H 6.78, N 1.55; found: C 58.44, H 6.79, N 1.52.

L4d: yield: 0.53 g (49%). ^{31}P NMR (C_6D_6): δ = 141.6 (s), 149.3 (s); ^{1}H NMR (C_6D_6): δ = 0.40 (s, 9H, CH_3Si), 0.41 (s, 9H, CH_3Si), 0.47 (s, 9H, CH_3Si), 0.57 (s, 9H, CH_3Si), 1.03 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 3.15 (m, 1H, NH), 3.38 (m,

1H, H-3), 3.58 (m, 1H, H-2), 3.89 (m, 1H, H-4), 4.13 (m, 2H, H-5, H-5′), 5.27 (d, 1H, H-1, $^3J_{1,2}$=3.6 Hz), 6.8–8.2 (m, 20H, CH=); ^{13}C NMR (C_6D_6): δ=0.6 (CH_3Si), 0.7 (CH_3Si), 0.8 (CH_3Si), 26.6 (CH_3), 27.0 (CH_3), 53.8 (d, C-3, $J_{C,P}$= 8.4 Hz), 64.5 (C-5), 80.3 (C-2), 80.5 (m, C-4), 104.4 (C-1), 112.2 (CMe_2), 125.1 (CH=), 125.2 (CH=), 125.5 (CH=), 127.1 (CH=), 127.3 (CH=), 127.4 (CH=), 127.5 (CH=), 127,6 (CH=), 128.7 (CH=), 129.1 (CH=), 129.2 (CH=), 129.6 (CH=), 131.4 (C), 131.8 (C), 132.8 (C), 133.1 (C), 133.4 (C), 134.5 (C), 134.9 (C), 136.9 (CH=), 137.6 (CH=), 137.9 (CH=), 152.7 (C),152.8 (C),153.4 (C), 153.9 (C); anal. calcd. (%) for $C_{60}H_{69}NO_8P_2Si_4$: C 65.13, H 6.29, N 1.27; found: C 65.32, H 6.31, N 1.33.

L4e: yield: 0.51 g (47%). ^{31}P NMR (C_6D_6): δ=144.3 (s), 153.1 (s); ^{1}H NMR (C_6D_6): δ=0.34 (s, 9H, CH_3Si), 0.46 (s, 9H, CH_3Si), 0.55 (s, 9H, CH_3Si), 0.57 (s, 9H, CH_3Si), 0.95 (s, 3H, CH_3), 0.98 (s, 3H, CH_3), 3.42 (m, 2H, NH, H-3), 3.69 (m, 1H, H-4), 3.82 (m, 1H, H-5′), 4.22 (m,1 1H, H-2), 4.49 (m, 1H, H-5), 5.41 (d, 1H, H-1, $^3J_{1,2}$=3.6 Hz), 6.8–8.2 (m, 20H, CH=); ^{13}C NMR (C_6D_6): δ=0.0 (CH_3Si), 0.3 (CH_3Si), 0.6 (CH_3Si), 26.4 (CH_3), 26.5 (CH_3), 54.6 (m, C-3), 63.9 (C-5), 79.9 (C-2), 81.0 (C-4), 104.2 (C-1), 112.0 (CMe_2), 124.8 (CH=), 125.2 (CH=), 125.5 (CH=), 126.7 (CH=), 127.0 (CH=), 127.6 (CH=), 128.4 (CH=), 128.6 (CH=), 129.1 (CH=), 130.8 (C), 131.2 (C), 131.4 (C), 132.5 (C), 132.6 (C), 132.7 (C), 134.0 (C), 134.5 (C), 136.6 (CH=), 137.0 (CH=), 137.4 (CH=), 137.5 (CH=), 152.3 (C), 152.6 (C), 154.4 (C), 154.2 (C); anal. calcd. (%) for $C_{60}H_{69}NO_8P_2Si_4$: C 65.13, H 6.29, N 1.27; found: C 65.45, H 6.38, N 1.29.

General Procedure for the Preparation of [Pd(η^3-allyl)(L)]BF_4 Complexes 24–34

The corresponding ligand (0.05 mmol) and the complex [Pd(μ-Cl)(η^3-1,3-allyl)]$_2$ (0.025 mmol) were dissolved in CD_2Cl_2 (1.5 mL) at room temperature under argon. $AgBF_4$ (9.8 mg, 0.5 mmol) was added after 30 min and the mixture was stirred for 30 min. The mixture was then filtered over celite under argon and the resulting solutions were analyzed by NMR. After the NMR analysis, the complexes were precipitated as pale yellow solids by addition of hexane.

