UNIVERSITAT ROVIRA I VIRGILI
SCREENING OF MODULAR CARBOHYDRATE LIGAND LIBRARIES
IN ASYMMETRIC METAL-CATALYZED C-C AND C-X BOND FORMATION REACTIONS
Yvette Angela Mata Campaña
ISBN:978-84-691-0375-3/DL:T.2193-2007

3.2. A carbohydrate-based phosphite-oxazoline ligand library for Pd-catalyzed allylic substitution reactions

Abstract. We have synthesized and screened a library of modular phosphite-oxazoline ligands for asymmetric allylic substitution reactions. The library is easily prepared from commercially available cheap D-glucosamine. The introduction of a phosphite moiety to the ligand design is highly advantageous for the product outcome. Therefore, this ligand library affords good-to-excellent reaction rates (TOF's up to 600 mol substrate x (mol Pd x h)$^{-1}$) and enantioselectivities (ee's up to 99%) and, at the same time, shows a broad scope for mono- and disubstituted linear hindered and unhindered substrates and cyclic substrates. The NMR studies on the Pd-π-allyl intermediates provide a deeper understanding about the effect of the ligand parameters on the origin of enantioselectivity.

3.2.1. Introduction

Palladium-catalyzed allylic substitution reactions are an efficient synthetic tool for constructing carbon-carbon and carbon-heteroatom bonds.[1] The chiral ligands used for highly enantioselective allylic substitution have mainly been mixed bidentate donor ligands.[1,2] Mixed phosphorus-nitrogen ligands have played a dominant role among heterodonor ligands. However, one disadvantage of these ligands is that they are often synthesized from expensive chiral sources or in tedious synthetic steps. Another common disadvantages of the most successful ligand families developed for this process is that they usually have low reaction rates and high substrate specificity (i.e ee's are high in disubstituted linear hindered substrates and low in cyclic and unhindered linear substrates, or vice versa) (Scheme 1).[1]

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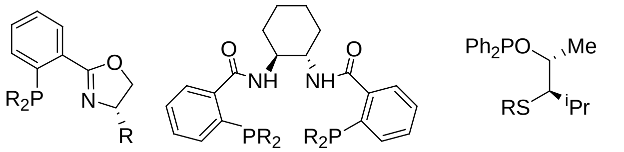
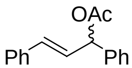
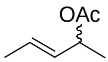
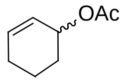
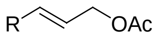


	PHOX ligands	Trost's ligands	Evans' ligands
	100% Yield (1 h) 99% ee	9% Yield (24 h) 52% ee	100% Yield (24 h) 98% ee
	99% Yield (1 h) 57% ee	92% Yield (24 h) 91% ee	87% Yield (24 h) 65% ee
	Yield not reported 72% ee	86% Yield (6 h) 96% ee	100% Yield (24 h) 90% ee
	99% Yield (18h) 47% regio; 84% ee	-	-

Scheme 1. Summary of the best results with several linear and cyclic substrates for three of the most representative ligand families developed for Pd-catalyzed allylic substitution reactions (reactions usually carried out with 2-4 mol% of Pd).

It is therefore of great importance nowadays to conduct research into more versatile and faster mixed P-N ligand systems that can be synthetized in few steps from simple starting materials. For this purpose, carbohydrates are particularly advantageous because of their low price and easy modular constructions.[3] Although they have been successfully used in other enantioselective reactions, they have only very recently shown their huge potential as a source of highly effective chiral ligands in this process.[3,4] Notable examples include two types of phosphorous-oxazoline ligands.[4e,5] In this context, Uemura and coworkers synthesized the phosphinite-oxazoline ligands **1** (Figure 1)[4e,5b] which proved to be effective in the allylic substitution of hindered substrate 1,3-diphenyl-3-acetoxyprop-1-ene but which had low enantioselectivity for unhindered cyclic and linear substrates.[4e] On the basis of this structure, in this paper we have designed a new ligand library in which the phosphinite group is replaced by a phosphite group (Figure 2). The advantage of incorporating a phosphite moiety into the ligand is that: (i) the substrate specificity decreases because the chiral pocket created

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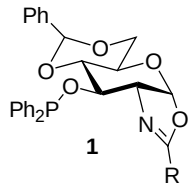
(the chiral cavity where the allyl is embedded) is smaller than for ligands **1**[1c,6] yet flexible enough[6] to allow the perfect coordination of hindered and unhindered substrates;[7] (ii) reaction rates increases because of the high π-acceptor capacity of the phosphite moiety;[8] and (iii) the regioselectivity towards the desired branched isomer in monosubstituted linear substrates increased because of the π-acceptor capacity of the phosphite moiety enhance the S_N-1 character of the nucleophilic attack.[9]



1

Figure 1. Phosphinite-oxazoline ligands developed by Uemura and coworkers.

We therefore report here the design of a library of 45 potential chiral phosphite-oxazoline ligands **L1-L5a-i** (Figure 2) for Pd-catalyzed allylic substitution reactions of several substrate types.[10] We also discuss the synthesis and characterization of the Pd-π-allyl intermediates to provide greater insight into the origin of the enantioselectivity. The library was synthesized and screened using a series of parallel reactors, each of which was equipped with 12 different positions. These new phosphite-oxazoline ligands **L1-L5a-i** also have the advantage of a more flexible ligand scaffold than ligands **1** because they can be easily tuned in two different regions (oxazoline and phosphite substituents) so that their effect on catalytic performance can be determined. Therefore, with this library we fully investigated the effects of different electronic and steric properties of the oxazoline moiety (**L1-L5**) and different substituents/configurations in the biaryl phosphite moieties (**a-i**). As a result, the highly enantioselective and active Pd-allylic substitution reactions are carried out for several substrates.

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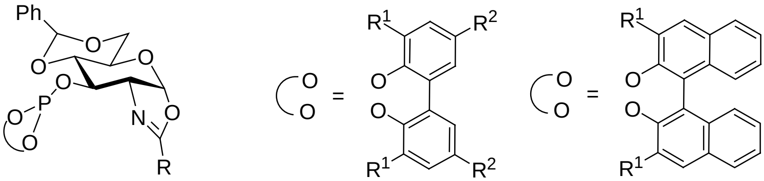

L1 R= Ph	**a** $R^1 = R^2 = {}^tBu$	**f** $(S)^{ax}$; R^1= H
L2 R= ^{i}Pr	**b** $R^1 = {}^tBu$; R^2 = OMe	**g** $(R)^{ax}$; R^1= H
L3 R= ^{t}Bu	**c** $R^1 = SiMe_3$; R^2 = H	**h** $(S)^{ax}$; $R^1 = SiMe_3$
L4 R= Me	**d** $R^1 = R^2$ = Me	**i** $(R)^{ax}$; $R^1 = SiMe_3$
L5 R= Bn	**e** $R^1 = R^2$ = H	

Figure 2. Phosphite-oxazoline ligand library **L1-L5a-i**.

3.2.2. Results and Discussion

3.2.2.1. Ligand synthesis.

The synthesis of the phosphite-oxazoline ligand library **L1-L5a-i** is straightforward (Scheme 2). They were efficiently synthesized in one step by reacting the corresponding sugar oxazoline-alcohols (**3**-**7**) with 1 equiv of the corresponding biaryl phosphorochloridite (**a**-**i**) in the presence of pyridine (Scheme 2). Oxazoline-alcohols **3**-**7** are easily prepared from inexpensive D-glucosamine **2** on a large scale.[4e] All the ligands were stable during purification on neutral alumina under an atmosphere of argon and isolated in moderate-to-good yields as white solids. They were stable at room temperature and very stable to hydrolysis. The elemental analysis were in agreement with the assigned structure. The ^{1}H and ^{13}C NMR spectra were as expected for these C_1 ligands. One singlet was observed in the ^{31}P NMR spectrum. Rapid ring inversions (atropoisomerization) in the biphenyl-phosphorus moieties occurred on the NMR time scale since the expected diastereoisomers were not detected by low-temperature phosphorus NMR.[11]

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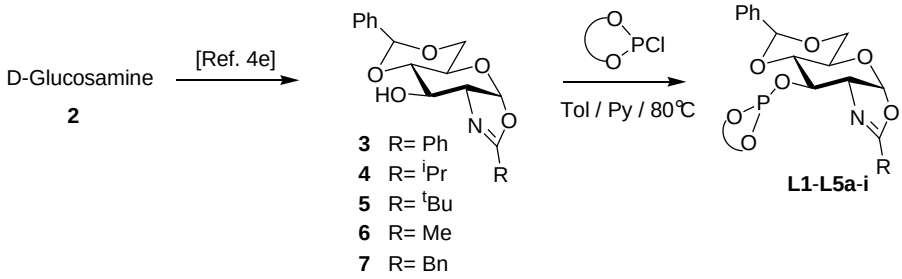
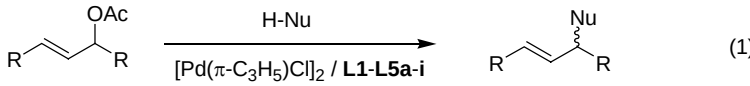


Scheme 2. Synthesis of phosphite-oxazoline ligand library **L1-L5a-i**.

3.2.2.2. Allylic substitution of disubstituted linear substrates

In this section, we report the use of the chiral phosphite-oxazoline ligand library (**L1-L5a-i**) in the Pd-catalyzed allylic substitution (equation 1) of two disubstituted linear substrates with different steric properties: *rac*-1,3-diphenyl-3-acetoxyprop-1-ene **S1** (widely used as a model substrate), and *rac*-1,3-dimethyl-3-acetoxyprop-1-ene **S2**. In all the cases, the catalysts were generated *in situ* from the π-allyl-palladium chloride dimer $[PdCl(\eta^3\text{-}C_3H_5)]_2$, the corresponding ligand and a catalytic amount of the corresponding base. Two nucleophiles were used. For the allylic alkylation, the nucleophile was generated from dimethyl malonate in the presence of *N*,*O*-bis(trimethylsilyl)-acetamide (BSA), while for the allylic amination, benzylamine was used as the nucleophile.



(1)

S1 R= Ph
S2 R= Me

8 R= Ph; H-Nu= H-CH(COOMe)$_2$
9 R= Ph; H-Nu= H-NHCH$_2$Ph
10 R= Me; H-Nu= H-CH(COOMe)$_2$

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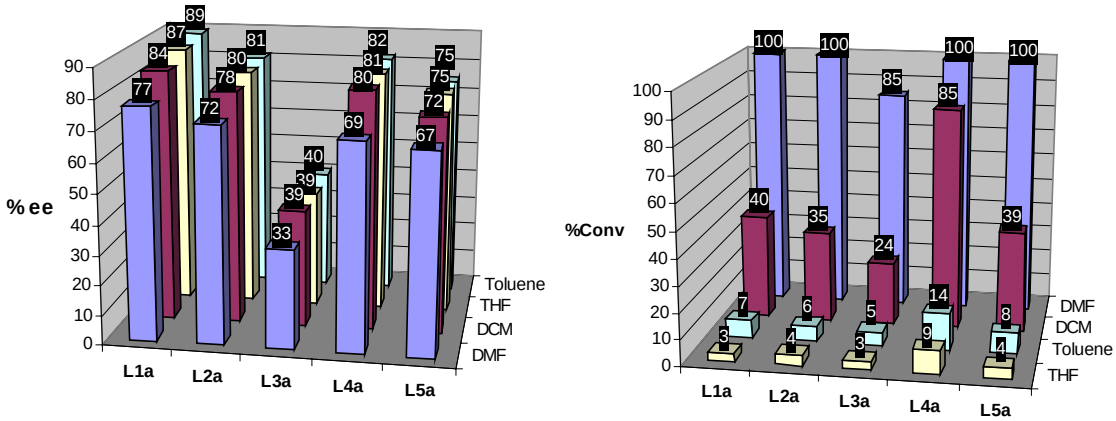
3.2.2.2.1. Allylic substitution of *rac*-1,3-diphenyl-3-acetoxyprop-1-ene S1 using dimethyl malonate and benzylamine as nucleophiles (equation 1)

For an initial evaluation of this new type of ligand in the palladium-catalysed asymmetric substitution reactions, we chose the allylic substitution of **S1** (equation 1, R= Ph) and used dimethyl malonate and benzylamine as nucleophiles. As these reactions were carried out with a variety of ligands carrying different donor groups, the efficacy of different ligand systems can be directly compared.[1]

We determined the optimal reaction conditions by conducting a first set of experiments in which the solvent, the ligand-to-palladium ratio and the base were varied. We first studied the effect of four solvents (tetrahydrofurane (THF), toluene, dimethylformamide (DMF) and dichloromethane (DCM), with five ligands (**L1a-L5a**). Figure 3 shows the results when dimethyl malonate was used as the nucleophile (trends were similar in the allylic amination of **S1**). The results show that the efficiency of the process strongly depended on the nature of the solvent. The enantioselectivity was highest with toluene, THF and dichloromethane. However, although toluene provided slightly higher enantioselectivity than dichloromethane, its activity was lower. On the other hand, dimethylformamide yielded the highest relative conversions, but its ee's were the lowest of the four solvents. So, the optimum trade-off between activities and enantioselectivities was obtained by using dichloromethane as the solvent (Figure 3).



(a) (b)

Figure 3. Results of the catalytic allylic alkylation of **S1** using ligands **L1a-L5a** in four solvents at room temperature and a ligand-to-palladium ratio of 1.1. (a) Enantioselectivities of product **8**. The positive numbers refer to the formation of the *S*-isomer in excess. (b) Conversions after 10 minutes.

We then studied the effect of varying the ligand-to-palladium ratio. Figure 4 shows the conversion and enantioselectivity when dichloromethane and ligands **L1a-L5a** were used (similar trends were observed for the other solvents). The results show that an excess of ligand is not needed for activities and enantioselectivities to be high. Interestingly, enantioselectivities were best with a ligand-to-palladium of 0.9. At a higher ligand-to-palladium ratio (1.1 or 2), enantioselectivies were lower. This is due to the fact that at a higher ligand-to-palladium ratio of 0.9 the phosphite-oxazoline ligand acts as a monodentate ligand (see section 3.2.2.5, Origin of enantioselectivity. Study of the Pd-π-allyl intermediates).

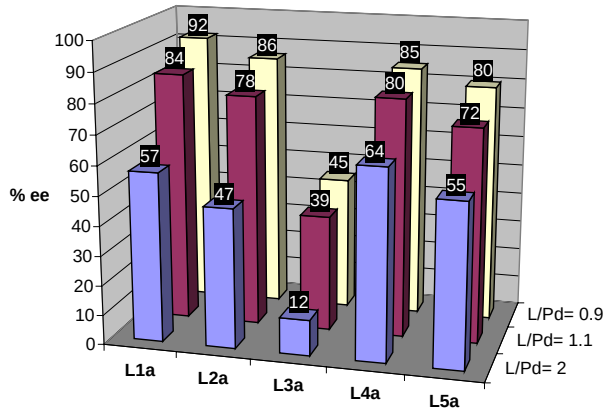


Figure 4. Enantioselectivities of product **8** using ligands **L1a-L5a** at different ligand-to-palladium ratio in dichloromethane at room temperature. The positive numbers refer to the formation of the *S*-isomer in excess. In all cases full conversion were obtained after 1 hour.

We then studied the effect of several bases. Table 1 shows the conversion and selectivity when dichloromethane was used as a solvent with ligands **L1a** and **L4a** (similar trends were observed for the other solvents and ligands). The best activities and enantioselectivities were obtained with KOAc and NaOAc (entries 1, 2, 5 and 6 vs 3, 4, 7 and 8).

For comparative purposes, the rest of the ligands were tested under conditions that provided optimum trade-off between enantioselectivities and reaction rates (i.e. a ligand-to-palladium ratio of 0.9, dichloromethane as the solvent and potassium acetate as the base). Table 2 shows the results when dimethyl malonate was used as the nucleophile. They indicate that catalytic performance (activities and enantioselectivities) is highly affected by the oxazoline substituents and the axial chirality and the substituents of the biaryl moieties. In general, activities (TOF's up to 600 mol **S1** x (mol Pd x h)$^{-1}$) and enantioselectivities (ee's up to 99%) were high.