[Pd(η^3-1,3-diphenylallyl)(L1a)]BF_4 (24): Isomer **A** (66%); ^{31}P NMR (CD_2Cl_2, 233 K): δ=128.6 (d, 1P, P–O, $^2J_{P,P}$= 181.9 Hz), 133.2 (d, 1P, P–N, $^2J_{P,P}$=181.9 Hz); ^{1}H NMR (CD_2Cl_2, 233 K): δ=1.15 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 1.28 (s, 9H, CH_3, *t*-Bu), 1.31 (s, 18H, CH_3, *t*-Bu), 1.43 (s, 18H, CH_3, *t*-Bu), 1.53 (s, 9H, CH_3, *t*-Bu), 1.59 (s, 9H, CH_3, *t*-Bu), 1.63 (s, 9H, CH_3, *t*-Bu), 3.42 (m, 2H, H-5 and H-5′), 3.52 (m, 1H, NH), 3.82 (m, 1H, H-2), 4.05 (m, 1H, H-4), 4.66 (m, 1H, H-3), 5.14 (m, 2H, CH allyl terminal), 5.79 (d, 1H, H-1, $^3J_{1,2}$=3.6 Hz), 6.62 (m, 1H, CH allyl central), 6.8–7.8 (m, 18H, CH=); ^{13}C NMR (CD_2Cl_2, 233 K): δ=26.1 (CH_3), 26.8 (CH_3), 31.1 (CH_3, *t*-Bu), 31.3 (CH_3, *t*-Bu), 31.5 (CH_3, *t*-Bu), 31.7 (CH_3, *t*-Bu), 32.1 (CH_3, *t*-Bu), 32.3 (CH_3, *t*-Bu), 34.6–36.0 (C, *t*-Bu), 39.3 (d, C-5, $J_{C,P}$=14.1 Hz), 76.4 (b, C-4), 82.9 (C-2), 83.4 (d, C-3, $J_{C,P}$=13.2 Hz), 87.5 (dd, CH allyl *trans* to P–O, $J_{C,P}$=40.3 Hz, $J_{C,P}$=8.5 Hz), 94.8 (dd, CH allyl *trans* to P–N, $J_{C,P}$=30.7 Hz, $J_{C,P}$=6.6 Hz), 104.9 (C-1), 112.6 (m, CH allyl central), 112.7 (CMe_2), 124.0–150.0 (aromatic carbons). Isomer **B** (34%); ^{31}P NMR (CD_2Cl_2, 233 K): δ=128.2 (d, 1P, P–O, $^2J_{P,P}$=179.1 Hz), 135.1 (d, 1P, P–N, $^2J_{P,P}$=179.1 Hz); ^{1}H NMR (CD_2Cl_2, 233 K): δ=1.09 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 1.31 (s, 9H, CH_3, *t*-Bu), 1.34 (s, 9H, CH_3, *t*-Bu), 1.46 (s, 18H, CH_3, *t*-Bu), 1.53 (s, 18H, CH_3, *t*-Bu), 1.64 (s, 18H, CH_3, *t*-Bu)3.42 (m, 3H, NH, H-5 and H-5′), 3.88 (m, 1H, H-2), 4.18 (m, 1H, H-4), 4.90 (m, 1H, H-3), 5.05 (m, 1H, CH allyl terminal), 5.17 (m, 1H, CH allyl terminal), 5.74 (d, 1H, H-1, $^3J_{1,2}$=4.0 Hz), 6.66 (m, 1H, CH allyl central), 6.8–7.8 (m, 18H, CH=); ^{13}C NMR (CD_2Cl_2, 233 K): δ=26.0 (CH_3), 26.6 (CH_3), 31.0 (CH_3, *t*-Bu), 31.1 (CH_3, *t*-Bu), 31.3 (CH_3, *t*-Bu), 31.4 (CH_3, *t*-Bu), 31.9 (CH_3, *t*-Bu), 32.3 (CH_3, *t*-Bu), 34.6–36.0 (C, *t*-Bu), 39.7 (d, C-5, $J_{C,P}$=14.8 Hz), 76.6 (b, C-4), 82.9 (C-2), 83.3 (m, C-3), 86.6 (dd, CH allyl *trans* to P–O, $J_{C,P}$=34.6 Hz, $J_{C,P}$=8.7 Hz), 96.4 (dd, CH allyl *trans* to P–N, $J_{C,P}$=34.8 Hz, $J_{C,P}$=7.2 Hz), 104.9 (C-1), 112.3 (CMe_2), 113.4 (m, CH allyl central), 124.0–150.0 (aromatic carbons); anal. calcd. (%) for $C_{79}H_{105}BF_4NO_8P_2Pd$: C 65.35, H 7.29, N 0.96; found: C 65.43, H 7.32, N 0.99.

[Pd(η^3-1,3-diphenylallyl)(L2a)]BF_4 (25): Isomer **A** (50%); ^{31}P NMR (CD_2Cl_2, 233 K): δ=146.2 (d, 1P, P–O, $^2J_{P,P}$= 149.4 Hz), 148.2 (d, 1P, P–N, $^2J_{P,P}$=149.4 Hz); ^{1}H NMR (CD_2Cl_2, 233 K): δ=1.18 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 1.32 (s, 9H, CH_3, *t*-Bu), 1.33 (s, 9H, CH_3, *t*-Bu), 1.45 (s, 18H, CH_3, *t*-Bu), 1.49 (s, 9H, CH_3, *t*-Bu), 1.53 (s, 9H, CH_3, *t*-Bu), 1.65 (s, 18H, CH_3, *t*-Bu), 3.57 (m, 2H, H-5 and H-5′), 3.92 (m, 2H, NH, H-4), 4.10 (m, 1H, H-3), 4.64 (m, 1H, H-2), 5.07 (m, 1H, CH allyl terminal), 5.23 (m, 1H, CH allyl terminal), 5.62 (d, 1H, H-1, $^3J_{1,2}$=4.0 Hz), 6.52 (m, 1H, CH allyl central), 6.7–7.8 (m, 18H, CH=); ^{13}C NMR (CD_2Cl_2, 233 K): δ=25.8 (CH_3), 26.2 (CH_3), 30.8–32.5 (CH_3, *t*-Bu), 34.6–36.0 (C, *t*-Bu), 38.5 (m, C-5), 73.8 (C-4), 76.3 (C-2), 77.8 (d, C-3, $J_{C,P}$=8.9 Hz), 92.2 (m, CH allyl *trans* to P–O), 97.4 (dd, CH allyl *trans* to P–N, $J_{C,P}$=33.7 Hz, $J_{C,P}$=7.2 Hz), 104.0 (C-1), 114.5 (m, CH allyl central), 115.1 (CMe_2), 124.0–150.0 (aromatic carbons). Minor isomer **B** (50%); ^{31}P NMR (CD_2Cl_2, 233 K): δ=145.4 (d, 1P, P–O, $^2J_{P,P}$= 120.6 Hz), 148.3 (d, 1P, P–N, $^2J_{P,P}$=120.6 Hz); ^{1}H NMR (CD_2Cl_2, 233 K): δ=1.24 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.29 (s, 9H, CH_3, *t*-Bu), 1.33 (s, 18H, CH_3, *t*-Bu), 1.45 (s, 9H, CH_3, *t*-Bu), 1.51 (s, 9H, CH_3, *t*-Bu), 1.56 (s, 9H, CH_3, *t*-Bu), 1.64 (s, 18H, CH_3, *t*-Bu), 3.57 (m, 2H, H-5 and H-5′), 3.92 (m, 2H, NH, H-4), 4.25 (m, 1H, H-3), 4.72 (m, 1H, H-2), 5.23 (m, 1H, CH allyl terminal), 5.34 (m, 1H, CH allyl terminal), 5.69 (d, 1H, H-1, $^3J_{1,2}$=4.0 Hz), 6.62 (m, 1H, CH allyl central), 6.7–7.8 (m, 18H, CH=); ^{13}C NMR (CD_2Cl_2, 233 K): δ=25.9 (CH_3), 26.1 (CH_3), 30.8–32.5 (CH_3, *t*-Bu), 34.6–36.0 (C, *t*-Bu), 38.5 (m, C-5), 73.8 (C-4), 76.6 (C-2), 77.4 (d, C-3, $J_{C,P}$=10.0 Hz), 91.9 (m, CH allyl *trans* to P–O), 98.2 (dd, CH allyl *trans* to P–N, $J_{C,P}$=30.4 Hz, $J_{C,P}$=6.6 Hz), 103.8 (C-1), 113.8 (m, CH allyl central), 115.1 (CMe_2), 124.0–150.0 (aromatic carbons); anal. calcd. (%) for $C_{79}H_{105}BF_4NO_8P_2Pd$: C 65.35, H 7.29, N 0.96; found: C 65.22, H 7.21, N 1.02.

[Pd(η^3-1,3-diphenylallyl)(L3a)]BF_4 (26): Isomer **A** (34%); ^{31}P NMR (CD_2Cl_2, 213 K): δ=124.2 (d, 1P, P–O, $^2J_{P,P}$= 159.9 Hz), 133.2 (d, 1P, P–N, $^2J_{P,P}$=159.9 Hz); ^{1}H NMR (CD_2Cl_2, 213 K): δ=1.18 (s, 3H, CH_3), 1.29 (s, 9H, CH_3, *t*-Bu), 1.32 (s, 18H, CH_3, *t*-Bu), 1.45 (s, 9H, CH_3, *t*-Bu), 1.49 (s, 3H, CH_3), 1.59 (s, 18H, CH_3, *t*-Bu), 1.64 (s, 9H, CH_3, *t*-Bu), 1.65 (s, 9H, CH_3, *t*-Bu), 4.05 (m, 2H, H-3, NH), 4.34 (m, 2H, H-5 and H-5′), 4.45 (m, 1H, H-4), 4.52 (m, 1H, H-2), 5.11 (m, 1H, CH allyl terminal), 5.35 (m, 1H, CH allyl terminal), 5.72 (d, 1H, H-1, $^3J_{1,2}$=3.6 Hz), 6.62 (m, 1H, CH

allyl central), 6.8–7.8 (m, 18H, CH=); ^{13}C NMR (CD_2Cl_2, 213 K): δ = 26.3 (CH_3), 27.1 (CH_3), 30.5–33.5 (CH_3, *t*-Bu), 35.0–36.3 (C, *t*-Bu), 56.3 (m, C-3), 65.4 (m, C-5), 75.6(C-4), 79.7 (C-2), 86.8 (m, CH allyl *trans* to P–O), 92.8 (m, CH allyl *trans* to P–N), 104.8 (C-1), 111.9 (CMe_2), 113.4 (m, CH allyl central), 124.0–150.0 (aromatic carbons). Isomer **B** (66%); ^{31}P NMR (CD_2Cl_2, 213 K): δ = 123.8 (d, 1P, $^2J_{P,P}$ = 156.2 Hz), 135.2 (d, 1P, $^2J_{P,P}$ = 156.2 Hz); ^{1}H NMR (CD_2Cl_2, 213 K): δ = 1.15 (s, 3H, CH_3), 1.30 (s, 9H, CH_3, *t*-Bu), 1.35 (s, 18H, CH_3, *t*-Bu), 1.41 (s, 3H, CH_3), 1.47 (s, 9H, CH_3, *t*-Bu), 1.55 (s, 18H, CH_3, *t*-Bu), 1.62 (s, 18H, CH_3, *t*-Bu), 4.09 (m, 2H, H-3, NH), 4.35 (m, 2H, H-5 and H-5′), 4.42 (m, 1H, H-4), 4.71 (m, 1H, H-2), 5.02 (m, 1H, CH allyl terminal), 5.55 (m, 1H, CH allyl terminal), 5.81 (d, 1H, H-1, $^3J_{1,2}$ = 4.0 Hz), 6.69 (m, 1H, CH allyl central), 6.8–7.8 (m, 18H, CH=); ^{13}C NMR (CD_2Cl_2, 213 K): δ = 26.0 (CH_3), 27.4 (CH_3), 30.5–33.5 (CH_3, *t*-Bu), 35.0–36.3 (C, *t*-Bu), 56.5 (C-3), 65.8 (m, C-5), 75.9 (C-4), 80.2 (m, C-2), 87.0 (m, CH allyl *trans* to P–O), 93.0 (m, CH allyl *trans* to P–N), 104.9 (C-1), 111.9 (CMe_2), 113.9 (m, CH allyl central), 124.0–150.0 (aromatic carbons); anal. calcd. (%) for $C_{79}H_{105}BF_4NO_8P_2Pd$: C 65.35, H 7.29, N 0.96; found: C 65.63, H 7.42, N 1.09.

[Pd(η^3-1,3-diphenylallyl)(L4a)]BF$_4$ (27): Isomer **A** (45%); ^{31}P NMR (CD_2Cl_2, 253 K): δ = 124.1 (d, 1P, P–O, $^2J_{P,P}$ = 181.8 Hz), 135.1 (d, 1P, P–N, $^2J_{P,P}$ = 181.8 Hz); ^{1}H NMR (CD_2Cl_2, 253 K): δ = 1.21 (s, 3H, CH_3), 1.29 (s, 9H, CH_3, *t*-Bu), 1.31 (s, 3H, CH_3), 1.35 (s, 18H, CH_3, *t*-Bu), 1.42 (s, 9H, CH_3, *t*-Bu), 1.45 (s, 9H, CH_3), 1.48 (s, 9H, CH_3, *t*-Bu), 1.64 (s, 9H, CH_3, *t*-Bu), 1.65 (s, 9H, CH_3, *t*-Bu), 3.45 (m, 1H, NH), 3.56 (m, 1H, C-3), 3.98 (m, 1H, H-4), 4.05 (m, 2H, H-5 and H-5′), 5.11 (m, 1H, CH allyl terminal), 5.25 (m, 1H, CH allyl terminal), 5.42 (m, 1H, H-2), 5.74 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 6.71 (m, 1H, CH allyl central), 6.8–7.8 (m, 18H, CH=); ^{13}C NMR (CD_2Cl_2, 253 K): δ = 26.0 (CH_3), 26.8 (CH_3), 31.0–33.0 (CH_3, *t*-Bu), 34.8–36.1 (C, *t*-Bu), 56.8 (m, C-3), 68.7 (m, C-5), 73.8 (C-4), 79.3 (C-2), 90.7 (m, CH allyl *trans* to P–O), 93.8 (m, CH allyl *trans* to P–N), 103.4 (C-1), 112.5 (CMe_2), 111.5 (m, CH allyl central), 124.0–150.0 (aromatic carbons). Isomer **B** (55%); ^{31}P NMR (CD_2Cl_2, 253 K): δ = 123.5 (d, 1P, P–O, $^2J_{P,P}$ = 170.3 Hz), 136.4 (d, 1P, P–N, $^2J_{P,P}$ = 170.3 Hz); ^{1}H NMR (CD_2Cl_2, 253 K): δ = 1.18 (s, 3H, CH_3), 1.25 (s, 9H, CH_3, *t*-Bu), 1.33 (s, 3H, CH_3), 1.39 (s, 18H, CH_3, *t*-Bu), 1.51 (s, 18H, CH_3, *t*-Bu), 1.60 (s, 18H, CH_3, *t*-Bu), 1.65 (s, 9H, CH_3, *t*-Bu), 3.51 (m, 1H, NH), 3.62 (m, 1H, C-3), 4.03 (m, 1H, H-4), 4.11 (m, 2H, H-5 and H-5′), 5.02 (m, 1H, CH allyl terminal), 5.21 (m, 1H, CH allyl terminal), 5.22 (m, 1H, H-2), 5.94 (d, 1H, H-1, $^3J_{1,2}$ = 4.0 Hz), 6.68 (m, 1H, CH allyl central), 6.8–7.8 (m, 18H, CH=); ^{13}C NMR (CD_2Cl_2, 253 K): δ = 25.8 (CH_3), 27.1 (CH_3), 31.0–33.0 (CH_3, *t*-Bu), 34.8–36.1 (C, *t*-Bu), 56.8 (m, C-3), 68.9 (m, C-5), 74.2 (C-4), 80.2 (C-2), 89.7 (m, CH allyl *trans* to P–O), 93.1 (dd, CH allyl *trans* to P–N, $J_{C,P}$ = 28.8 Hz, $J_{C,P}$ = 6.2 Hz), 103.5 (C-1), 112.5 (CMe_2), 113.1 (m, CH allyl central), 124.0–150.0 (aromatic carbons); anal. calcd. (%) for $C_{79}H_{105}BF_4NO_8P_2Pd$: C 65.35, H 7.29, N 0.96; found: C 65.13, H 7.22, N 0.91.