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Table 1. Pd-catalyzed allylic substitution of **S1** using ligands **L1a** and **L4a**. Effect of the base.[a]

Entry	Ligand	Base	% Conv (min)[b]	% ee[c]
1	**L1a**	KOAc	100 (30)	92 (*S*)
2	**L1a**	NaOAc	100 (30)	92 (*S*)
3	**L1a**	K_2CO_3	100 (60)	85 (*S*)
4	**L1a**	Li_2CO_3	100 (60)	89 (*S*)
5	**L4a**	KOAc	100 (15)	85 (*S*)
6	**L4a**	NaOAc	100 (15)	85 (*S*)
7	**L4a**	K_2CO_3	90 (30)	78 (*S*)
8	**L4a**	Li_2CO_3	100 (30)	77 (*S*)

[a] All reactions were run at 23 ºC. 0.5 mol% $[PdCl(\eta^3\text{-}C_3H_5)]_2$. Dichloromethane as solvent. 0.9 mol% ligand. [b] Reaction time shown in parentheses. [c] Enantiomeric excesses. The absolute configuration appears in parentheses.

The effect of the oxazoline substituent was studied with ligands **L1a**-**L5a** (Table 2, entries 1, 10-12 and 14). We found that these substituents affected both activities and enantioselectivities. The results showed that enantioselectivity is dependent on both the electronic and steric properties of the substituents in the oxazoline moiety. Therefore, enantioselectivities were best with ligand **L1a**, which contains a phenyl-oxazoline group (Table 2, entry 1). This behavior contrasts with the effect of the oxazoline-substituent observed for related phosphinite-oxazoline ligands **1**, for which enantioselectivities were higher when a methyl substituent was present.[4e] However, activities were controlled by the steric properties of the substituents in the oxazoline groups. They were higher when less sterically demanding substituents were present (i.e. Me>Ph≈Bn>^{i}Pr>^{t}Bu).

The effects of phosphite moieties were studied using ligands **L1a-i** (Table 2, entries 1-9). It was observed that these moieties affected both activity and enantioselectivity. The results indicated that the substituents at the *ortho* positions of the biphenyl moiety mainly affected activities, while the substituents at the *para* positions mainly affected enantioselectivities. Activities and enantioselectitivies were

therefore highest when *tert*-butyl groups were present at both the *ortho* and *para* positions of the biphenyl phosphite moiety (ligand **L1a**, Table 2, entry 1). To further investigate how enantioselectivity was influenced by the axial chirality of the biaryl moiety, ligands **L1f-L1i** containing different enantiomerically pure binapthyl moieties were also tested (Table 2, entries 6-9). The results indicate that there is a cooperative effect between the configuration of the biaryl moiety and the configurations of the ligand backbone on enantioselectivity. This leads to a matched combination for ligands **L1f** and **L1h**, which contains an *S*-binaphthyl moiety (Table 2, entries 6 and 8 vs 7 and 9). In addition, comparing the results obtained using ligands **L1c** with binaphthyl ligands **L1h** and **L1i** (Table 2, entry 3 vs 8 and 9), we can also conclude that the atropoisomeric biphenyl moiety in ligands **L1a-d** adopts an *S*-configuration when coordinated in the Pd-π-allyl intermediate species.

To sum up, the best result was obtained with ligand **L1a**, which contains the optimal combination of substituents in the oxazoline and in the biaryl phosphite moieties. These results clearly show the efficiency of using highly modular scaffolds in ligand design.

In addition to the effect of structural parameters on enantioselectivity, the reaction parameters can also be controlled to further improved selectivity. In this case, enantioselectivity was further improved (ee's up to 95%) with ligand **L1a** by lowering the reaction temperature to 0 ºC (Table 2, entry 15). As expected, changing the solvent from dichloromethane to toluene increased enantioselectivity even further (ee's up to 99%, Table 2, entry 16). Interestingly, when this result is compared with the enantioselectivities obtained with their corresponding Pd-phosphinite-oxazoline **1** system (ee's up to 96% at 0 °C), we can concluded that adding a phosphite moiety to ligands **L1-L5a-i** has been advantageous. These results are among the best that have been reported.[1]

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Table 2. Selected results for the Pd-catalyzed allylic alkylation of **S1** using phosphite-oxazoline ligand library **L1-L5a-i**[a]

Entry	Ligand	% Conv (min)[b]	% ee[c]
1	**L1a**	100 (30)	92 (*S*)
2	**L1b**	89 (30)	84 (*S*)
3	**L1c**	95 (30)	86 (*S*)
4	**L1d**	85 (30)	89 (*S*)
5	**L1e**	57 (30)	86 (*S*)
6	**L1f**	82 (30)	81 (*S*)
7	**L1g**	80 (30)	9 (*S*)
8	**L1h**	100 (30)	84 (*S*)
9	**L1i**	99 (30)	62 (*S*)
10	**L2a**	92 (30)	86 (*S*)
11	**L3a**	67 (30)	45 (*S*)
12	**L4a**	100 (15)	85 (*S*)
13	**L4c**	88 (15)	83 (*S*)
14	**L5a**	99 (30)	80 (*S*)
15[d]	**L1a**	54 (300)	95 (*S*)
16[d,e]	**L1a**	100 (360)	99 (*S*)

[a] All reactions were run at 23 ºC. 0.5 mol% $[PdCl(\eta^3\text{-}C_3H_5)]_2$. Dichloromethane as solvent. 0.9 mol% ligand. [b] Reaction time shown in parentheses. [c] Enantiomeric excesses. The absolute configuration appears in parentheses. [d] T= 0 ºC. [e] 2 mol% Pd, toluene as solvent.

We then tested ligands **L1-L5a-i** in the Pd-catalyzed allylic amination of **S1** with benzylamine (equation 1). The catalytic results are summarized in Table 3. We observed that the catalytic performance follows the same trend as for the allylic alkylation of **S1**. Therefore, the enantioselectivities were highest (even higher than in the alkylation of this substrate) with ligand **L1a** (ee's up to 94% at room temperature and dichloromethane as the solvent). As expected, the activity was lower than in the alkylation reaction of **S1**. The stereoselectivity of the amination was the same as for the

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alkylation reaction, though the CIP descriptor was inverted due to the change in priority of the groups.

Table 3. Selected results for the Pd-catalyzed allylic amination of **S1** using phosphite-oxazoline ligand library **L1-L5a-i**[a]

Entry	Ligand	% Conv [b]	% ee[c]
1	**L1a**	60	94 (*R*)
2	**L1b**	53	87 (*R*)
3	**L1c**	58	90 (*R*)
4	**L1d**	54	92 (*R*)
5	**L1e**	34	87 (*R*)
10	**L2a**	59	89 (*R*)
11	**L3a**	35	34 (*R*)
12	**L4a**	79	89 (*R*)
14	**L5a**	61	85 (*R*)

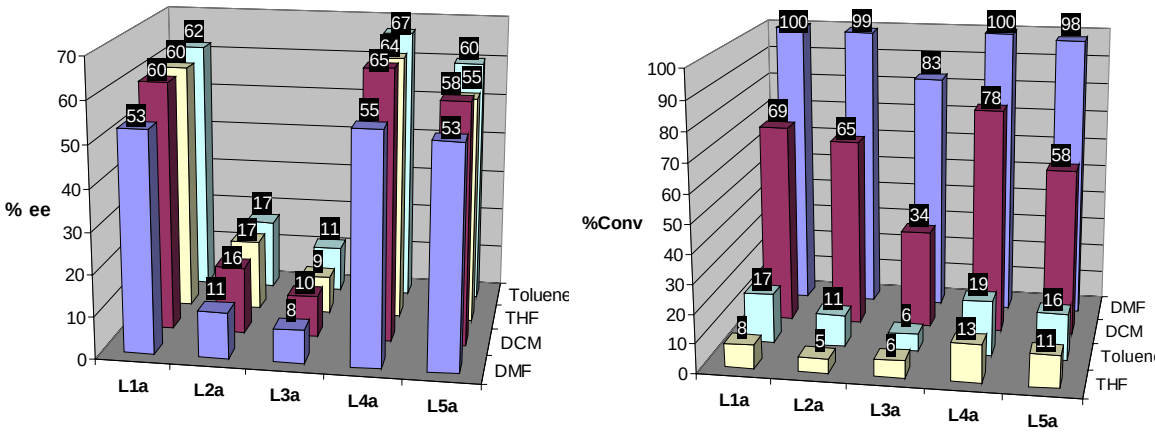
[a] All reactions were run at 23 ºC. 1 mol% $[PdCl(\eta^3\text{-}C_3H_5)]_2$. Dichloromethane as solvent. 1.8 mol% ligand. [b] Conversion after 24 hours. [c] Enantiomeric excesses. The absolute configuration appears in parentheses.

3.2.2.2.2. Allylic alkylation of *rac*-1,3-dimethyl-3-acetoxyprop-1-ene S2 using dimethyl malonate as the nucleophile (equation 1)

We also evaluated the phosphite-oxazoline ligand library **L1-L5a-i** in the allylic alkylation of the linear substrate **S2** (equation 1, R= Me). This substrate is less sterically demanding than substrate **S1,** which we had used before. The 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 where the allyl is embedded) around the metal center, mainly because of the presence of less sterically demanding methyl *syn* substituents.[1] Therefore, few catalytic systems have provided high enantioselectivities.[8b,12] Due to the presence of bulky biaryl phosphite

moiety in ligands **L1-L5a-i**, which are know to be flexible and to provide large bite angles, we expected to be able to tune the size of the chiral pocket adequately and therefore to obtain also high enantioselectivity for this substrate.

The preliminary investigations into the solvent (Figure 5) and ligand-to-palladium ratio (Figure 6) revealed a trend that was similar to that of the previously tested substrate **S1**. The trade-off between selectivities and activities was therefore best when dichloromethane was used and the ligand-to-palladium ratio was 0.9. However, it should be noted that the negative effect of adding excess ligand is less pronounced for this unhindered substrate than for the previously tested hindered substrate **S1** (Figure 4 vs 6). This maybe because substrate **S2** is less sterically hindered than substrate **S1** (see section 3.2.2.5, Origin of enantioselectivity. Study of the Pd-π-allyl intermediates).



(a) (b)

Figure 5. Results of the catalytic allylic alkylation of **S2** using ligands **L1a-L5a** in four solvents at room temperature and a ligand-to-palladium ratio of 0.9. (a) Enantioselectivities of product **10**. The positive numbers refer to the formation of the *R*-isomer in excess. (b) Conversions after 30 minutes.

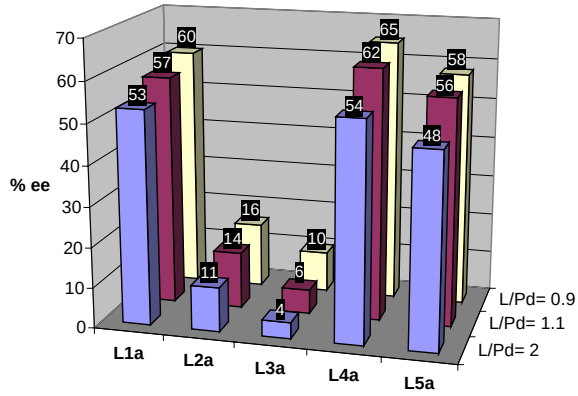


Figure 6. Enantioselectivities of product **10** using ligands **L1a**-**L5a** at different ligand-to-palladium ratio in dichloromethane at room temperature. The positive numbers refer to the formation of the *R*-isomer in excess. In all cases full conversions were obtained after 2 hours.

Table 4 summarizes the results of using the phosphite-oxazoline ligand library **L1**-**L5a-i** under the optimized conditions. In general, activities and enantioselectivities were also high (ee's up to 89%) in the alkylation of **S2**. Again, activities and enantioselectivities were affected by the substituents in both the oxazoline and phosphite moiety and the cooperative effect between stereocenters. However, the effect of these parameters on enantioselectivity was different from their effect on the alkylation of hindered substrate **S1**. Thus, enantioselectivity was best with ligand **L4h** (ee's up to 89%). These results again clearly shows the importance of using modular scaffolds in the ligand design.

Regarding the effect of the oxazoline substituents, the presence of bulky substituents in this position considerably decreased activities and enantioselectivities (Table 4, entries 1, 10-12 and 15). Therefore, in contrast to the alkylation of **S1**, both the activities and enantioselectivities were only dependent on the steric properties of the substituents in the oxazoline moiety and their were higher when a methyl substituent was present (ligand **L4a**, Table 4, entry 12).

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Table 4. Pd-catalyzed allylic substitution of **S2** using phosphite-oxazoline ligand library **L1-L5a-i**[a]

Entry	Ligand	% Conv (min)[b]	% ee[c]
1	**L1a**	69 (30)	60 (*R*)
2	**L1b**	63 (30)	60 (*R*)
3	**L1c**	68 (30)	32 (*R*)
4	**L1d**	61 (30)	40 (*R*)
5	**L1e**	42 (30)	22 (*R*)
6	**L1f**	50 (30)	68 (*R*)
7	**L1g**	12 (30)	9 (*S*)
8	**L1h**	28 (30)	77 (*R*)
9	**L1i**	49 (30)	9 (*R*)
10	**L2a**	65 (30)	16 (*R*)
11	**L3a**	34 (30)	10 (*R*)
12	**L4a**	78 (30)	65 (*R*)
13	**L4c**	77 (30)	48 (*R*)
14	**L4h**	31 (30)	80 (*R*)
15	**L5a**	58 (30)	58 (*R*)
16[d]	**L1f**	100 (360)	81 (*R*)
17[d]	**L1h**	83 (600)	87 (*R*)
18[d]	**L4h**	88 (600)	89 (*R*)

[a] All reactions were run at 23 ºC. 0.5 mol% $[PdCl(\eta^3\text{-}C_3H_5)]_2$. Dichloromethane as solvent. 0.9 mol% ligand. [b] Reaction time shown in parentheses. [c] Enantiomeric excesses. The absolute configuration appears in parentheses. [d] T= 0 ºC.

As far as the effect of the phosphite moiety on catalytic performance is concerned, bulky substituents need to be in the *ortho* position of the biphenyl moieties and substituents of any group except hydrogen need to be in the *para* positions if enantioselectivity is to be high (Table 4, entries 1 and 2 *vs* 3-5). Therefore, ligands **L1a** and **L1b** containing bulky substituents in the *ortho* positions and either *tert*-butyl or methoxy groups in the *para* positions of the biphenyl moieties provided higher

enantioselectivities than ligands **L1c** (without substituents in the *para* positions), **L1d** (with small methyl substituents in *ortho* positions) and **L1e** (with an unsubstituted biphenyl moiety). The effect of the configuration of the biaryl naphthyl moiety (ligands **L1f-i**) is similar to the effect in the previous alkylation of **S1** (Table 4, entries 6-9). Therefore, ligands **L1f** and **L1h** with an *S*-binaphthyl moiety provided higher enantioselectivities than ligands **L1g** and **L1i** with a *R*-binaphthyl group. Interestingly, and in contrast to the substitution of **S1**, this cooperative effect is highly advantageous. Enantioselectivities increased from 60% to 77% ee at room temperature (Table 4, entry 1 vs 8).

In summary, results were best with ligand **L4h**, which contains the optimal combination of subsitutents in the oxazoline and in the biaryl phosphite moieties (ee’s up to 89%). If this result is compared with the low-to-moderate enantioselectivities obtained with their related Pd-phosphinite-oxazoline **1** ligand systems (ee’s up to 57% at 0 °C) in the alkylation of substrate **S2**, we can conclude again that the addition of a phosphite moiety has been highly advantageous in terms of activity and enantioselectivity. These results are among the best that have been reported.[8b,12]

3.2.2.3. Allylic alkylation of cyclic substrates (equation 2)

As for the unhindered substrate **S2**, enantioselectivity in cyclic substrates is difficult to control, mainly because of the presence of less sterically *syn* substituents. These *syn* substituents are thought to play a crucial role in the enantioselection observed with cyclic substrates in the corresponding Pd-allyl intermediate.[1]

This section shows that the chiral phosphite-oxazoline ligand library **L1-L5a-i** applied above to the Pd-catalyzed allylic substitution of linear substrates (**S1** and **S2**) can also be used for cyclic substrates (ee’s up to 94%). In this case, two cyclic substrates were tested (equation 2): *rac*-3-acetoxycyclohexene **S3** (which is widely used as a model substrate) and *rac*-3-acetoxycycloheptene **S4**.