[Pd(η^3-1,3-diphenylallyl)(L1e)]BF$_4$ (28): Isomer **A** (20%); ^{31}P NMR (CD_2Cl_2, 263 K): δ = 140.5 (d, 1P, P–O, $^2J_{P,P}$ = 154.4 Hz), 146.3 (d, 1P, P–N, $^2J_{P,P}$ = 154.4 Hz); ^{1}H NMR (CD_2Cl_2, 263 K): δ = 0.51 [s, 9H, $Si(CH_3)_3$], 0.75–0.92 [m, 27H, $Si(CH_3)_3$], 1.24 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 3.02 (m, 1H, NH), 3.42 (m, 2H, H-5 and H-5′), 4.02 (m, 2H, H-2 and H-4), 4.62 (m, 1H, H-3), 4.86 (m, 1H, CH allyl terminal), 5.18 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 5.61 (m, 1H, CH allyl terminal), 6.21 (m, 2H, CH=), 6.41 (m, 1H, CH allyl central), 6.5–8.5 (m, 20H, CH=); ^{13}C NMR (CD_2Cl_2, 263 K): δ = 0.8–2.4 [$Si(CH_3)_3$], 24.9 (CH_3), 26.5 (CH_3), 37.2 (C-5), 78.7 (m, C-4), 79.4 (m, C-2), 82.5 (C-3), 88.0 (dd, CH allyl *trans* to P–O, $J_{C,P}$ = 36.5 Hz, $J_{C,P}$ = 6.0 Hz), 99.8 (m, CH allyl *trans* to P–N), 105.3 (C-1), 113.0 (CMe_2), 114.0 (m, CH allyl central), 120.0–155.0 (aromatic carbons). Isomer **B** (80%); ^{31}P NMR (CD_2Cl_2, 263 K): δ = 142.8 (d, 1P, P–O, $^2J_{P,P}$ = 151.2 Hz), 147.2 (d, 1P, P–N, $^2J_{P,P}$ = 151.2 Hz); ^{1}H NMR (CD_2Cl_2, 263 K): δ = 0.44 [s, 9H, $Si(CH_3)_3$], 0.75–0.92 [m, 27H, $Si(CH_3)_3$], 1.27 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 2.85 (m, 1H, H-5), 3.02 (m, 1H, NH), 3.21 (m, 1H, H-5′), 4.02 (m, 2H, H-2 and H-4), 4.80 (m, 1H, H-3), 5.05 (m, 1H, CH allyl terminal), 5.20 (d, 1H, H-1, $^3J_{1,2}$ = 4.0 Hz), 5.72 (m, 1H, CH allyl terminal), 6.21 (m, 2H, CH=), 6.47 (m, 1H, CH allyl central), 6.5–8.5 (m, 20H, CH=); ^{13}C NMR (CD_2Cl_2, 263 K): δ = 0.8–2.4 [$Si(CH_3)_3$], 24.7 (CH_3), 26.6 (CH_3), 37.0 (C-5), 78.7 (m, C-4), 79.5 (m, C-2), 82.7 (C-3), 84.7 (dd, CH allyl *trans* to P–O, $J_{C,P}$ = 37.2 Hz, $J_{C,P}$ = 7.2 Hz), 102.9 (m, CH allyl *trans* to P–N), 105.7 (C-1), 112.6 (m, CH allyl central), 113.0 (CMe_2), 120.0–155.0 (aromatic carbons); anal. calcd. (%) for $C_{75}H_{81}BF_4NO_8P_2PdSi_4$: C 60.38, H 5.47, N 0.94; found: C 60.54, H 5.63, N 0.99.