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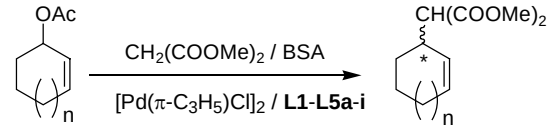

(2)

S3 n=1
S4 n=2

11 n=1
12 n=2

We initially studied the allylic alkylation of *rac*-3-acetoxycyclohexene **S3** using ligands **L1-L5a-i**. Preliminary investigations into the solvent effect and ligand-to-palladium ratio showed the same trends as in the unhindered linear substrate **S2** tested previously. The trade-off between enantioselectivities and reaction rates was therefore optimum with dichloromethane and a ligand-to-palladium ratio of 0.9.

Table 5 summarizes the results of using the phosphite-oxazoline ligand library **L1-L5a-i** under the optimized conditions. In general, activities and enantioselectivities were also high (ee's up to 85%) in the alkylation of **S3**. Again, activities and enantioselectivities were affected by the substituents in the oxazoline moiety and the substituents/configuration of the phosphite moiety. However, the effect of these parameters was different from the effect observed in the substitution of linear substrates **S1** and **S2**. Therefore, results were best with ligand **L1i**.

While the effect of the oxazoline substituents on activities is similar to the effect in the alkylation of **S1** and **S2**, the effect of the phosphite moiety is different. Therefore, activities were better when less sterically demanding oxazoline substituents were present (Table 5, entries 1 and 12 *vs* 10, 11 and 14) and when bulky substituents were present at both *ortho* and *para* positions of the biphenyl moieties (Table 5, entries 1-5).

If enantioselectivity was to be high, we found that a phenyl substituent in the oxazoline moiety (Table 5, entries 1 vs 10-12 and 14) and either *ortho* trimethylsilyl disubstituted binaphthyl moiety (Table 5, entries 8 and 9) or *ortho* and *para* tetrasubstituted *tert*-butyl biphenyl moiety (Table 5, entry 1) were needed. Interestingly, in contrast to the alkylation of **S1** and **S2**, the cooperative effect resulted in a matched

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combination for ligand **L1i**, which contains an *R*-binapthyl phosphite group (Table 5, entries 9 and 16).

This phosphite-oxazoline ligand library **L1-L5a-i** was also effective (ee's up to 94%) in the allylic alkylation of the seven-membered ring substrate **S4** (Table 5, entries 17-19).

Table 5. Selected results for the Pd-catalyzed allylic alkylation of **S3** and **S4** using phosphite-oxazoline ligand library **L1-L5a-i**[a]

Entry	Ligand	Substrate	% Conv (h)[b]	% ee[c]
1	**L1a**	**S3**	100 (24)	75 (*R*)
2	**L1b**	**S3**	68 (24)	22 (*R*)
3	**L1c**	**S3**	72 (24)	54 (*R*)
4	**L1d**	**S3**	62 (24)	32 (*R*)
5	**L1e**	**S3**	21 (24)	5 (*R*)
6	**L1f**	**S3**	23 (24)	28 (*R*)
7	**L1g**	**S3**	28 (24)	38 (*S*)
8	**L1h**	**S3**	42 (24)	73 (*R*)
9	**L1i**	**S3**	23 (24)	83 (*R*)
10	**L2a**	**S3**	79 (24)	43 (*R*)
11	**L3a**	**S3**	51 (24)	49 (*R*)
12	**L4a**	**S3**	100 (24)	34 (*R*)
13	**L4c**	**S3**	89 (24)	28 (*R*)
14	**L5a**	**S3**	98 (24)	13 (*R*)
15[d]	**L1a**	**S3**	69 (36)	81 (*R*)
16[d]	**L1i**	**S3**	37 (36)	85 (*R*)
17	**L1a**	**S4**	100 (24)	78 (*R*)
18[d]	**L1a**	**S4**	43 (36)	92 (*R*)
19[d]	**L1i**	**S4**	19 (36)	94 (*R*)

[a] All reactions were run at 23 ºC. 0.5 mol% $[PdCl(\eta^3\text{-}C_3H_5)]_2$. Dichloromethane as solvent. 0.9 mol% ligand. [b] Reaction time in hours shown in parentheses. [c] Enantiomeric excesses. The absolute configuration appears in parentheses. [d] T= -5 ºC.

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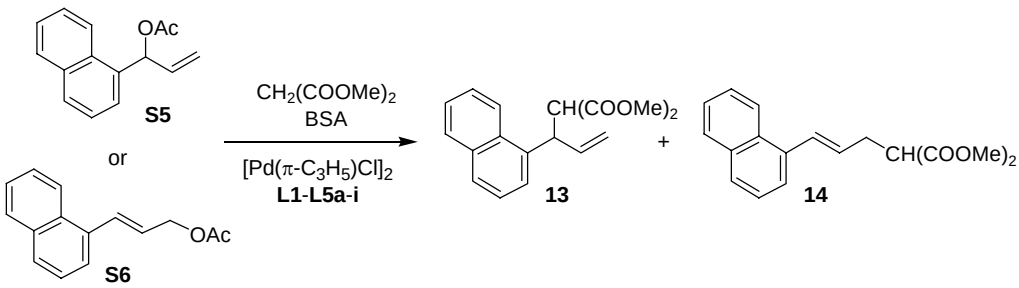
In summary, results were best with ligand **L1i**, which contains the optimal combination of configuration/substituents in the biaryl moiety and in the oxazoline group. Again the replacement of a phosphinite moiety by a phosphite group in the ligand design is seen to lead to higher enantioselectivities than when related ligands **1** are used (ee's up to 74% at 0 °C). These results are among the best that have been reported.[1d,4h,8b,12a,13]

3.2.2.4. Allylic substitution of monosubstituted linear substrates (equation 3)

Encouraged by the excellent results obtained for several disubstituted linear substrates and cyclic substrates, we examined the regio- and stereoselective allylic alkylation 1-(1-naphthyl)allyl acetate **S5** and 1-(1-naphthyl)-3-acetoxyprop-1-ene **S6** with dimethyl malonate (equation 3). It is not only the enantioselectivity of the process that needs to be controlled for these substrates; the regioselectivity is also a problem, because a mixture of regioisomers may be obtained. Most Pd-catalysts developed to date favor the formation of achiral linear product **14** rather than the desired branched isomer **13**. Therefore, the development of highly regio- and enantioselective Pd-catalysts is still a challenge.[8b,9,14] Because the π-acceptor capacity of the biaryl phosphite moiety in ligands **L1-L5a-i** is high, we expected to enhance the S_N-1 character of the nucleophilic attack, which would favor the formation of the branched isomer **13**.[9]



(3)

Adv. Synth. Catal. **2005**, *347*, 1943 and submitted to *Chem. Eur. J.*

Table 6 summarizes the results obtained with the phosphite-oxazoline ligand library **L1-L5a-i**. In general, enantioselectivities were high (ee's up to 96 %) and regioselectivities good (up to 85%) for the branched product **13** under standard reaction conditions. The results indicated that the trade-off between regio- and enantioselectivities was best for ligands that contain a phenyl substituent in the oxazoline moiety and trimethylsilyl substituents at the *ortho* positions of the biaryl group. Therefore, ligands **L1c** and **L1i** produced the desired branched isomer **13** as the major product with high enantioselectivity (Table 6, entries 3 and 7). These results are among the best reported for this type of substrates.[8b,9,14]

Table 6. Selected results for the Pd-catalyzed allylic alkylation of monosubstituted substrate **S5** and **S6** using the ligand library **L1-L5a-i** under standard conditions[a]

Entry	Ligand	Substrate	% Conv[b] (min)	**13**/**14**[c]	% ee[d]
1	**L1a**	**S5**	100 (60)	65/35	83 (*S*)
2	**L1b**	**S5**	100 (60)	55/45	90 (*S*)
3	**L1c**	**S5**	100 (60)	80/20	90 (*S*)
4	**L1d**	**S5**	100 (60)	65/35	63(*S*)
5	**L1e**	**S5**	100 (60)	55/45	42 (*S*)
6	**L1h**	**S5**	100 (60)	50/50	96 (*S*)
7	**L1i**	**S5**	100 (60)	85/15	88 (*S*)
8	**L2a**	**S5**	100 (60)	55/45	32 (*S*)
9	**L3a**	**S5**	100 (60)	55/45	32 (*S*)
10	**L4a**	**S5**	100 (60)	50/50	78 (*S*)
11	**L4c**	**S5**	100 (60)	75/25	80 (*S*)
12	**L5a**	**S5**	100 (60)	60/40	72 (*S*)
13	**L1c**	**S6**	100 (60)	80/20	91 (*S*)

[a] All reactions were run at 23 ºC. 1 mol% $[PdCl(\eta^3\text{-}C_3H_5)]_2$. Dichloromethane as solvent. 1.8 mol% ligand. [b] Reaction time in minutes shown in parentheses. [c] Percentage of branched (**13**) and linear (**14**) isomers [d] Enantiomeric excesses. The absolute configuration appears in parentheses.

It should be noted that the enantioselectivity was best (up to 96%) with ligand **L1h**, but selectivity towards the formation of the desired branched isomer was only

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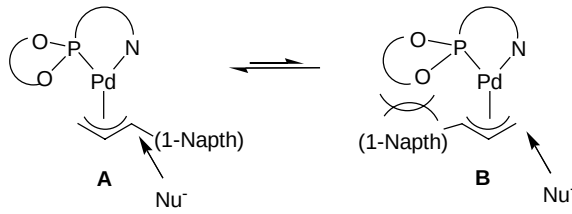
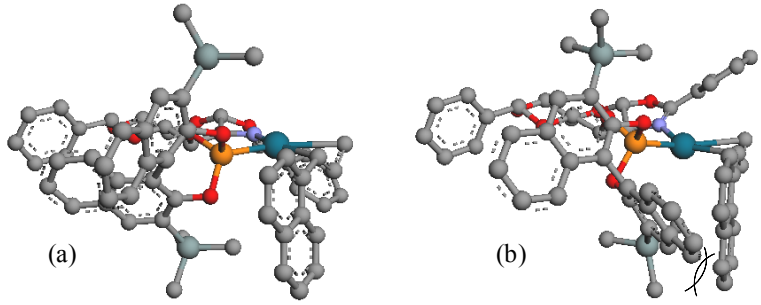
moderate (Table 6, entry 6). Interestingly, the **L1i** with the opposite configuration of the binaphthyl phosphite moiety affords product **13** in 85% yield and 88% ee (Table 6, entry 7). Assuming that the nucleophilic attack takes place *trans* to the phosphite moiety (the best π-acceptor moiety) (vide infra) and taking into account that the nucleophilic attack by an S_N-2 type process should take place preferentially at the less substituted allyl terminus (Scheme 3, species **B**),[9] the study of the models (Scheme 4) indicates that the Pd-π-allyl isomer containing ligand **L1i**, with an *R*-binaphthyl, produced a steric repulsion between the phosphite moiety and the naphthyl of the substrate (Scheme 4(b)) that shifts the equilibrium to species **A** and favored the formation of regioisomer **13** (Scheme 3). In contrast, ligand **L1h** has an *S*-binaphthyl moiety and a different spatial orientation of the biaryl phosphite moiety, which reduces the steric repulsion between the phosphite and the substrate **S5** (Scheme 4(a)), thus favoring the formation of the **B** isomer.



Scheme 3. Nucleophilic attack in the Pd-catalyzed allylic alkylation of substrate **S5** with ligand **L1i**.



Scheme 4. Draws of the Pd-π-allyl intermediates containing ligand (a) **L1h** and (b) **L1i**. H atoms are omitted for clarity.

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3.2.2.5. Origin of enantioselectivity. Study of the Pd-π-allyl intermediates

In order to provide further insight into how ligand parameters affect catalytic performance, we studied the Pd-π-allyl compounds **15-24**, [Pd(η^3-allyl)(L)]BF_4 (L= phosphite-oxazoline 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 methodology previously described from the corresponding Pd-allyl dimer and the appropriate ligand in the presence of silver tetrafluoroborate (Scheme 5).[15] The complexes were characterized by elemental analysis and by ^{1}H, ^{13}C and ^{31}P NMR spectroscopy. The spectral assignments (see Experimental Section) were based on information from ^{1}H-^{1}H, ^{31}P-^{1}H and ^{13}C-^{1}H correlation measurements in combination with ^{1}H-^{1}H NOESY experiments. Unfortunately, it was not possible to obtain any crystal of sufficient quality to perform X ray diffraction measurements.

$$[Pd(\eta^3\text{-allyl})(\mu\text{-Cl})]_2 + L \xrightarrow{AgBF_4} 2\ [Pd(\eta^3\text{-allyl})(L)]BF_4$$

15 allyl = 1,3-Ph_2-C_3H_3; L= **L1a**
16 allyl = 1,3-Ph_2-C_3H_3; L= **L1f**
17 allyl = 1,3-Ph_2-C_3H_3; L= **L1b**
18 allyl = 1,3-Ph_2-C_3H_3; L= **L3a**
19 allyl = 1,3-Me_2-C_3H_3; L= **L1a**
20 allyl = 1,3-Me_2-C_3H_3; L= **L3a**
21 allyl = 1,3-Me_2-C_3H_3; L= **L1c**
22 allyl = *cyclo*-C_6H_9; L= **L1a**
23 allyl = *cyclo*-C_6H_9; L= **L1b**
24 allyl = *cyclo*-C_6H_9; L= **L4a**

Scheme 5. Preparation of [Pd(η^3-allyl)(L)]BF_4 complexes **15-24**.

3.2.2.5.1. Palladium 1,3-diphenyl-allyl complexes

When the phosphite-oxazoline ligand library **L1-L5a-i** was used in the allylic substitution of disubstituted hindered substrate **S1**, the catalytic results indicated that for enantioselectivity to be high the combination of the substituent/configuration of the

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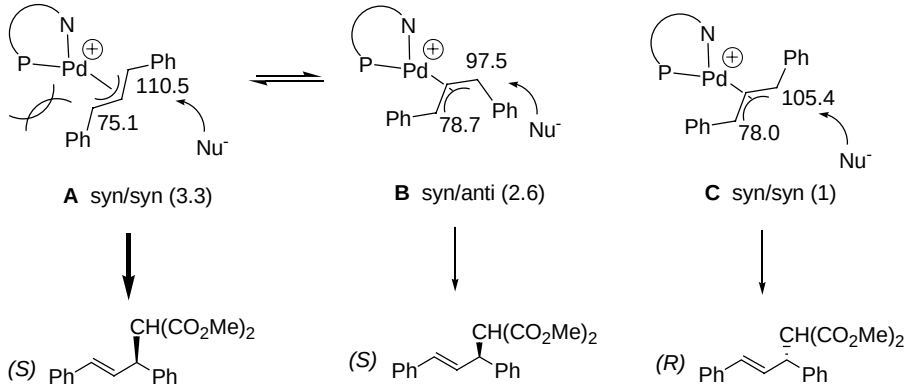
biaryl moieties and oxazoline substituent had to be correct. Therefore, a phenyl substituent in the oxazoline group and an *ortho* and *para* bulky substituted biphenyl phosphite moiety are required if enantioselectivity is to be high. In addition, the ligand-to-palladium ratio was found to have an important effect on enantioselectivity. To understand this catalytic behavior, we decided to study the Pd-π-allyl complexes **15-18** which contain ligands **L1a, L1f**, **L1b** and **L3a**, respectively, at a ligand-to-palladium ratio of 0.9 and 2. While ligand **L1a** containing a phenyl substituent in the oxazoline moiety and a tetrasubstituted *tert*-butyl biphenyl phosphite moiety provided high enantioselectivity (ee's up to 92% at room temperature), ligand **L1b**, with methoxy substituents at the *para* position of the biphenyl phosphite moiety, and ligand **L3a**, with a bulky *tert*-butyl group in the oxazoline group, were less enantioselective (ee's up to 84% and 45%, respectively, at room temperature).