[Pd(η^3-1,3-dimethylallyl)(L1e)]BF$_4$ (29): Isomer **A** (50%); ^{31}P NMR (CD_2Cl_2, 223 K): δ = 142.3 (d, 1P, P–O, $^2J_{P,P}$ = 122.0 Hz), 145.1 (d, 1P, P–N, $^2J_{P,P}$ = 122.0 Hz); ^{1}H NMR (CD_2Cl_2, 223 K): δ = 0.30–0.55 [m, 36H, $Si(CH_3)_3$], 0.85 (m, 3H, CH_3 allyl), 1.11 (s, 3H, CH_3), 1.18 (m, 3H, CH_3 allyl), 1.27 (s, 3H, CH_3), 3.18 (m, 1H, H-5), 3.23 (d, 1H, H-2, $^3J_{1,2}$ = 3.6 Hz), 3.62 (m, 2H, H-5' and NH), 3.95 (m, 1H, CH allyl terminal), 4.11 (m, 1H, H-4), 4.22 (m, 1H, CH allyl terminal), 4.95 (m, 1H, H-3), 5.15 (m, 1H, CH allyl central), 5.49 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 7.2–7.8 (m, 20H, CH=); ^{13}C NMR (CD_2Cl_2, 223 K): δ = 0.4–2.0 [$Si(CH_3)_3$], 17.7 (CH_3 allyl), 18.2 (d, CH_3 allyl, $J_{C,P}$ = 7.5 Hz), 26.0 (CH_3), 26.6 (CH_3), 36.4 (m, C-5), 78.7 (m, C-4 and C-3), 83.2 (C-2), 87.0 (d, CH allyl *trans* to P–O, $J_{C,P}$ = 35.6 Hz), 100.4 (d, CH allyl *trans* to P–N, $J_{C,P}$ = 34.9 Hz), 105.5 (C-1), 113.2 (CMe_2), 118.3 (m, CH allyl central), 122.0–157.0 (aromatic carbons). Isomer **B** (50%); ^{31}P NMR (CD_2Cl_2, 223 K): δ = 142.9 (d, 1P, P–O, $^2J_{P,P}$ = 115.1 Hz), 146.4 (d, 1P, P–N, $^2J_{P,P}$ = 115.1 Hz); ^{1}H NMR (CD_2Cl_2, 223 K): δ = 0.30–0.55 [m, 36H, $Si(CH_3)_3$], 1.08 (m, 6H, CH_3 allyl and CH_3), 1.18 (m, 3H, CH_3 allyl), 1.40 (s, 3H, CH_3), 3.20 (m, 1H, H-5), 3.55 (m, 2H, H-5' and NH), 3.82 (d, 1H, H-2, $^3J_{1,2}$ = 3.6 Hz), 3.99 (m, 1H, CH allyl terminal), 4.11 (m, 1H, H-4), 4.27 (m, 1H, CH allyl terminal), 4.99 (m, 1H, H-3), 5.19 (m, 1H, CH allyl central), 5.60 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 7.2–7.8 (m, 20H, CH=); ^{13}C NMR (CD_2Cl_2, 223 K): δ = 0.4–2.0 [$Si(CH_3)_3$], 17.9 (CH_3 allyl), 18.6 (d, CH_3 allyl, $J_{C,P}$ = 7.0 Hz), 26.2 (CH_3), 29.4 (CH_3), 36.7 (m, C-5), 78.7 (m, C-4 and C-3), 83.5 (C-2), 85.1 (d, CH allyl *trans* to P–O, $J_{C,P}$ = 34.8 Hz), 97.4 (d, CH allyl *trans* to P–N, J_{C-P} = 35.1 Hz), 105.8 (C-1), 113.2 (CMe_2), 118.2 (m, CH allyl central), 122.0–157.0 (aromatic carbons); anal. calcd. (%) for $C_{65}H_{77}BF_4NO_8P_2PdSi_4$: C 57.08, H 5.67, N 1.02; found: C 57.14, H 5.72, N 1.07.

[Pd(η^3-1,3-dimethylallyl)(L2e)]BF$_4$ (30): Isomer **A** (45%); ^{31}P NMR (CD_2Cl_2, 253 K): δ = 140.8 (d, 1P, P–O, $^2J_{P,P}$ = 144.1 Hz), 144.3 (d, 1P, P–N, $^2J_{P,P}$ = 144.1 Hz); ^{1}H NMR (CD_2Cl_2, 253 K): δ = 0.30–0.90 [m, 36H, $Si(CH_3)_3$],

1.05 (m, 3H, CH_3 allyl), 1.19 (s, 3H, CH_3), 1.25 (m, 6H, CH_3 allyl and CH_3), 3.21 (m, 1H, H-5), 3.43 (m, 2H, H-2 and NH), 3.57 (m, 1H, H-5′), 3.86 (m, 1H, CH allyl terminal), 4.20 (m, 1H, H-4), 4.29 (m, 1H, CH allyl terminal), 4.83 (m, 1H, H-3), 5.33 (m, 1H, CH allyl central), 5.39 (d, 1H, H-1, $^3J_{1,2}=3.6$ Hz), 7.2–7.8 (m, 20H, CH=); ^{13}C NMR (CD_2Cl_2, 253 K): δ = 0.2–2.0 [$Si(CH_3)_3$], 16,8 (d, CH_3 allyl, $J_{C,P}=7.5$ Hz), 18.3 (d, CH_3 allyl, $J_{C,P}=7.2$ Hz), 26.2 (CH_3), 27.3 (CH_3), 37.2 (m, C-5), 78.9 (C-4), 80.1 (C-3), 83.5 (C-2), 86.1 (d, CH allyl *trans* to P–O, $J_{C,P}=35.2$ Hz), 96.9 (d, CH allyl *trans* to P–N, $J_{C,P}=34.7$ Hz), 105.3 (C-1), 113.9 (CMe_2), 117.9 (m, CH allyl central), 120.0–156.0 (aromatic carbons). Isomer **B** (55%); ^{31}P NMR (CD_2Cl_2, 253 K): δ = 141.5 (d, 1P, P–O, $^2J_{P,P}=147.2$ Hz), 142.6 (d, 1P, P–N, $^2J_{P,P}=147.2$ Hz); ^{1}H NMR (CD_2Cl_2, 253 K): δ = 0.30–0.90 [m, 36H, $Si(CH_3)_3$], 1.11 (m, 3H, CH_3 allyl), 1.22 (s, 3H, CH_3), 1.29 (m, 3H, CH_3), 1.33 (s, 3H, CH_3 allyl), 3.33 (m, 2H, H-5 and NH), 3.49 (m, 1H, H-2), 3.57 (m, 1H, H-5′), 3.93 (m, 1H, CH allyl terminal), 4.20 (m, 1H, H-4), 4.33 (m, 1H, CH allyl terminal), 4.89 (m, 1H, H-3), 5.29 (m, 1H, CH allyl central), 5.43 (d, 1H, H-1, $^3J_{1,2}=3.6$ Hz), 7.2–7.8 (m, 20H, CH=); ^{13}C NMR (CD_2Cl_2, 253 K): δ = 0.2–2.0 [$Si(CH_3)_3$], 17.2 (d, CH_3 allyl, $J_{C,P}=7.2$ Hz), 18.8 (d, CH_3 allyl, $J_{C,P}=7.6$ Hz), 26.5 (CH_3), 27.8 (CH_3), 37.8 (m, C-5), 78.9 (C-4), 80.5 (C-3), 83.8 (C-2), 86.4 (d, CH allyl *trans* to P–O, $J_{C,P}=35.2$ Hz), 101.3 (d, CH allyl *trans* to P–N, $J_{C,P}=35.0$ Hz), 105.3 (C-1), 114.1 (CMe_2), 117.5 (m, CH allyl central), 120.0–156.0 (aromatic carbons); anal. calcd. (%) for $C_{65}H_{77}BF_4NO_8P_2PdSi_4$: C 57.08, H 5.67, N 1.02; found: C 57.23, H 5.81, N 0.95.