The NMR study of Pd-allyl intermediate **15,** which contains ligand **L1a**, performed at a ligand-to-palladium ratio of 0.9 had a mixture of three isomers in a ratio of 3.3:2.6:1 (see Experimental Section). The major **A** and the minor **C** isomers were assigned by NOE to the two *syn*/*syn endo* and *exo* isomers, while the isomer **B** was assigned to the *syn*/*anti* isomer (Scheme 6). In addition, the NMR spectra showed an equilibrium between isomers **A** and **B** (Scheme 7). Therefore, exchange signals between *syn*/*syn* isomer **A** and *syn*/*anti* isomer **B** were observed in the NOESY spectra. Exchange between H_A^{anti} at 6.69 ppm of the **A** isomer and H_B^{syn} at 5.15 ppm of the **B** isomer confirm η^3- η^1- η^3 movement for the exchange between isomers **A** and **B**.[16] In addition, the fact that no other H^{anty}-H^{syn} exchange is observed indicates that the exchange mechanism takes place by opening selectively one of the terminal Pd-C bond. Accordingly, the study of the models indicated that the change in configuration of the biphenyl phosphite moiety (atropoisomerism) in the major **A** intermediate increases the steric repulsion between the biaryl phosphite group and one of the phenyl substituents in **S1** (Scheme 8, species **A'**). The formation of the *syn*/*anti* isomer **B** minimizes this new steric interaction. Therefore, the open Pd-C bond belongs to the less electrophilic carbon atom containing the substituent that undergoes the biggest steric hindrance with

the biaryl phosphite fragment. The study of the models also indicates that in isomer **A** there is a stabilizing π-stacking interaction between the phenyl oxazoline group and one of the phenyl substituents in **S1**. This explains the preferentially formation of *syn*/*syn* isomer **A** respect to *syn*/*syn* isomer **C**. For all isomers, the carbon NMR chemical shifts indicate that the most electrophilic allyl carbon terminus is *trans* to the phosphite moiety. Assuming that the nucleophilic attack takes place at the most electrophilic carbon atom, the attack at the *syn*/*syn* isomer **A** and *syn*/*anti* isomer **B** will lead to the formation of (*S*)-**8** while the attack at the *syn*/*syn* isomer **C** will lead to the formation of the opposite enantiomer of the alkylation product **8**. The fact that the enantiomeric excess of alkylation product **8** (ee's up to 92% (*S*) at room temperature) is higher than the diastereoisomeric excesses of the Pd-intermediates (de= 72%) indicated that isomer **A** must react faster than isomers **B** and **C**. This is also consistent with the fact that for all isomers, the most electrophilic allylic terminal carbon atom is the one *trans* to the phosphite in the major **A** isomer. Therefore, it can be concluded that the nucleophilic attack takes place preferentially at the allyl terminus *trans* to the phosphite moiety of the major **A** Pd-intermediate.



Scheme 6. Diastereoisomer Pd-allyl intermediates **15** 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.

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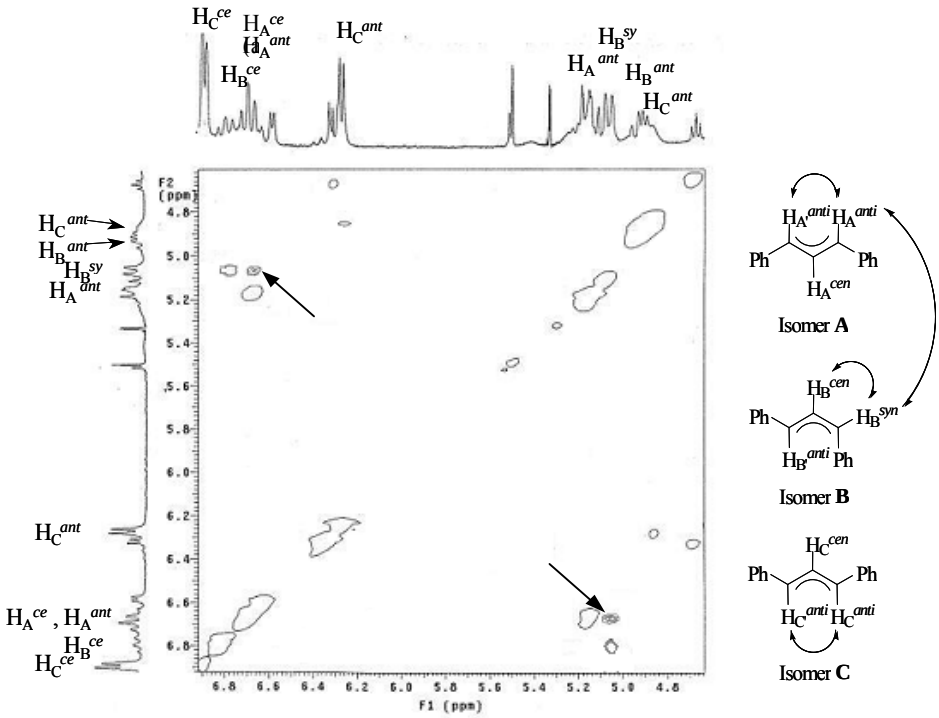
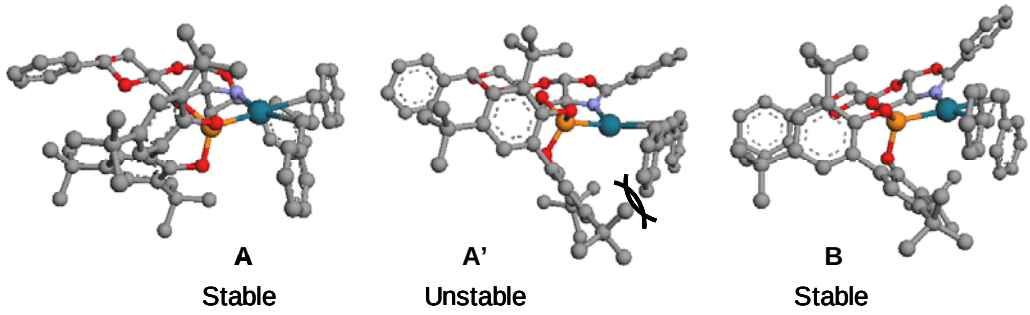


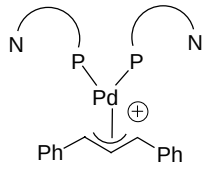
Scheme 7. Part of the NOESY spectrum (6.9-4.7 ppm) of **15**. Arrows indicate NOE exchange signals.



Scheme 8. Draws of the Pd-allyl intermediates **15A**, **15A'** and **15B** for **S1** with ligand **L1a**. H atoms are omitted for clarity.

We next performed the NMR study of Pd-allyl intermediate **15** at a ligand-to-palladium ratio of 2. The ^{31}P NMR indicated that a new species at 137.4 ppm was the major one (40%) (Scheme 9). This species was attributed to Pd-allyl complex **25**

([Pd(η^3-allyl)(**L1a**)$_2$]BF_4) in which two phosphite-oxazoline **L1a** ligands are coordinated in a monodentate fashion through the phosphite moiety. This intermediate reacts with less enantiodiscrimination than Pd-bidentate species because it has more degrees of freedom.[17] This explains the drop in enantioselectivity observed at higher ligand-to-palladium ratios than 0.9 when the Pd/**L1a** catalyst system was used (see Figure 4).



25

Scheme 9. Pd-intermediate with two phosphite-oxazoline **L1a** ligands coordinated as monodentated ones through the phosphite moiety.

To provide further evidence that the *syn-anti* isomerism observed in complex **15** is caused by the atropoisomerism of the biphenyl moieties, we studied the palladium allyl intermediate [Pd(η^3-1,3-diphenylallyl)(**L1f**)]BF_4 (**16**), which contains enantiopure *S*-binaphthyl ligand **L1f**. As expected, and in contrast to complex **15**, the VT-NMR study performed at a ligand-to-palladium ratio of 0.9 showed a mixture of two isomers in a ratio of 6:1 (see Experimental Section). No changes were observed down to –80 °C. Both isomers (**A** and **B**) were unambiguously assigned by NOE to the two *syn*/*syn* endo and exo isomers (Scheme 10). For both isomers, the carbon NMR chemical shifts indicate that the most electrophilic allyl carbon terminus is *trans* to the phosphite moiety. Assuming that the nucleophilic attack takes place at the most electrophilic carbon terminus and on the basis of the observed stereochemical outcome of the reaction, 81% (*S*) in product **8,** and the fact that the enantiomeric excess of alkylation product **8** is higher than the diastereoisomeric excesses of the Pd-intermediates, the **A** isomer must react faster than the **B** isomer.

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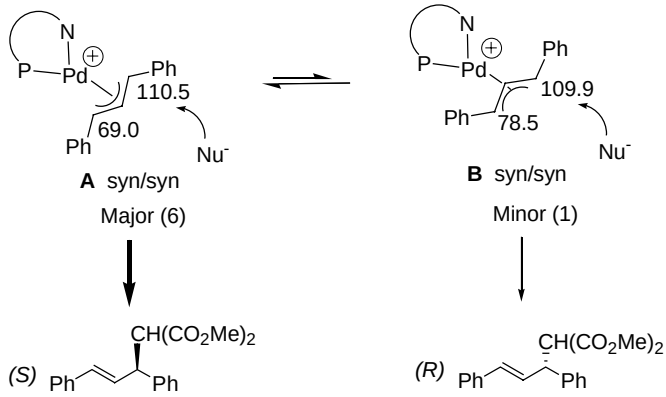

Scheme 10. Diastereoisomer Pd-allyl intermediates **16** for **S1** with ligand **L1f**. The relative amounts of each isomer are drawn in parenthesis. The chemical shifts (in ppm) of the allylic terminal carbons are shown.

We next studied the Pd-allyl intermediate **17** (at a ligand-to-palladium ratio of 0.9) containing ligand **L1b**. This complex has the same substituent in the oxazoline moiety but differs from ligand **L1a** in the *para*-substituents in the biaryl phosphite moiety. The NMR study showed a mixture of three isomers in a ratio of 2:1:1.3 (see Experimental Section). The major **A** and the minor **C** isomers were assigned by NOE to the two *syn*/*syn endo* and *exo* isomers, while the isomer **B** was assigned to the *syn*/*anti* isomer (Scheme 11). As for complex **15**, the NMR spectra showed and equilibrium between isomers **A** and **B**. Again, this *syn*/*syn* – *syn*/*anti* equilibrium is due to the atropoisomerism of the biphenyl phosphite moiety (vide supra). As for complex **15**, it should be noted that, for all isomers, the most electrophilic allyl carbon terminus is *trans* to the phosphite moiety and the isomer **A** reacts faster than the other isomers. Assuming that the nucleophilic attack takes place at the most electrophilic carbon atom, the attack at the *syn*/*syn* isomer **A** and at the *syn*/*anti* isomer **B** will lead to the formation of (*S*)-**8,** while the attack at the *syn*/*syn* isomer **C** will lead to the formation of the opposite enantiomer of alkylation product **8**. Therefore, the fact that the enantioselectivity was lower when the Pd/**L1b** catalyst was used (ee's up to 84%) than when the Pd/**L1a** catalyst was used (ee's up to 92%) may be due to the decrease in the

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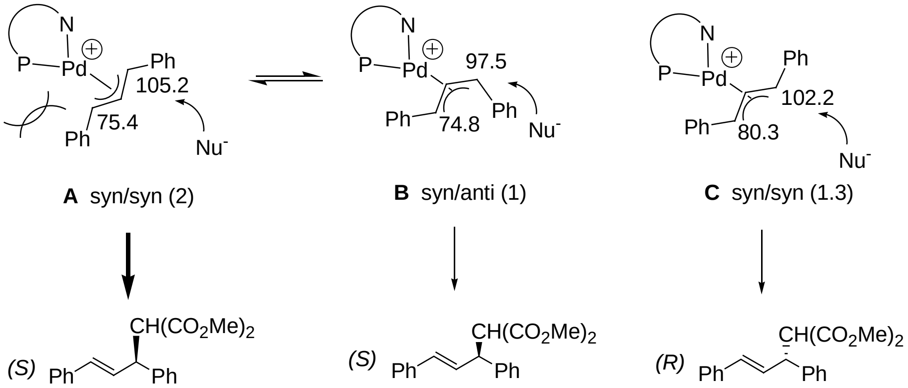
relative amount of species that provides the *S*-enantiomer (**A** and **B**) respect the ones that provides *R*-**8** (**C**) compared to the population of isomers (**A** and **B** respect to **C**) for complex **15**.



Scheme 11. Diastereoisomer Pd-allyl intermediates **17** for **S1** with ligand **L1b**. The relative amounts of each isomer are drawn in parenthesis. The chemical shifts (in ppm) of the allylic terminal carbons are shown.

Finally, we studied the Pd-allyl intermediate **18** (at a ligand-to-palladium ratio of 0.9) containing ligand **L3a**, which has a different substituent in the oxazoline moiety and provides much lower enantioselectivity (ee's up to 45%) than the previously studied Pd/**L1a** catalyst. In contrast to complexes **15-17** studied above, the NMR spectra showed that species with two phosphite-oxazoline ligands coordinated in a monodentate fashion are the major ones (70%). We believe that this is due to the increase in the steric bulk of the oxazoline moiety because a phenyl (ligands **L1a-b** and **L1f**) was replaced with a *tert*-butyl group (**L3a**). The presence of this species fully accounts for the low enantioselectivity observed for this catalyst.

In summary, the study of the allyl intermediates indicates that: (a) changes in the substituents at the biaryl phosphite moieties mean that there are changes in the ratio of the species that provides both enantiomers of alkylation product **8**, while changes in the oxazoline substituents mean that there are changes in the amount of species with

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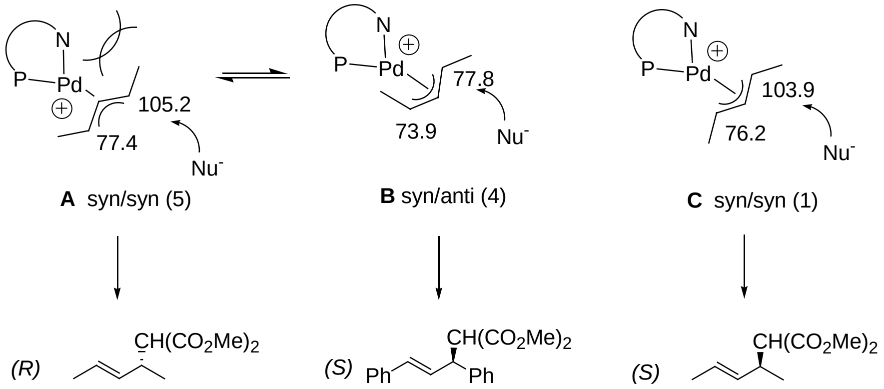
ligands coordinated in monodentate fashion and (b) the formation of species with monodentate ligands increases when the ligand-to-palladium ratio is higher than 0.9 and when there is a bulky substituent in the oxazoline moiety. Therefore, if enantioselectivity is to be high, the ligand-to-palladium ratio must be 0.9, and there must be an *ortho* and *para* bulky substituted biphenyl phosphite moiety and a phenyl substituent in the oxazoline group.