[Pd(η³-1,3-cyclohexylallyl)(L1a)]BF_4 (31): Isomer **A** (45%); ^{31}P NMR (CD_2Cl_2, 223 K): δ = 140.4 (d, 1P, P–O, $^2J_{P,P}=79.3$ Hz), 144.8 (d, 1P, P–N, $^2J_{P,P}=79.3$ Hz); ^{1}H NMR (CD_2Cl_2, 213 K): δ = 0.95 (m, 2H, CH_2), 1.15 (m, 2H, CH_2), 1.25–1.61 (m, 78H, CH_3 and CH_3, *t*-Bu), 1.72 (m, 2H, CH_2), 3.41 (m, 1H, H-5), 3.85(m, 1H, H-5′), 4.31 (m, 2H, H-3, CH allyl terminal), 4.42 (m, 2H, H-2, NH), 4.59 (m, 1H, H-4), 4.81 (m, 1H, CH allyl central), 5.78 (d, 1H, H-1, $^3J_{1,2}=3.6$ Hz), 5.92 (m, 1H, CH allyl terminal), 7.2–7.8 (m, 8H, CH=); ^{13}C NMR (CD_2Cl_2, 213 K): δ = 20.3 (b, CH_2), 26.5 (CH_3), 26.8 (CH_3), 27.2 (b, CH_2), 27.9 (b, CH_2), 31.4–33.5 (CH_3, *t*-Bu), 35.2–36.0 (C, *t*-Bu), 38.0 (m, C-5), 75.0 (m, CH allyl *trans* to P–O), 77.8 (C-4), 80.2 (C-2), 83.5 (C-3), 98.7 (m, CH allyl *trans* to P–N), 105.5 (C-1), 111.4 (m, CH allyl central), 113.6 (CMe_2), 124.0–150.0 (aromatic carbons). Isomer **B** (55%); ^{31}P NMR (CD_2Cl_2, 223 K): δ = 143.1 (d, 1P, $^2J_{P,P}=72.8$ Hz), 147.1 (d, 1P, $^2J_{P,P}=72.8$ Hz); ^{1}H NMR (CD_2Cl_2, 213 K): δ = 0.95 (m, 2H, CH_2), 1.15 (m, 2H, CH_2), 1.25–1.61 (m, 78H, CH_3 and CH_3, *t*-Bu), 1.72 (m, 2H, CH_2), 3.38 (m, 1H, H-5), 3.80 (m, 1H, H-5′), 4.29 (m, 1H, H-3), 4.42 (m, 2H, H-2, NH), 4.53 (m, 2H, H-4 and CH allyl terminal), 4.81 (m, 1H, CH allyl central), 5.82 (d, 1H, H-1, $^3J_{1,2}=3.6$ Hz), 5.87 (m, 1H, CH allyl terminal), 7.2–7.8 (m, 8H, CH=); ^{13}C NMR (CD_2Cl_2, 213 K): δ = 20.3 (b, CH_2), 26.3 (CH_3), 26.7 (CH_3), 27.2 (b, CH_2), 27.9 (b, CH_2), 31.4–33.5 (CH_3, *t*-Bu), 35.2–36.0 (C, *t*-Bu), 38.0 (m, C-5), 76.3 (m, CH allyl *trans* to P–O), 77.9 (C-4), 80.0 (C-2), 83.1 (C-3), 99.2 (m, CH allyl *trans* to P–N), 105.3 (C-1), 111.1 (m, CH allyl central), 113.6 (CMe_2), 124.0–150.0 (aromatic carbons); anal. calcd. (%) for $C_{70}H_{101}BF_4NO_8P_2Pd$: C 62.76, H 7.60, N 1.05; found: C 62.55, H 7.71, N 1.09.

[Pd(η³-1,3-cyclohexylallyl)(L2a)]BF_4 (32): Isomer **A** (55%); ^{31}P NMR (CD_2Cl_2, 233 K): δ = 145.5 (d, 1P, P–O, $^2J_{P,P}=80.5$ Hz), 147.3 (d, 1P, P–N, $^2J_{P,P}=80.5$ Hz); ^{1}H NMR (CD_2Cl_2, 233 K): δ = 0.98 (m, 2H, CH_2), 1.15 (m, 2H, CH_2), 1.21 (s, 3H, CH_3), 1. 1.32 (s, 9H, CH_3, *t*-Bu), 1.35 (s, 12H, CH_3 and CH_3, *t*-Bu), 1.47 (s, 18H, CH_3, *t*-Bu), 1.50 (s, 18H, CH_3, *t*-Bu), 1.53 (s, 9H, CH_3, *t*-Bu), 1.62 (s, 9H, CH_3, *t*-Bu), 1.79 (m, 2H, CH_2), 3.52 (m, 1H, H-5), 3.73 (m, 1H, H-5′), 4.11 (m, 2H, NH, H-4), 4.41 (m, 1H, CH allyl terminal), 4.62 (m, 1H, H-3), 4.71 (m, 1H, H-2), 5.12 (m, 1H, CH allyl central), 5.81 (d, 1H, H-1, $^3J_{1,2}=4.0$ Hz), 5.98 (m, 1H, CH allyl terminal), 7.1–7.8 (m, 8H, CH=); ^{13}C NMR (CD_2Cl_2, 233 K): δ = 18.3 (CH_2), 26.3 (CH_3), 26.8 (CH_3), 28.2 (b, CH_2), 31.1–32.7 (CH_3, *t*-Bu), 35.2–36.1 (C, *t*-Bu), 38.7 (m, C-5), 74.9 (b, C-3 and CH allyl *trans* to P–O), 77.0 (C-4), 78.0 (C-2), 101.9 (d, CH allyl *trans* to P–N, $J_{C,P}=37.0$ Hz), 104.2 (C-1), 114.5 (m, CH allyl central), 115.3 (CMe_2), 124.0–150.0 (aromatic carbons). Minor isomer **B** (45%); ^{31}P NMR (CD_2Cl_2, 233 K): δ = 144.4 (d, 1P, P–O, $^2J_{P,P}=79.3$), 149.4 (d, 1P, P–N, $^2J_{P,P}=79.3$); ^{1}H NMR (CD_2Cl_2, 233 K): δ = 0.98 (m, 2H, CH_2), 1.15 (m, 2H, CH_2), 1.29 (s, 3H, CH_3), 1. 1.33 (s, 9H, CH_3, *t*-Bu), 1.35 (s, 21H, CH_3 and CH_3, *t*-Bu), 1.47 (s, 8H, CH_3, *t*-Bu), 1.57 (s, 27H, CH_3, *t*-Bu), 1.62 (s, 9H, CH_3, *t*-Bu), 1.79 (m, 2H, CH_2), 3.55 (m, 1H, H-5), 3.62 (m, 1H, H-5′), 4.11 (m, 2H, NH, H-4), 4.49 (m, 1H, CH allyl terminal), 4.62 (m, 1H, H-3), 4.77 (m, 2H, H-2 and CH allyl terminal), 4.98 (m, 1H, CH allyl central), 5.85 (d, 1H, H-1, $^3J_{1,2}=4.0$ Hz), 7.1–7.8 (m, 8H, CH=); ^{13}C NMR (CD_2Cl_2, 233 K): δ = 18.7 (CH_2), 26.4 (CH_3), 27.0 (CH_3), 28.2 (b, CH_2), 31.1–32.7 (CH_3, *t*-Bu), 35.2–36.1 (C, *t*-Bu), 38.7 (m, C-5), 74.6 (b, C-3), 77.0 (C-4), 78.0 (C-2 and CH allyl *trans* to P–O), 91.9 (d, CH allyl *trans* to P–N, $J_{C,P}=36.6$ Hz), 104.4 (C-1), 113.8 (m, CH allyl central), 115.3 (CMe_2), 124.0–150.0 (aromatic carbons); anal. calcd. (%) for $C_{70}H_{101}BF_4NO_8P_2Pd$: C 62.76, H 7.60, N 1.05; found: C 62.89, H 7.63, N 1.01.