3.2.2.5.2. Palladium 1,3-dimethyl-allyl complexes

When the phosphite-oxazoline ligand library **L1-5a-i** was used in the allylic substitution of unhindered linear **S2** substrate, the catalytic results revealed that bulky substituents in the oxazoline group decreased enantioselectivities. On the other hand, enantioselectivities were high when bulky substituents were in the *ortho* position of the biphenyl moieties and the *para* positions of the biphenyl moieties were substituted with a group other than hydrogen. The ligand-to-palladium ratio was also found to have an effect on enantioselectivity. To understand this catalytic behavior, we studied the $[Pd(\eta^3\text{-allyl})(L)]BF_4$ complexes **19-21** which contain ligands **L1a**, **L3a** and **L1c**, at a ligand-to-palladium ratio of 0.9 and 2. Thus, while ligand **L1a**, which contains bulky *tert*-butyl groups at the *ortho* and *para* positions of the biaryl moiety, provided good enantioselectivities, ligand **L1c**, without substituents in the *para* positions of the biphenyl moiety, and ligand **L3a**, with a bulky *tert*-butyl group in the oxazoline group, were less enantioselective.

The NMR study of Pd-1,3-dimethyl allyl intermediate **19** at a ligand-to-palladium ratio of 0.9, which contains ligand **L1a**, indicated the presence of a mixture of three isomers at a ratio of 5:4:1 (see Experimental Section). The major **A** and the minor **C** isomers were assigned by NOE to the two *syn*/*syn endo* and *exo* isomers, while the isomer **B** was assigned to the *syn*/*anti* isomer (Scheme 12). In contrast to complex **15**, the major *syn*/*syn* isomer **19A** adopts a W spatial arrangement. This is due to the absence of the favorable π-stacking interaction observed in related complex **15**. The

NMR spectra showed a *syn-anti* equilibrium between isomers **A** and **B**, which was attributed to the atropoisomerism of the biphenyl phosphite in isomer **A** as it was in the related Pd-1,3-diphenylallyl complexes **15** and **17**. However, the study of the models indicates that the change in configuration of the biphenyl phosphite moiety results in a new steric interaction between the oxazoline phenyl group and one of the methyl substituents in **S2** (isomer **A'**, Scheme 13). The formation of the *syn*/*anti* isomer **B** minimizes this steric interaction (Scheme 13). Therefore, the open Pd-C bond belongs to the more electrophilic carbon atom containing the substituent that undergoes the biggest steric hindrance with the phenyl oxazoline fragment. Again, the most electrophilic allyl carbons are *trans* to the phosphite moiety in *syn*/*syn* isomer **A** and *syn*/*syn* isomer **C**, and the carbon in isomer **B** is far less electrophilic ($\Delta(\delta^{13}C) \approx 30$ ppm). Assuming that the nucleophilic attack takes place at the most electrophilic carbon terminus and on the basis of the relative abundance of isomers **A** and **C**, the calculated diastereomeric excess matches the enantiomeric excess obtained experimentally for product **10** (ee = 60% (*R*)).



Scheme 12. Diastereoisomer Pd-allyl intermediates **19** for **S2** 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.

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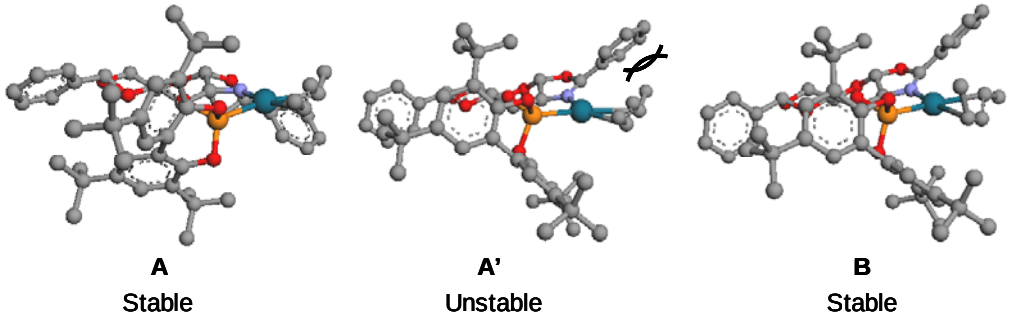
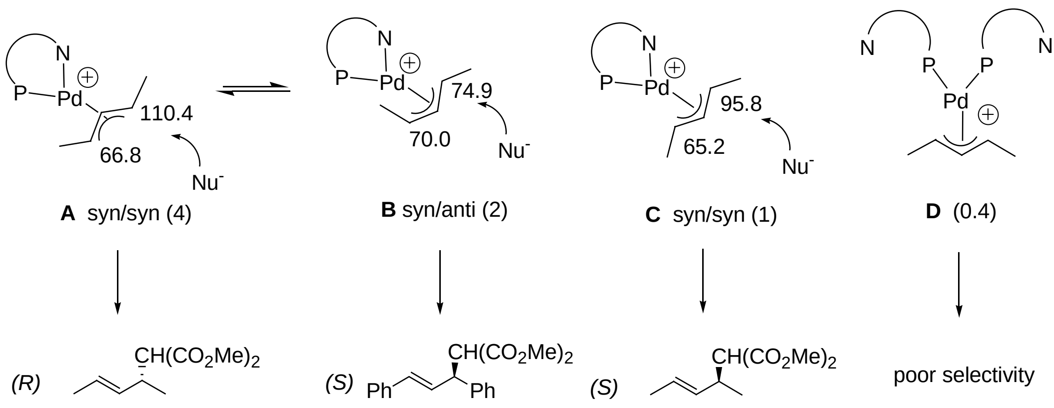


Scheme 13. Draws of the Pd-allyl intermediates **19A**, **19A'** and **19B** for **S2** with ligand **L1a**. H atoms are omitted for clarity.

We also performed the NMR study of Pd-allyl intermediate **19** at a ligand-to-palladium ratio of 2. The ^{31}P NMR indicated the presence of a new species (10 %, δ= 136.9 ppm) which was attributed to the Pd-allyl complex in which two phosphite-oxazoline **L1a** ligands are coordinated in a monodentate fashion through the phosphite moiety ([Pd(1,3-dimethyl-allyl)(**L1a**)$_2$]BF_4). Interestingly, in contrast to the Pd-1,3-diphenyl allyl intermediate **15**, the amount of this ([Pd(1,3-dimethyl-allyl)(**L1a**)$_2$]BF_4) species is lower. This is probably due to the presence of less sterically hindered 1,3-dimethyl allyl and explains why the enantioselectivity observed at higher than 0.9 ligand-to-palladium ratios in the alkylation of **S2** decreased less than in the alkylation of **S1**.

The NMR study of Pd-1,3-dimethyl allyl intermediate **20**, which contains ligand **L3a** with a bulky *tert*-butyl group at the oxazoline, indicated the presence of a mixture of four isomers in a ratio of 4:2:1:0.4 at a ligand-to-palladium ratio of 0.9 (see Experimental Section). Isomers **A**, **B** and **C** were assigned by NOE to the *syn*/*syn endo, syn/anti and syn/syn exo* isomers, respectively, while isomer **D** was attributed to the isomer that contains two ligands coordinated in a monodentate fashion (Scheme 14). As for complex **19**, isomers **A** and **B** were in equilibrium and the most electrophilic allyl carbons were *trans* to the phosphite moiety in *syn*/*syn* isomer **A** and *syn*/*syn* isomer **C**,

being the carbon in isomer **B** less electrophilic ($\Delta(\delta^{13}C) \approx 30$ ppm). Therefore, the fact that the enantioselectivity with the Pd/**L3a** catalyst system is lower than with the Pd/**L1a** catalyst system may be due to the presence of less enantioselective isomer **D** and the decrease in the relative amount of isomers **A** and **C** (5:1 ratio for complex **19** and 4:1 ratio for complex **20**).



Scheme 14. Diastereoisomer Pd-allyl intermediates **20** for **S2** 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.

We next studied Pd-allyl intermediate **21** (at a ligand-to-palladium ratio of 0.9) containing ligand **L1c**. This complex has the same substituent in the oxazoline moiety as complex **19** but differs from ligand **L1a** in the substituents of the biphenyl phosphite moiety. The NMR study showed a mixture of three isomers at a ratio of 1:1:2 (see Experimental Section) (Scheme 15). As for complex **19**, these were assigned to the two *syn*/*syn endo* (**A**) and *exo* (**C**) isomers and to the *syn*/*anti* isomer (**B**). Again, isomers **A** and **B** are in equilibrium and the most electrophilic allyl carbon atoms are found in species **A** and **C**. However, in contrast to complex **19**, the allylic carbon atoms *trans* to the phosphite moiety in isomer **A** is much more electrophilic than the one in isomer **C** ($\Delta(\delta^{13}C) \approx 7$ ppm). Therefore, isomer **A** should react faster than isomer **C**. Despite this,

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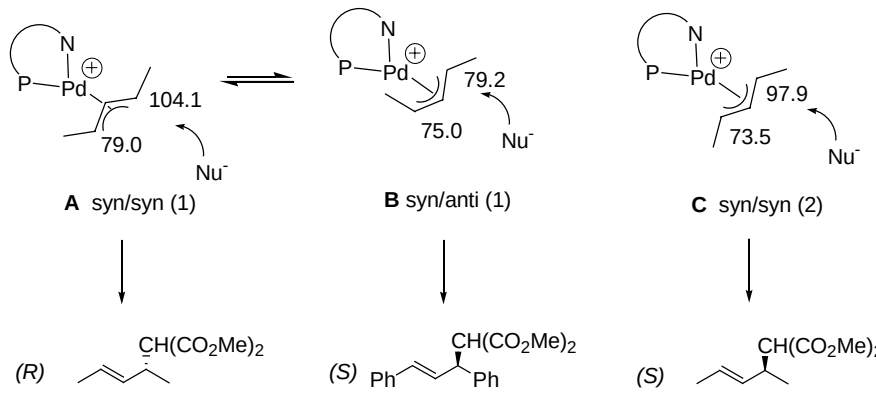
the fact that isomer **C** is the major one may explain why the enantioselectivity with this catalytic system is lower than with Pd/**L1a**.



Scheme 15. Diastereoisomer Pd-allyl intermediates **21** for **S2** with ligand **L1c**. The relative amounts of each isomer are drawn in parenthesis. The chemical shifts (in ppm) of the allylic terminal carbons are shown.

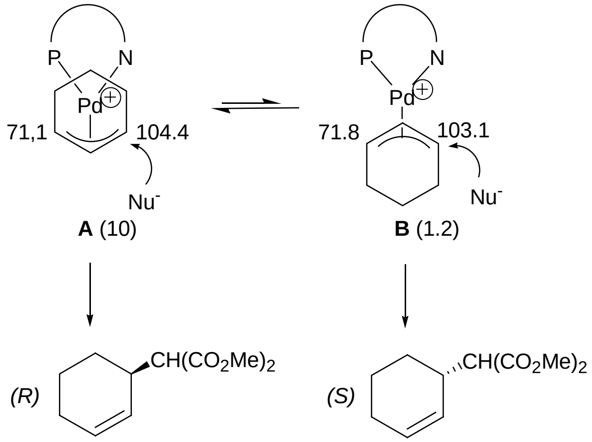
In summary, the study of the allyl intermediate indicates that: (a) changes in the substituents in the biaryl phosphite moieties mean that there are also changes in the ratio of the species that provide both enantiomers of alkylation product **10**, while changes in the oxazoline substituents mean that there are changes in both the ratio of species and the amount of species with ligands coordinated in monodentate fashion and (b) the formation of species with monodentate ligands increases when the ligand-to-palladium ratio is higher than 0.9.

3.2.2.5.3. Palladium 1,3-cyclohexenyl-allyl complexes

When the phosphite-oxazoline ligand library **L1-5a-i** was used in the allylic substitution of cyclic substrate **S3**, the catalytic results revealed that bulky *tert*-butyl substituents in *ortho* and *para* positions of the biphenyl phosphite moiety and a phenyl substituent in the oxazoline group are needed if enantioselectivity is to be high. To

understand this catalytic behavior we studied the Pd-π-allyl complexes **22-24** which contain ligands **L1a**, **L4a** and **L1b**. Thus, while ligand **L1a**, which contains bulky *tert*-butyl groups at the *ortho* and *para* positions of the biaryl moiety, provided good enantioselectivities, ligand **L1b**, with methoxy substituent in the *para* positions of the biphenyl moiety, and ligand **L4a**, with a methyl substituent in the oxazoline group, were less enantioselective.

The NMR study of Pd-1,3-cyclohexenyl allyl intermediate **22**, which contains ligand **L1a**, showed a mixture of two isomers at a ratio of 10:1.2 at a ligand-to-palladium ratio of 0.9 (see Experimental Section). Both isomers were assigned by NOE to the two *syn*/*syn* isomers (Scheme 16). For both isomers, the carbon NMR chemical shifts indicated that the most electrophilic allylic terminus carbon is *trans* to the phosphite moiety. Assuming that the nucleophilic attack takes place at the most electrophilic carbon terminus and on the basis of the relative abundance of isomers **A** and **B**, the calculated diastereomeric excess matched the enantiomeric excess obtained experimentally for product **11** (ee = 75% (*R*)).



Scheme 16. Diastereoisomer Pd-allyl intermediates **22** for **S3** 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.

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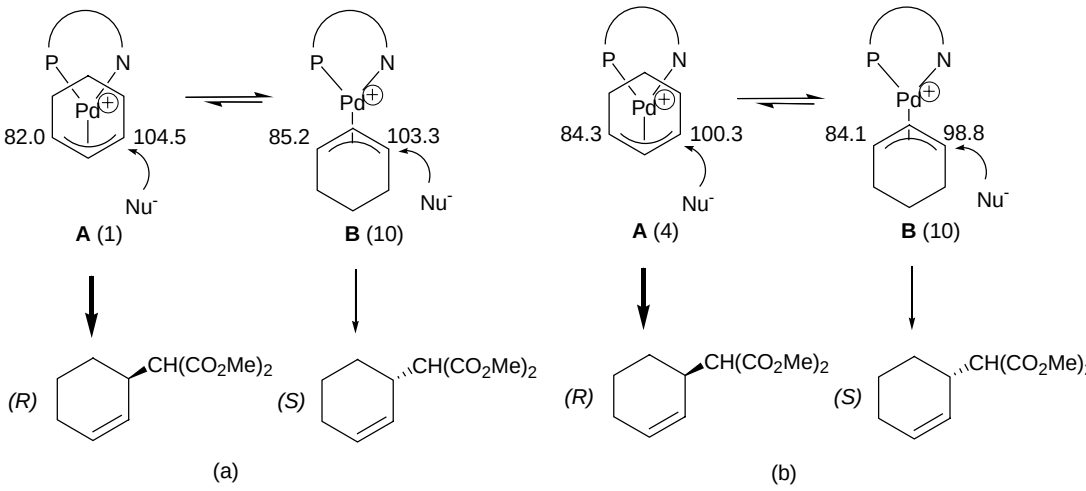
The NMR study of Pd-1,3-cyclohexenyl allyl intermediates **23** and **24**, which contain ligands **L1b** and **L4a**, showed a mixture of two isomers in a ratio of 1:10 and 4:10, respectively (at a ligand-to-palladium ratio of 0.9, see Experimental Section). All the species were assigned by NOE to the two *syn*/*syn* isomers possible for each Pd-allyl complex (Scheme 17). For all isomers, the carbon NMR chemical shifts indicated that the most electrophilic allylic terminus carbon is *trans* to the phosphite moiety. However, in contrast to complex **22**, the nucleophilic attack at the major isomers **B** will lead to the formation of (*S*)-**11** product. Therefore, the difference between the diastereoisomeric ratio and enantioselectivity observed in the alkylation of **S3** (d.e= 80% (*S*) vs ee= 22% (*R*) for Pd/**L1b**; d.e= 40% (*S*) vs ee= 34% (*R*) for Pd/**L4a**) indicates that the nucleophile reacts faster with the minor isomer **A**.



Scheme 17. Diastereoisomer Pd-allyl intermediates (a) **23** for **S3** with ligand **L1b** and (b) **24** for **S3** 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.

In summary, the NMR data indicates that the fact that the enantioselectivity obtained for Pd/**L1b** and Pd/**L4a** was lower than for Pd/**L1a** may be due to the decrease

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in the relative amount of species that provide the *R*-enantiomer (**A**) with respect to the ones that provide *S*-**11** (**B**) compared to the population observed for Pd/**L1a** complex.

3.2.3. Conclusions

A library of phosphite-oxazoline ligands **L1-L5a-i** has been synthesized for the Pd-catalyzed allylic substitution reactions of several substrates with different electronic and steric properties. These series of ligands have four main advantages: (1) they can be prepared in a few steps from readily available D-glucosamine; (2) the π-acceptor character of the phosphite moiety increases reaction rates; (3) the flexibility and larger bite angle created by the biaryl phosphite moiety increases versatility and (4) their modular nature enables the substituents in the oxazoline moiety and the substituents/configurations in the biaryl phosphite moiety to be easily and systematically varied. Thus, by carefully selecting the ligand components, high enantioselectivities (ee’s up to 99%) and good activities have been achieved in a wide range of substrates with different steric and electronic properties. In general, activities and enantioselectivies are mainly affected by the substituents in both the oxazoline and the phosphite moieties and the cooperative effect between stereocenters. However, the effect of these parameters depends on each substrate class.

The study of the Pd-1,3-diphenyl, 1,3-dimethyl and 1,3-cyclohexenyl allyl intermediates by NMR spectroscopy makes it possible to understand the catalytic behaviour observed. This study also indicates that the nucleophilic attack takes place predominantly at the allylic terminal carbon atom located *trans* to the phosphite moiety.

To sum up, the combination of high enantioselectivities (ee's up to 99%), high activities, high substrate versatility and the low cost of the ligands opens up the allylic alkylation of a wide range of substrates to the potential effective use of readily available and highly modular sugar-based phosphite-oxazoline ligands. The efficiency of this ligand design is also corroborated by the fact that these Pd-phosphite-oxazoline

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catalysts provided higher enantioselectivity than their phosphinite-oxazoline analogues in several substrates types.

3.2.4. Experimental section

3.2.4.1. General comments

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.[18] Racemic substrates **S1-S6** were prepared as previously reported.[19-22] $[Pd(\eta^3\text{-}1,3\text{-}Ph_2\text{-}C_3H_3)(\mu\text{-}Cl)]_2$,[23] $[Pd(\eta^3\text{-}1,3\text{-}Me_2\text{-}C_3H_3)(\mu\text{-}Cl)]_2$[24] and $[Pd(\eta^3\text{-cyclohexenyl})(\mu\text{-}Cl)]_2$[25] were prepared as previously described. ^1H, $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR spectra were recorded using a 400 MHz spectrometer. Chemical shifts are relative to that of $SiMe_4$ (^1H and ^{13}C) as internal standard or H_3PO_4 (^{31}P) as external standard. ^1H, ^{13}C and ^{31}P assignments were done based on ^1H-^1H gCOSY, ^1H-^{13}C gHSQC and ^1H-^{31}P gHMBC experiments.

3.2.4.2. General procedure for the preparation of ligands L1-L5a-i

The corresponding phosphorochloridite (3.0 mmol) produced *in situ* was dissolved in toluene (12.5 mL) and pyridine (1.14 mL, 14 mmol) was added. The corresponding hydroxyl-oxazoline compound (2.8 mmol) was azeotropically dried with toluene (3 x 2 mL) and then dissolved in toluene (12.5 mL) to which pyridine (1.14 mL, 14 mmol) was added. The oxazoline solution was transferred slowly at 0 ºC to the solution of phosphorochloridite. The reaction mixture was stirred overnight at 80 ºC, and the pyridine salts were removed by filtration. Evaporation of the solvent gave a white foam, which was purified by flash chromatography in alumina (toluene/NEt_3= 100/1) to produce the corresponding ligand as a white solid.

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L1a: Yield: 0.98 g, 44 %.^{31}P ($CDCl_3$), δ: 149.9 (s). ^{1}H ($CDCl_3$), δ: 1.29 (s, 9H, CH_3, ^{t}Bu), 1.31 (s, 9H, CH_3, ^{t}Bu), 1.34 (s, 9H, CH_3, ^{t}Bu), 1.52 (s, 9H, CH_3, ^{t}Bu), 3.64 (m, 2H, H-5, H-6'), 3.80 (m, 1H, H-4), 4.34 (m, 1H, H-6), 4.41 (dd, 1H, H-2, $^3J_{1-2}$= 7.6 Hz, $^3J_{2-3}$= 3.8 Hz), 4.73 (m, 1H, H-3), 5.47 (s, 1H, H-7), 6.05 (d, 1H, H-1, $^3J_{1-2}$= 7.6 Hz), 7.09-7.47 (m, 12H, CH=), 7.96 (m, 2H, CH=).^{13}C ($CDCl_3$), δ: 31.3 (CH_3, ^{t}Bu), 31.5 (CH_3, ^{t}Bu), 31.6 (CH_3, ^{t}Bu), 31.7 (CH_3, ^{t}Bu), 34.8 (C, ^{t}Bu), 34.9 (C, ^{t}Bu), 35.5 (C, ^{t}Bu), 35.7 (C, ^{t}Bu), 63.2 (C-5), 68.9 (C-6), 69.3 (C-2), 77.2 (C-3), 79.6 (C-4), 101.7 (C-7), 102.1 (C-1), 124.4 (CH=), 125.5 (CH=), 126.4 (CH=), 126,7 (CH=), 126.9 (CH=), 127.2 (CH=), 128.3 (CH=), 128.5 (CH=), 128,6 (CH=), 129.2 (CH=), 129.3 (CH=), 132.1 (C), 132.6 (C), 133.4 (C), 137.1 (C), 138.1 (C), 140.1 (C), 140.7 (C), 145.4 (C), 146.4 (C), 146.8 (C), 163.7 (C). Anal. calcd (%) for $C_{48}H_{58}NO_7P$: C 72.80, H 7.38, N 1.77; found: C 72.61, H 7.39, N 1.72.

L1b: Yield: 0.40 g, 20 %.^{31}P ($CDCl_3$), δ: 148.9 (s). ^{1}H ($CDCl_3$), δ= 1.35 (s, 9H, CH_3, ^{t}Bu), 1.53 (s, 9H, CH_3, ^{t}Bu), 3.70 (m, 2H, H-6', H-5), 3.81 (s, 3H, OMe), 3.81 (s, 3H, Ome), 3. 83 (m, 1H, H-4), 4.39 (m, 1H, H-6), 4.46 (dd, 1H, H-2, $^3J_{2,1}$= 7.6 Hz, $^3J_{2,3}$= 3.2 Hz), 4.77 (m, 1H, H-3), 5.52 (s, 1H, H-7), 6.10 (d, 1H, H-1, $^3J_{1,2}$= 7.6 Hz), 6.71 (m, 2H, CH=), 6.98 (m, 2H, CH=), 7.1-7.6 (m, 8H, CH=), 7.99 (m, 2H, CH=). ^{13}C ($CDCl_3$), δ: 31.1 (CH_3, ^{t}Bu), 31.3 (CH_3, ^{t}Bu), 35.5 (C, ^{t}Bu), 35.7 (C, ^{t}Bu), 55.8 (OCH_3), 63.1 (C-5), 68.9 (C-6), 69.3(C-2), 77.4 (C-3), 79.5 (C-4), 101.7 (C-7), 102.1 (C-1), 112.8 (CH=), 113.0 (CH=), 114.5 (CH=), 125.5 (CH=), 126.4 (CH=), 127.2 (CH=), 128.3 (CH=), 128.5 (CH=), 128.6 (CH=), 128.7 (CH=), 129.3 (CH=), 132.1 (C), 134.2 (C), 137.1 (C), 138.1 (C), 140.1 (C), 140.8 (C), 145.4 (C), 146.3 (C), 146.8 (C), 156.4 (C), 157.1 (C), 173.9 (C). Anal. calcd (%) for $C_{42}H_{46}NO_7P$: C 68.19, H 6.27, N 1.89; found: C 68.09, H 6.31, N 1.81.

L1c: Yield: 0.50 g, 25 %.^{31}P ($CDCl_3$), δ: 150.3 (s). ^{1}H ($CDCl_3$), δ: 0.36 (s, 9H, $Si(CH_3)_3$), 0.43 (s, 9H, $Si(CH_3)_3$), 3.68 (m, 2H, H-6', H-5), 3.92 (m, 1H, H-4), 4.41 (dd,

1H, H-6, $^{3}J_{6-6'}$=9.6 Hz, $^{3}J_{6-5}$= 4.2 Hz), 4.46 (dd, 1H, H-2, $^{3}J_{2-1}$= 7.6 Hz, $^{3}J_{2-3}$= 2.4), 4.87 (m, 1H, H-3), 5.52 (s, 1H, H-7), 6.12 (d, 1H, H-1, $^{3}J_{1-2}$= 7.6 Hz), 7.2-7.5 (m, 14H, CH=), 8.01 (m, 2H, CH=). ^{13}C ($CDCl_3$), δ: 0.3 ($Si(CH_3)_3$), 0.4 ($Si(CH_3)_3$), 62.9 (C-5), 69 (C-6), 69.8 (C-2), 75.9 (d, C-3, J_{C-P}= 13.6 Hz), 80.2 (d, C-4, J_{C-P}= 3.2 Hz), 101.2 (C-7), 101.5 (C-1), 124.8 (CH=), 125.0 (CH=), 125.5 (CH=), 126.5 (CH=), 127.0 (C), 128.3 (CH=), 128.4 (CH=), 128.6 (CH=), 129.2 (CH=), 129.3 (CH=), 132.0 (C), 133.9 (C), 132.1 (CH=), 132.5 (CH=), 132.6 (CH=), 135.3 (CH=), 137.1 (C), 138.4 (C), 163.9 (C). Anal. calcd (%) for $C_{38}H_{42}NO_7PSi_2$: C 64.11, H 5.95, N 1.97; found: C 64.19, H 5.91, N 1.89.

L1d: Yield: 0.17 g, 28 %. ^{31}P NMR (C_6D_6) δ= 150.3 (s). ^{1}H NMR (C_6D_6) δ= 2.27 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 3.50 (m, 1H, H-6'), 3.67 (m, 2H, H-4, H-5), 4.20 (m, 1H, H-6), 4.31 (m, 1H, H-2), 4.81 (m, 1H, H-3), 5.47 (s, 1H, H-7), 5.70 (d, 1H, H-1, $^{2}J_{1-2}$= 7.5 Hz), 7.0-8.3 (m, 14H, CH=). ^{13}C NMR (C_6D_6) δ= 17.2 (CH_3), 17.4 (CH_3), 21.1 (CH_3), 63.9 (C-5), 68.9 (C-6), 69.5 (C-2), 78.6 (d, C-3, $^{2}J_{c-p}$= 20 Hz), 79.0 (C-4), 102.2 (C-7), 103.5 (C-1), 126.0 (CH=), 127.2 (CH=), 129.0 (CH=), 129.3 (CH=), 129.4 (CH=), 129.6 (CH=), 131.0 (C), 131.6 (CH=), 131.7 (CH=), 132.3 (CH=), 134.3 (CH=), 138.2 (C), 138.31 (C), 139.3 (C), 146.9 (C), 164.1 (C). Anal. calcd (%) for $C_{36}H_{34}NO_7P$: C 69.33, H 5.50, N 2.25; found: C 69.39, H 5.52, N 2.23.

L1e: Yield: 0.14 g, 12 %.^{31}P ($CDCl_3$), δ: 152.9 (s). ^{1}H ($CDCl_3$), δ: 3.78 (m, 2H, H-5, H-6'), 3.84 (m, 1H, H-4), 4.44 (m, 2H, H-6, H-2), 4.65 (m, 1H, H-3), 5.68 (s, 1H, H-7), 6.19 (d, 1H, H-1, $^{3}J_{1,2}$= 7.2 Hz), 7.15-7.59 (m, 12H, CH=), 8.03 (m, 2H, CH=). ^{13}C ($CDCl_3$), δ: 63.4 (C-5), 68.8 (C-6), 69.1 (C-2), 77.4 (C-3), 79.0 (C-4), 101.7 (C-7), 102.8 (C-1), 122.3 (CH=), 122.6 (CH=), 125.4 (CH=), 125.5 (CH=), 126.3 (CH=), 128.4 (CH=), 128.5 (CH=), 128.6 (CH=), 128.7 (CH=), 129.2 (CH=), 129.3 (CH=), 129.4 (CH=), 130.0 (CH=), 132.3 (C), 137.1 (C), 138.1 (C), 163.9 (C). Anal. calcd (%) for $C_{32}H_{26}NO_7P$: C 67.72, H 4.62, N 2.47; found: C 67.84, H 4.66, N 2.39.

L1f: Yield: 0.1 g, 16 %. ^{31}P NMR (C_6D_6) δ= 154.7 (s). ^{1}H NMR (C_6D_6) δ= 3.40 (m, 1H, H-6'), 3.53 (m, 2H, H-4, H-5), 4.06 (m, 2H, H-2, H-6), 4.66 (m, 1H, H-3), 5.44 (d, 1H, H-1, $^{2}J_{1\text{-}2}$= 7.8 Hz), 5.51 (s, 1H, H-7), 6.90-8.15 (m, 22H, CH=). ^{13}C NMR (C_6D_6) δ= 63.7 (C-5), 68.8 (C-6), 69.3 (C-2), 78.7 (d, C-3, $^{2}J_{c\text{-}p}$= 13.7 Hz), 78.8 (C-4), 101.9 (C-7), 103.5 (C-1), 122.6 (CH=), 123.0 (CH=), 125.5 (CH=), 126.9 (CH=), 127.0 (CH=), 127.8 (CH=), 127.9 (CH=), 128.9 (CH=), 129.0 (CH=), 129.1 (CH=), 129.6 (CH=), 130.2 (CH=), 131.1 (CH=), 132.0 (C), 132.3 (CH=), 132.4 (C), 133.7 (C), 133.9 (C), 138.3 (C), 148.7 (C), 148.8 (C), 164.1 (C). Anal. calcd (%) for $C_{40}H_{30}NO_7P$: C 71.96, H 4.53, N 2.10; found: C 71.59, H 4.59, N 2.07.

L1g: Yield: 0.08 g, 12 %. ^{31}P NMR (C_6D_6) δ= 154.2 (s). ^{1}H NMR (C_6D_6) δ= 3.27 (m, 1H, H-6'), 3.45 (m, 2H, H-4, H-5), 4.02 (m, 1H, H-6), 4.14 (dd, 1H, H-2, $^{2}J_{2\text{-}1}$= 7.6 Hz, $^{2}J_{2\text{-}3}$= 5.2 Hz), 4.62 (m, 1H, H-3), 5.29 (s, 1H, H-7), 5.55 (d, 1H, H-1, $^{2}J_{1\text{-}2}$= 7.6 Hz), 6.90-8.15 (m, 22H, CH=). ^{13}C NMR (C_6D_6) δ= 63.1 (C-5), 68.7 (C-6), 69.2 (C-2), 78.3 (d, C-3, $^{2}J_{c\text{-}p}$= 19.0 Hz), 78.7 (C-4), 101.7 (C-7), 103.5 (C-1), 122.5 (CH=), 123.5 (CH=), 125.5 (CH=), 125.6 (CH=), 126.9 (CH=), 127.0 (CH=), 127.1 (CH=), 127.8 (CH=), 127.9 (CH=), 128.8 (C), 128.9 (CH=), 129.0 (CH=), 129.1 (CH=), 129.5 (CH=), 129.8 (C), 130.4 (CH=), 131.1 (CH=), 132.1 (C), 132.4 (CH=), 133.6 (C), 133.8 (CH=), 138.5 (CH=), 147.8 (C), 147.9 (C), 164.2 (C). Anal. calcd (%) for $C_{40}H_{30}NO_7P$: C 71.96, H 4.53, N 2.10; found: C 71.74, H 4.56, N 2.12.