[Pd(η³-1,3-cyclohexylallyl)(L3a)]BF_4 (33): Isomer **A** (57%); ^{31}P NMR (CD_2Cl_2, 223 K): δ = 140.0 (d, 1P, P–O, $^2J_{P,P}=76.9$ Hz), 145.7 (d, 1P, P–N, $^2J_{P,P}=76.9$ Hz); ^{1}H NMR (CD_2Cl_2, 213 K): δ = 0.99 (m, 2H, CH_2), 1.17 (m, 2H, CH_2), 1.3–1.6 (m, 78H, CH_3 and CH_3, *t*-Bu), 1.7.5 (m, 2H, CH_2), 3.25 (m, 1H, NH), 4.05 (m, 1H, H-3), 4.42 (m, 1H, H-4), 4.55 (m, 2H, H-5 and H-5′), 4.58 (m, 1H, H-2), 4.69 (m, 1H, CH allyl terminal), 5.01 (m, 1H, CH allyl central), 5.80 (d, 1H, H-1, $^3J_{1,2}=3.6$ Hz), 5.94 (m, 1H, CH allyl terminal), 7.2–7.8 (m, 8H, CH=); ^{13}C NMR (CD_2Cl_2, 213 K): δ = 19.0 (b, CH_2), 26.3 (CH_3), 26.5 (CH_3), 28.2 (b, CH_2), 31.5–33.5 (CH_3, *t*-Bu), 35.2–36.2 (C, *t*-Bu), 56.3 (m, C-3), 63.8 (m, C-5), 77.7 (C-4), 77.7 (b, CH allyl *trans* to P–O), 85.6 (C-2), 98.9 (m, CH allyl *trans* to P–N), 104.4 (C-1), 113.3 (m, CMe_2 and CH allyl central), 124.0–150.0 (aromatic carbons). Isomer **B** (43%); ^{31}P NMR (CD_2Cl_2, 223 K): δ = 144.2 (d, 1P, $^2J_{P,P}=72$ Hz), 149.2 (d, 1P, $^2J_{P,P}=72$ Hz); ^{1}H NMR (CD_2Cl_2, 213 K): δ = 0.99 (m, 2H, CH_2), 1.17 (m, 2H, CH_2), 1.3–1.6 (m, 78H, CH_3 and CH_3, *t*-Bu), 1.7.5 (m, 2H, CH_2), 3.25 (m, 1H, NH), 4.11 (m, 1H, H-3), 4.38 (m, 1H, H-4), 4.42 (m, 1H, H-5), 4,52 (m ,1H, H-5′), 4.60 (m, 1H, H-2), 4.62 (m, 1H, CH allyl terminal), 4.95 (m, 1H, CH allyl central), 5.84 (d, 1H, H-1, $^3J_{1,2}=3.6$ Hz), 5.86 (m, 1H, CH allyl terminal), 7.2–7.8 (m, 8H, CH=); ^{13}C NMR (CD_2Cl_2, 213 K): δ = 19.0 (b, CH_2), 26.3 (CH_3), 26.7 (CH_3), 28.2 (b, CH_2), 31.5–33.5 (CH_3, *t*-Bu), 35.2–36.2 (C, *t*-Bu), 56.5 (m, C-3), 63.3 (m, C-5), 77.5 (C-4), 77.7 (b, CH allyl *trans* to P–O), 85.5 (C-2), 93.0 (m, CH allyl *trans* to P–N), 104.4 (C-1),

113.2 (CMe_2), 114.0 (m, CH allyl central), 124.0–150.0 (aromatic carbons); anal. calcd. (%) for $C_{70}H_{101}BF_4NO_8P_2Pd$: C 62.76, H 7.60, N 1.05; found: C 62.72, H 7.54, N 1.11.

[Pd(η^3-1,3-cyclohexylallyl)(L4a)]BF_4 (34): Isomer **A** (45%); ^{31}P NMR (CD_2Cl_2, 223 K): $\delta = 143.2$ (d, 1P, P–O, $^2J_{P,P} = 72.9$ Hz), 148.9 (d, 1P, P–N, $^2J_{P,P} = 72.9$ Hz); ^{1}H NMR (CD_2Cl_2, 213 K): $\delta = 0.97$ (m, 2H, CH_2), 1.17 (m, 2H, CH_2), 1.3–1.6 (m, 78H, CH_3 and CH_3, *t*-Bu), 1.84 (m, 2H, CH_2), 4.11 (m, 2H, H-3, NH), 4.38 (m, 1H, CH allyl terminal), 4.45 (m, 2H, H-5 and H-5′), 4.54 (m, 1H, H-4), 4.62 (m, 1H, H-2), 4.70 (m, 1H, CH allyl central), 5.81 (d, 1H, H-1, $^3J_{1,2} = 3.6$ Hz), 5.98 (m, 1H, CH allyl terminal), 7.2–7.8 (m, 8H, CH=); ^{13}C NMR (CD_2Cl_2, 213 K): $\delta = 18.7$ (CH_2), 26.2 (CH_3), 27.0 (CH_3), 28.3 (b, CH_2), 30.5–33.9 (CH_3, *t*-Bu), 35.0–36.5 (C, *t*-Bu), 53.3 (m, C-3), 65.2 (m, C-5), 75.9 (C-4), 77.5 (b, CH allyl *trans* to P–O), 78.1 (C-2), 92.8 (m, CH allyl *trans* to P–N), 104.9 (C-1), 112.9 (CMe_2), 113.2 (m, CH allyl central), 124.0–150.0 (aromatic carbons). Isomer **B** (55%); ^{31}P NMR (CD_2Cl_2, 223 K): $\delta = 145.4$ (d, 1P, $^2J_{P,P} = 79.3$ Hz), 148.2 (d, 1P, $^2J_{P,P} = 79.3$ Hz); ^{1}H NMR (CD_2Cl_2, 213 K): $\delta = 0.97$ (m, 2H, CH_2), 1.17 (m, 2H, CH_2), 1.3–1.6 (m, 78H, CH_3 and CH_3, *t*-Bu), 1.84 (m, 2H, CH_2), 4.14 (m, 2H, H-3, NH), 4.41 (m, 1H, CH allyl terminal), 4.49 (m, 2H, H-5 and H-5′), 4.56 (m, 1H, H-4), 4.62 (m, 1H, H-2), 4.73 (m, 1H, CH allyl central), 5.79 (m, 1H, CH allyl terminal), 5.83 (d, 1H, H-1, $^3J_{1,2} = 3.6$ Hz), 7.2–7.8 (m, 8H, CH=); ^{13}C NMR (CD_2Cl_2, 213 K): $\delta = 18.9$ (CH_2), 26.1 (CH_3), 27.3 (CH_3), 28.3 (b, CH_2), 30.5–33.9 (CH_3, *t*-Bu), 35.0–36.5 (C, *t*-Bu), 53.6 (m, C-3), 65.2 (m, C-5), 74.5 (C-4), 77.5 (b, CH allyl *trans* to P–O), 78.4 (C-2), 96.0 (m, CH allyl *trans* to P–N), 104.9 (C-1), 112.9 (CMe_2), 113.4 (m, CH allyl central), 124.0–150.0 (aromatic carbons); anal. calcd. (%) for $C_{70}H_{101}BF_4NO_8P_2Pd$: C 62.76, H 7.60, N 1.05; found: C 62.86, H 7.77, N 0.99.

Study on the Reactivity of [Pd(η^3-allyl)(L)]BF_4 with Sodium Malonate by *in situ* NMR[38]

A solution of *in situ* prepared [Pd(η^3-allyl)(L)]BF_4 (L = phosphite-phosphoroamidite ligand, 0.05 mmol) in CD_2Cl_2 (1 mL) was cooled in the NMR spectrometer at −80 °C. At this temperature, a solution of cooled sodium malonate (0.1 mmol) was added. The reaction was then followed by ^{31}P NMR. The relative reaction rates were calculated using a capillary containing a solution of triphenylphosphine in CD_2Cl_2 as external standard.

Typical Procedure for Allylic Alkylation of Disubstituted Linear (S1 and S2) and Cyclic (S5 and S6) Substrates

A degassed solution of [PdCl(η^3-C_3H_5)]$_2$ (0.9 mg, 0.0025 mmol) and the corresponding phosphite-phosphoroamidite (0.0055 mmol) in dichloromethane (0.5 mL) was stirred for 30 min. Subsequently, a solution of the corresponding substrate (0.5 mmol) in dichloromethane (1.5 mL), dimethyl malonate (171 μL, 1.5 mmol), *N,O*-bis(trimethylsilyl)acetamide (370 μL, 1.5 mmol) and a pinch of the corresponding base were added. The reaction mixture was stirred at room temperature. After the desired reaction time the reaction mixture was diluted with Et_2O (5 mL) and saturated aqueous NH_4Cl solution (25 mL) was added. The mixture was extracted with Et_2O (3 × 10 mL) and the extract dried over $MgSO_4$. For substrate **S1**, solvent was removed and conversion was measured by ^{1}H NMR. To determine the *ee* by HPLC (Chiralcel OD, 0.5% 2-propanol/hexane, flow 0.5 mL min^{-1}), a sample was filtered over basic alumina using dichloromethane as the eluent.[39] For substrates **S2**, **S5** and **S6**, conversion and enantiomeric excess was determined by GC.[40]

Typical Procedure for Allylic Alkylation of Monosubstituted Substrates S3 and S4

A degassed solution of [PdCl(η^3-C_3H_5)]$_2$ (1.8 mg, 0.005 mmol) and the corresponding phosphite-phosphoroamidite (0.011 mmol) in dichloromethane (0.5 mL) was stirred for 30 min at room temperature. Subsequently, a solution of substrate (0.5 mmol) in dichloromethane (1.5 mL), dimethyl malonate (171 μL, 1.5 mmol), *N,O*-bis(trimethylsilyl)acetamide (370 μL, 1.5 mmol) and a pinch of KOAc were added. After 2 h at room temperature, the reaction mixture was diluted with Et_2O (5 mL) and saturated aqueous NH_4Cl solution (25 mL) was added. The mixture was extracted with Et_2O (3 × 10 mL) and the extract dried over $MgSO_4$. Solvent was removed and conversion and regioselectivity were measured by ^{1}H NMR. To determine the *ee* by HPLC (Chiralcel OJ, 13% 2-propanol/hexane, flow 0.7 mL min^{-1}), a sample was filtered over basic alumina using dichloromethane as the eluent.[41]

Typical Procedure for Allylic Amination of Disubstituted Linear Substates (S1 and S2)

A degassed solution of [PdCl(η^3-C_3H_5)]$_2$ (0.9 mg, 0.0025 mmol) and the corresponding phosphite-phosphoroamidite (0.0055 mmol) in dichloromethane (0.5 mL) was stirred for 30 min. Subsequently, a solution of the corresponding substrate (0.5 mmol) in dichloromethane (1.5 mL) and benzylamine (131 μL, 1.5 mmol) were added. The reaction mixture was stirred at room temperature. After the desired reaction time, the reaction mixture was diluted with Et_2O (5 mL) and saturated aqueous NH_4Cl solution (25 mL) was added. The mixture was extracted with Et_2O (3 × 10 mL) and the extract dried over $MgSO_4$. For substrate **S1**, solvent was removed and conversion was measured by ^{1}H NMR. To determine the *ee* by HPLC (Chiralcel OJ, 13% 2-propanol/hexane, flow 0.5 mL min^{-1}), a sample was filtered over silica using 10% Et_2O/hexane mixture as the eluent.[39] For substrate **S2**, conversion and enantiomeric excess was determined by GC.[42]

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that isomer **28B** reacts around 20 times faster than isomer **28A**.
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