L1h: Yield: 0.40 g, 17 %. ^{31}P NMR (C_6D_6) δ: 151.7 (s, 1P). ^{1}H NMR (C_6D_6) δ: 0.57 (s, 9H, $Si(CH_3)_3$), 0.65 (s, 9H, $Si(CH_3)_3$), 3.37 (m, 1H, H-6'), 3.52 (m, 1H, H-5), 3.91 (m, 1H, H-4), 4.02 (m, 1H, H-6), 4.23 (m, 1H, H-2), 5.12 (m, H-3), 5.40 (d, 1H, H-1, $^{3}J_{1\text{-}2}$= 8.0 Hz), 5.47 (s, 1H, H-7), 6.86-8.19 (m, 22H, CH=). ^{13}C NMR (C_6D_6) δ: 0.6 ($Si(CH_3)_3$), 0.9 ($Si(CH_3)_3$), 63.1 (C-5), 69.1 (C-6), 70.1 (C-2), 77.0 (d, C-3, $^{2}J_{c\text{-}p}$= 13.6 Hz), 80.5 (d, C-4, $^{2}J_{c\text{-}p}$= 4.1 Hz), 101.8 (C-7), 102.2 (C-1), 110.4 (C), 124.4 (CH=), 124.7 (CH=), 125.5 (CH=), 126.0 (CH=), 127.1 (CH=), 127.3 (CH=), 127.4 (CH=), 127.6 (CH=), 127.8 (CH=), 127.9 (CH=), 128.1 (CH=), 128.4 (CH=), 128.6 (CH=),

128.8 (CH=), 129.1 (CH=), 129.1 (CH=), 129.3 (CH=), 129.3 (CH=), 129.7 (CH=), 130.2 (C), 131.7 (C), 132.0 (C), 132.8 (C), 135.0 (C), 135.1 (C), 135.4 (C), 137.4 (CH=), 138.0 (CH=), 138.2 (CH=), 138.6 (CH=), 152.5 (C), 152.9 (C), 163.6 (C). Anal. calcd (%) for $C_{46}H_{46}NO_7PSi_2$: C 68.04, H 5.71, N 1.72; found: C 68.12, H 5.78, N 1.69.

L1i: Yield: 0.40 g, 17 %. ^{31}P NMR (C_6D_6) δ: 150.5 (s). ^{1}H NMR (C_6D_6) δ: 0.41 (s, 9H, $Si(CH_3)_3$), 0.55 (s, 9H, $Si(CH_3)_3$), 3.18 (m, 1H, H-6'), 3.49 (m, 1H, H-5), 3.66 (m, 1H, H-4), 3.90 (m, 1H, H-6), 4.41 (dd, 1H, H-2, $^{3}J_{2\text{-}1}$= 8.0 Hz, $^{3}J_{2\text{-}3}$= 2.4 Hz) 5.00 (s, 1H, H-7), 5.04 (m, 1H, H-3), 5.64 (d, 1H, H-1, $^{3}J_{1\text{-}2}$= 8.0 Hz), 6.80-8.01 (m, 22H, CH=). ^{13}C NMR (C_6D_6) δ= 0.5 ($Si(CH_3)_3$), 0.9 ($Si(CH_3)_3$), 63.4 (C-5), 69.0 (C-6), 70.9 (C-2), 77.1 (d, C-3, $^{2}J_{c\text{-}p}$= 9.1 Hz), 81.0 (C-4), 101.7 (C-1), 102.0 (C-7), 124.4 (C), 124.7 (C), 125.4 (CH=), 126.0 (CH=), 127.2 (CH=), 127.3 (CH=), 127.6 (CH=), 127.7 (CH=), 127.8 (CH=), 128.1 (CH=), 128.4 (CH=), 128.6 (CH=), 128.7 (CH=), 128.8 (CH=), 128.9 (CH=), 129.0 (CH=), 129.1 (CH=), 129.2 (CH=), 129.6 (C), 131.6 (CH=), 131.9 (CH=), 132.3 (CH=), 133.1 (CH=), 134.9 (C), 135.1 (C), 137.3 (CH=), 137.8 (CH=), 138.0 (C), 152.8 (C), 153.0 (C), 164.3 (C). Anal. calcd (%) for $C_{46}H_{46}NO_7PSi_2$: C 68.04, H 5.71, N 1.72; found: C 68.23, H 5.84, N 1.63.

L2a: Yield: 0.94 g, 35 %.^{31}P ($CDCl_3$), δ: 148.3 (s). ^{1}H ($CDCl_3$), 1.22 (m, 6H, CH_3, ^{i}Pr), 1.29 (s, 18H, CH_3, ^{t}Bu), 1.38 (s, 9H, CH_3, ^{t}Bu), 1.49 (s, 9H, CH_3, ^{t}Bu), 2.60 (sp, 1H, CH, ^{i}Pr, $^{3}J_{H\text{-}H}$= 7.2 Hz), 3.56 (m, 1H, H-5), 3.67 (m, 1H, H-6'), 3.80 (m, 1H, H-4), 4.21 (m, 1H, H-2), 4.38 (dd, 1H, H-6, $^{2}J_{6\text{-}6'}$= 10 Hz, $^{3}J_{6\text{-}5}$= 4.4Hz), 4.66 (m, 1H, H-3), 5.51 (s, 1H, H-7), 5.89 (d, 1H, H-1, $^{3}J_{1\text{-}2}$= 7.6 Hz), 7.1-7.6 (m, 9H, CH=). ^{13}C ($CDCl_3$), δ: 19.5 (CH_3, ^{i}Pr), 19.6 (CH_3, ^{i}Pr), 28.6 (CH, ^{i}Pr), 31.3 (CH_3, ^{t}Bu), 31.4 (CH_3, ^{t}Bu), 31.5 (CH_3, ^{t}Bu), 31.7 (CH_3, ^{t}Bu), 34.8 (C, ^{t}Bu), 34.9 (C, ^{t}Bu), 35.5 (C, ^{t}Bu), 35.7 (C, ^{t}Bu), 63.0 (C-5), 68.8 (C-2), 68.9 (C-6), 77.4 (C-3), 79.7 (C-4), 101.5 (C-1 and C-7), 124.4 (CH=), 125.5 (CH=), 126.3 (CH=), 126.6 (CH=), 126.9 (CH=), 128.4 (CH=), 128.5 (CH=), 129.2 (CH=), 129.3 (CH=), 132.2 (C), 133.1 (C), 137.1 (C), 138.1 (C), 140.1

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(C), 140.7 (C), 146.3 (C), 146.7 (C), 172.0 (C). Anal. calcd (%) for $C_{45}H_{60}NO_7P$: C 71.31, H 7.98, N 1.85; found: C 71.44, H 7.89, N 1.88.

L3a: Yield: 1.13 g, 48 %.^{31}P ($CDCl_3$), δ: 148.5 (s). ^{1}H ($CDCl_3$), δ: 1.27 (s, 9H, CH_3, ^{t}Bu), 1.36 (s, 18H, CH_3, ^{t}Bu), 1.41 (s, 9H, CH_3, ^{t}Bu), 1.54 (s, 9H, CH_3, ^{t}Bu), 3.58 (m, 1H, H-5), 3.70 (m, 1H, H-6'), 3.79 (dd, 1H, H-4, $^3J_{4,5}$= 9.6 Hz, $^3J_{4,3}$= 7.6 Hz), 4.24 (dd, 1H, H-2, $^3J_{2,1}$= 8.0 Hz, $^3J_{2,3}$= 3.6 Hz), 4.41 (dd, 1H, H-6, $^3J_{6,6'}$= 10.8 Hz, $^3J_{6,5}$= 5.2 Hz), 4.65 (m, 1H, H-3), 5.54 (s, 1H, H-7), 5.91 (d, 1H, H-1, $^3J_{1,2}$= 8.0 Hz), 7.1-7.6 (m, 9H, CH=). ^{13}C ($CDCl_3$), δ: 27.7 (CH_3, ^{t}Bu), 31.4 (CH_3, ^{t}Bu), 31.5 (CH_3, ^{t}Bu), 31.8 (CH_3, ^{t}Bu), 33.7 (C, ^{t}Bu), 34.8 (C, ^{t}Bu), 34.9 (C, ^{t}Bu), 35.6 (C, ^{t}Bu), 35.7 (C, ^{t}Bu), 63.0 (C-5), 68.9 (C-2 and C-6), 77.5 (d, C-3, $J_{C,P}$= 6.9 Hz), 79.6 (C-4), 101.5 (C-7), 101.9 (C-1), 124.4 (CH=), 125.5 (CH=), 126.3 (CH=), 126.6 (CH=), 126.9 (CH=), 128.4 (CH=), 128.5 (CH=), 129.2 (CH=), 129.3 (CH=), 132.7 (C), 133.5 (C), 137.1 (C), 138.1 (C), 140.1 (C), 140.8 (C), 145.4 (C), 146.3 (C), 146.8 (C), 173.9 (C). Anal. calcd (%) for $C_{46}H_{62}NO_7P$: C 71.57, H 8.10, N 1.81; found: C 71.64, H 8.05, N 1.78.

L4a: Yield: 0.28 g, 15 %.^{31}P ($CDCl_3$), δ: 148.0 (s). ^{1}H ($CDCl_3$), δ: 1.33 (s, 9H, CH_3, ^{t}Bu), 1.35 (s, 9H, CH_3, ^{t}Bu), 1.37 (s, 9H, CH_3, ^{t}Bu), 1.52 (s, 9H, CH_3, ^{t}Bu), 2.05 (d, CH_3, J_{H-P}= 1.6 Hz), 3.62 (m, 2H, H-5, H-6'), 3.82 (dd, 1H, H-4, $^3J_{4-3}$= 9.6 Hz, $^3J_{4-5}$= 6.8 Hz), 4.20 (bd, 1H, H-2, $^3J_{1-2}$= 7.6 Hz), 4.36 (dd, 1H, H-6, $^3J_{6-6'}$= 10 Hz, $^3J_{6-5}$= 4.4 Hz), 4.74 (m, 1H, H-3), 5.50 (s, 1H, H-7), 5.89 (d, 1H, H-1, $^3J_{1-2}$= 7.6 Hz), 7.1-7.5 (m, 9H, CH=). ^{13}C ($CDCl_3$), δ: 14.5 (CH_3), 31.3 (CH_3, ^{t}Bu), 31.4 (CH_3, ^{t}Bu), 31.5 (CH_3, ^{t}Bu), 31.7 (CH_3, ^{t}Bu), 34.8 (C, ^{t}Bu), 35.5 (C, ^{t}Bu), 35.7 (C, ^{t}Bu), 63.0 (C-5), 69.0 (C-6), 69.2 (C-2), 76.4 (d, C-3, J_{C-P}= 19.7 Hz), 80.2 (b, C-4), 101.4 (C-1), 101.8 (C-7), 124.4 (CH=), 125.5 (CH=), 126.4 (CH=), 126,7 (CH=), 126.9 (CH=), 128.4 (CH=), 128.5 (CH=), 129.3 (CH=), 137.1 (C), 138.1 (C), 140.2 (C), 140.5 (C), 146.4 (C), 146.7 (C), 165.2 (C).

UNIVERSITAT ROVIRA I VIRGILI
SCREENING OF MODULAR CARBOHYDRATE LIGAND LIBRARIES
IN ASYMMETRIC METAL-CATALYZED C-C AND C-X BOND FORMATION REACTIONS
Yvette Angela Mata Campaña
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L4c: Yield: 0.22g, 30 %. ^{31}P NMR (C_6D_6) δ= 150.2 (s). ^{1}H NMR (C_6D_6) δ= 0.42 (s, 9H, CH_3-Si), 0.50 (s, 9H, CH_3-Si), 1.55 (d, 3H, CH_3, J_{H-P}= 1.6 Hz), 3.37 (m, 1H, H-6'), 3.52 (m, 1H, H-5), 3.84 (dd, 1H, H-4, $^{3}J_{4-3}$= 10 Hz, $^{3}J_{4-5}$= 7.6 Hz), 4.05 (m, 1H, H-2), 4.10 (m, 1H, H-6, $^{3}J_{6-6'}$= 10 Hz, $^{3}J_{6-5}$= 5.2 Hz), 4.91 (m, 1H, H-3), 5.37 (d, 1H, H-1, $^{2}J_{1-2}$= 7.6 Hz), 5.40 (s, 1H, H-7), 7.0-7.6 (m, 11H, CH=). ^{13}C NMR (C_6D_6) δ= 0.8 (CH_3-Si), 14.2 (CH_3), 63.4 (C-5), 69.4 (C-6), 70.2 (C-2), 72.2 (d, C-3, $^{2}J_{c-p}$= 13.7 Hz), 80.9 (C-4), 101.9 (C-1), 102.4 (C-7), 125.6 (CH=), 125.8 (CH=), 127.4 (CH=), 128.9 (CH=), 129.6 (CH=), 129.9 (C), 132.3 (C), 132.4 (C), 133.3 (CH=), 134.4 (C), 136.0 (CH=), 136.1 (CH=), 137.9 (C), 138.2 (C), 153.8 (C), 155.1 (C), 164.0 (C). Anal. calcd (%) for $C_{43}H_{56}NO_7P$: C 70.76, H 7.73, N 1.92; found: C 70.79, H 7.74, N 1.95.

L4h: Yield: 0.59 g, 35 %. ^{31}P NMR (C_7D_8), δ: 152.2 (b). ^{1}H NMR (C_6D_6) δ: 0.50 (s, 9H, $Si(CH_3)_3$), 0.59 (s, 9H, $Si(CH_3)_3$), 1.45 (s, 3N, CH_3-N), 3.34 (m, 1H, H-6'), 3.46 (m, 1H, H-5), 3.82 (m, 1H, H-4), 3.86 (m, 1H, H-2), 4.06 (m, 1H, H-6), 4.87 (m, H-3), 5.18 (d, 1H, H-1, $^{3}J_{1-2}$= 7.6 Hz), 5.45 (s, 1H, H-7), 6.80-8.13 (m, 15H, CH=). ^{13}C NMR (C_6D_6) δ: 0.6 ($Si(CH_3)_3$), 0.8 ($Si(CH_3)_3$), 13.9 (N-CH_3), 63.1 (C-5), 69.2 (C-6), 69.6 (C-2), 77.2 (d, C-3, $^{2}J_{c-p}$= 15.1 Hz), 80.2 (C-4), 101.7 (C-1), 102.2 (C-7), 125.3 (CH=), 125.4 (CH=), 126.0 (C), 127.2 (CH=), 127.3 (CH=), 128.7 (CH=), 128.9 (CH=), 129.0 (CH=), 129.5 (CH=), 129.7 (CH=), 131.6 (C), 131.9 (C), 132.8 (C), 135.1 (C), 137.3 (CH=), 138.0 (CH=), 153.0 (C), 164.4 (C). Anal. calcd (%) for $C_{41}H_{44}NO_7PSi_2$: C 65.66, H 5.91, N 1.87; found: C 65.77, H 5.98, N 1.91.

L5a: Yield: 0.90 g, 40 %. ^{31}P ($CDCl_3$), δ: 150.1 (s, 1P). ^{1}H ($CDCl_3$), δ: 1.41 (s, 9H, CH_3, ^{t}Bu), 1.42 (s, 9H, CH_3, ^{t}Bu), 1.71 (s, 9H, CH_3, ^{t}Bu), 1.74 (s, 2H, CH_2), 1.85 (s, 9H, CH_3, ^{t}Bu), 3.50 (m, 1H, H-6'), 3.65 (m, 1H, H-5), 3.81 (m, 1H, H-4), 4.13 (m, 1H, H-2), 4.24 (dd, 1H, H-6, $^{2}J_{6-6'}$= 10.0 Hz, $^{3}J_{6-5}$= 4.8 Hz), 4.92 (m, 1H, H-3), 5.49 (d, 1H, H-1, $^{3}J_{1-2}$= 7.6 Hz), 5.53 (s, 1H, H-7), 7.14-7.83 (m, 14H, CH=). ^{13}C ($CDCl_3$), δ: 15.2 (CH_2), 32.9 (CH_3, ^{t}Bu), 33.1 (CH_3, ^{t}Bu), 36.0 (C, ^{t}Bu), 36.1 (C, ^{t}Bu), 37.1 (C, ^{t}Bu), 37.2 (C, ^{t}Bu), 64.4 (C-5), 70.1 (C-6), 70.4 (C-2), 79.0 (d, C-3, $^{2}J_{C-P}$= 20.5 Hz), 81.0 (C-4),

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103.0 (C-7), 103.2 (C-1), 125.7 (CH=), 125.8 (CH=), 127.0 (CH=), 128,1 (CH=), 128.4 (CH=), 128.6 (CH=), 129.1 (CH=), 129.4 (CH=), 129,6 (CH=), 129.7 (CH=), 129.9 (CH=), 130.4 (CH=), 130.7 (CH=), 135.1 (C), 135.7 (C), 139.2 (C), 139.2 (C), 141.9 (C), 142.5 (C), 147.6 (C), 147.9 (C), 148.3(C), 146.8 (C), 165.7 (C). Anal. calcd (%) for $C_{49}H_{60}NO_7P$: C 73.02, H 7.50, N 1.74; found: C 73.14, H 7.54, N 1.73.

3.2.4.3. General procedure for the preparation of [Pd(η^3-allyl)(L)]BF_4 complexes 15-25

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 minutes and the mixture was stirred for 30 minutes. 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 adding hexane as pale yellow solids.

[Pd(η^3-1,3-diphenylallyl)(L1a)]BF_4 (15). Isomer **A** (48%): ^{31}P NMR (CD_2Cl_2), δ: 134.3 (s). ^{1}H NMR (CD_2Cl_2), δ: 1.3-1.9 (36H, CH_3, *t*-Bu), 4.01 (m, 2H, H-5, H-6'), 4.24 (m, 1H, H-3), 4.34 (m, 1H, H-6), 4.41 (m, 1H, H-4), 4.54 (m, 1H, H-2), 5.18 (m, 1H, CH terminal), 5.49 (s, 1H, H-7), 6.27 (m, 1H, H-1), 6.69 (m, 2H, CH terminal, CH central), 7.0-7.9 (m, 24 H, CH=). ^{13}C NMR(CD_2Cl_2), δ: 31.2-33.0 (CH_3, *t*-Bu), 34.8-36.3 (C, *t*-Bu), 65.2 (C-5), 67.0 (C-2), 67.9 (C-6), 74.7 (m, C-3), 75.1 (m, CH terminal), 83.4 (C-4), 101.6 (C-7), 104.9 (C-1), 110.5 (m, CH terminal), 111.8 (m, CH central), 123-150 (aromatic carbons), 170.4 (C=N). Isomer **B** (38%): ^{31}P NMR (CD_2Cl_2), δ: 134.8 (s). ^{1}H NMR (CD_2Cl_2), δ: 1.3-1.9 (27H, CH_3, *t*-Bu), 3.84 (m, 1H, H-6'), 4.01 (m, 2H, H-5, H-6), 4.24 (m, 1H, H-3), 4.41 (m, 1H, H-4), 4.64 (m, 1H, H-2), 4.93 (m, 1H, CH terminal), 5.15 (m, 1H, CH terminal), 5.53 (s, 1H, H-7), 6.31 (m, 1H, H-1), 6.87 (m, 1H, CH central), 7.0-7.9 (m, 24 H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 31.2-33.0 (CH_3, *t*-Bu), 34.8-36.3 (C, *t*-Bu), 61.5 (C-6), 65.2 (C-5), 67.0 (C-2), 74.7 (m, C-3), 78.7 (CH

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terminal), 83.4 (C-4), 97.5 (d, CH terminal, $J_{C\text{-}P}$= 33.4 Hz), 101.3 (C-7), 104.9 (C-1), 112.7 (m, CH central), 123-150 (aromatic carbons), 169.4 (C=N). Isomer **C** (14%): ^{31}P NMR (CD_2Cl_2), δ: 133.1 (s). ^{1}H NMR (CD_2Cl_2), δ: 1.3-1.9 (27H, CH_3, *t*-Bu), 3.84 (m, 1H, H-6'), 4.01 (m, 2H, H-5, H-6), 4.24 (m, 1H, H-3), 4.41 (m, 1H, H-4), 4.54 (m, 1H, H-2), 4.92 (m, 1H, CH terminal), 5.49 (s, 1H, H-7), 6.28 (m, 1H, CH terminal), 6.34 (m, 1H, H-1), 6.79 (m, 1H, CH central), 7.0-7.9 (m, 24 H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 31.2-33.0 (CH_3, *t*-Bu), 34.8-36.3 (C, *t*-Bu), 61.5 (C-6), 65.7 (C-5), 67.0 (C-2), 74.7 (m, C-3), 78.0 (m, CH terminal), 83.4 (C-4), 101.6 (C-7), 104.9 (C-1), 105.4 (m, CH terminal), 111.6 (m, CH central), 123-150 (aromatic carbons), 170.4 (C=N). Anal. calcd (%) for $C_{63}H_{71}BF_4NO_7PPd$: C 64.21, H 6.07, N 1.19; found: C 64.33, H 6.15, N 1.23.

[Pd(η^3-1,3-diphenylallyl)(L1a)$_2$]BF$_4$ (25). ^{31}P NMR (CD_2Cl_2), δ: 137.4 (s). ^{1}H NMR (CD_2Cl_2), δ: 1.3-1.9 (36H, CH_3, *t*-Bu), 3.82 (m, 2H, H-6'), 4.01 (m, 8H, H-3, H-4, H-5, H-6), 4.87 (m, 2H, H-2), 5.11 (m, 1H, CH terminal), 5.15 (m, 1H, CH terminal), 5.62 (s, 2H, H-7), 6.20 (m, 2H, H-1), 6.72 (m, 1H, CH central), 6.8-7.9 (m, 38 H, CH=).

[Pd(η^3-1,3-diphenylallyl)(L1f)]BF$_4$ (16). Isomer **A** (86%): ^{31}P NMR (CD_2Cl_2), δ: 143.4 (s). ^{1}H NMR (CD_2Cl_2), δ: 3.21 (m, 1H, H-6'), 3.74 (m, 2H, H-5, H-3), 3.99 (m, 1H, H-6), 4.41 (m, 1H, H-4), 4.95 (m, 1H, CH terminal), 5.02 (m, 1H, H-2), 5.15 (s, 1H, H-7), 6.05 (m, 1H, CH central), 6.35 (m, 2H, H-1, CH=), 6.55 (m, 1H, CH=), 6.75 (m, 1H, CH terminal), 7.0-8.5 (m, 20 H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 65.6 (C-5), 66.6 (C-2), 67.7 (C-6), 69.0 (m, CH terminal), 74.4 (m, C-3), 81.2 (C-4), 101.6 (C-7), 105.6 (C-1), 110.5 (d, CH terminal, $J_{C\text{-}P}$= 25.8 Hz), 112.8 (m, CH central), 132-147 (aromatic carbons), 170.4 (C=N). Isomer **B** (14%): ^{31}P NMR (CD_2Cl_2), δ: 142.9 (s). ^{1}H NMR (CD_2Cl_2), δ: 3.21 (m, 1H, H-6'), 3.42 (m, 1H, H-6), 3.59 (m, 1H, H-5), 3.64 (m, 1H, H-3), 4.38 (m, 1H, CH terminal), 4.59 (m, 1H, H-4), 4.68 (m, 1H, H-2), 5.32 (s, 1H, H-7), 6.05 (m, 1H, CH central), 6.20 (m, 1H, H-1), 6.35 (m, 1H, CH=), 6.52 (m, 2H, CH terminal, CH=), 6.9-8.5 (m, 20 H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 62.6 (C-6), 66.0 (C-5), 66.6 (C-2), 74.1 (m, C-3), 78.5 (CH terminal), 84.0 (C-4), 101.6 (C-7), 105.6 (C-1),

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109.9 (d, CH terminal, $J_{C\text{-}P}$= 25.8 Hz), 112.7 (m, CH central), 132-147 (aromatic carbons), 170.9 (C=N). Anal. calcd (%) for $C_{55}H_{43}BF_4NO_7PPd$: C 62.67, H 4.11, N 1.33; found: C 62.71, H 4.09, N 1.32.

[Pd(η^3-1,3-diphenylallyl)(L1b)]BF_4 (17). Isomer **A** (46%): ^{31}P NMR (CD_2Cl_2), δ: 134.1 (s). ^{1}H NMR (CD_2Cl_2), δ: 1.36 (s, 9H, CH_3, *t*-Bu), 1.68 (s, 9H, CH_3, *t*-Bu), 3.71 (m, 1H, H-6'), 3.79 (m, 3H, CH_3O), 3.82 (m, 3H, CH_3O), 3.95 (m, 1H, H-5), 4.14 (m, 1H, H-3), 4.25 (m, 1H, H-4), 4.36 (m, 1H, H-6), 4.51 (m, 1H, H-2), 5.10 (m, 1H, CH terminal), 5.56 (s, 1H, H-7), 6.21 (m, 1H, H-1), 6.59 (m, 1H, CH central), 6.93 (m, 1H, CH terminal), 6.8-7.9 (m, 24 H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 31.7-33.0 (CH_3, *t*-Bu), 35.0-36.5 (C, *t*-Bu), 55.9-56.3 (CH_3O), 65.4 (C-5), 67.2 (C-2), 68.3 (C-6), 74.8 (m, C-3), 75.4 (CH terminal), 81.8 (C-4), 101.3 (C-7), 105.2 (d, CH terminal, $J_{C\text{-}P}$= 28.6 Hz), 105.5 (C-1), 114.2 (m, CH central), 124-158 (aromatic carbons), 169.2 (C=N). Isomer **B** (23%): ^{31}P NMR (CD_2Cl_2), δ: 133.5 (s). ^{1}H NMR (CD_2Cl_2), δ: 1.36 (s, 9H, CH_3, *t*-Bu), 1.78 (s, 9H, CH_3, *t*-Bu), 3.71 (m, 1H, H-6'), 3.80 (m, 3H, CH_3O), 3.83 (m, 3H, CH_3O), 3.91 (m, 1H, H-6), 3.95 (m, 1H, H-5), 4.14 (m, 1H, H-3), 4.25 (m, 1H, H-4), 4.58 (m, 1H, H-2), 4.95 (m, 1H, CH terminal), 5.53 (s, 1H, H-7), 6.26 (m, 1H, H-1), 6.39 (m, 1H, CH terminal), 6.92 (m, 1H, CH terminal), 6.8-7.9 (m, 24 H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 31.7-33.0 (CH_3, *t*-Bu), 35.0-36.5 (C, *t*-Bu), 55.9-56.3 (CH_3O), 61.8 (C-6), 64.9 (C-5), 67.2 (C-2), 74.8 (m, 2C, C-3, CH terminal), 81.8 (C-4), 97.5 (d, CH terminal, $J_{C\text{-}P}$= 32 Hz), 101.3 (C-7), 105.5 (C-1), 113.9 (m, CH central), 124-158 (aromatic carbons), 170.6 (C=N). Isomer **C** (31%): ^{31}P NMR (CD_2Cl_2), δ: 132.5 (s). ^{1}H NMR (CD_2Cl_2), δ: 1.39 (s, 9H, CH_3, *t*-Bu), 1.42 (s, 9H, CH_3, *t*-Bu), 3.71 (m, 1H, H-6'), 3.82 (m, 3H, CH_3O), 3.92 (m, 1H, H-6), 3.94 (m, 3H, CH_3O), 3.95 (m, 1H, H-5), 4.14 (m, 1H, H-3), 4.25 (m, 1H, H-4), 4.36 (m, 1H, H-6), 4.51 (m, 1H, H-2), 4.91 (m, 1H, CH terminal), 5.17 (m, 1H, CH terminal), 5.56 (s, 1H, H-7), 6.21 (m, 1H, H-1), 6.57 (m, 1H, CH central), 6.8-7.9 (m, 24 H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 31.7-33.0 (CH_3, *t*-Bu), 35.0-36.5 (C, *t*-Bu), 55.9-56.3 (CH_3O), 61.8 (C-6), 64.3 (C-5), 67.2 (C-2), 74.8 (m, C-3), 80.3 (m, CH terminal), 81.8 (C-4), 101.3 (C-7), 102.2 (m, CH terminal),

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105.5 (C-1), 114.7 (m, CH central), 124-158 (aromatic carbons), 170.4 (C=N). Anal. calcd (%) for $C_{57}H_{59}BF_4NO_9PPd$: C 60.79, H 5.28, N 1.24; found: C 60.82, H 5.29, N 1.31.

[Pd(η^3-1,3-diphenylallyl)(L3a)$_2$]BF_4 (18). ^{31}P NMR (CD_2Cl_2), δ: 135.8 (s). ^{1}H NMR (CD_2Cl_2), δ: 0.88 (s, 18H, CH_3, N-*t*-Bu), 1.33 (s, 18H, CH_3, *t*-Bu), 1.39 (s, 18H, CH_3, *t*-Bu), 1.42 (s, 18H, CH_3, *t*-Bu), 1.72 (s, 18H, CH_3, *t*-Bu), 3.77 (m, 2H, H-6'), 3.99 (m, 6H, H-3, H-4, H-5), 4.07 (m, 2H, H-6), 4.93 (m, 2H, H-2), 5.07 (m, 1H, CH terminal), 5.16 (m, 1H, CH terminal), 5.56 (s, 2H, H-7), 6.24 (m, 2H, H-1), 6.67 (m, 1H, CH central), 6.8-7.9 (m, 28 H, CH=).

[Pd(η^3-1,3-dimethylallyl)(L1a)]BF_4 (19). Isomer **A** (50%): ^{31}P NMR (CD_2Cl_2), δ: 134.2 (s). ^{1}H NMR (CD_2Cl_2), δ: 0.85-0.95 (m, 6H, CH_3), 1.2-1.7 (36H, CH_3, *t*-Bu), 3.56 (m, 1H, CH terminal), 4.03 (m, 2H, H-6, H-6'), 4.09 (m, 2H, H-5, H-4), 4.51 (m, 1H, H-3), 4.69 (m, 1H, H-2), 4.98 (m, 1H, CH terminal), 5.37 (m, 1H, CH central), 5.62 (s, 1H, H-7), 6.69 (m, 1H, H-1), 7.1-8.1 (m, 14H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 18.5 (CH_3), 18.7 (CH_3), 31.6-33.0 (CH_3, *t*-Bu), 35.0-36.5 (C, *t*-Bu), 62.3 (C-6), 65.2 (C-5), 67.5 (C-2), 75.3 (C-4), 77.4 (m, CH terminal), 81.3 (C-3), 101.8 (C-7), 105.2 (m, C-1, CH terminal), 122.9 (m, CH central), 125-152 (aromatic carbons), 170.1 (C=N). Isomer **B** (40%): ^{31}P NMR (CD_2Cl_2), δ: 133.9 (s). ^{1}H NMR (CD_2Cl_2), δ: 0.85-0.95 (m, 6H, CH_3), 1.2-1.7 (36H, CH_3, *t*-Bu), 3.64 (m, 1H, CH terminal), 4.00 (m, 1H, CH terminal), 4.03 (m, 1H, H-6'), 4.09 (m, 2H, H-5, H-4), 4.42 (m, 1H, H-6), 4.63 (m, 2H, H-2, H-3), 5.42 (m, 1H, CH central), 5.62 (s, 1H, H-7), 6.62 (m, 1H, H-1), 7.1-8.1 (m, 14H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 18.2 (CH_3), 18.7 (CH_3), 31.6-33.0 (CH_3, *t*-Bu), 35.0-36.5 (C, *t*-Bu), 65.2 (C-5), 67.5 (C-2), 68.1 (C-6), 73.9 (m, CH terminal), 75.3 (C-4), 77.8 (m, CH terminal), 81.3 (C-3), 101.8 (C-7), 105.2 (C-1), 123.6 (m, CH central), 125-152 (aromatic carbons), 170.1 (C=N). Isomer **C** (10%): ^{31}P NMR (CD_2Cl_2), δ: 132.8 (s). ^{1}H NMR (CD_2Cl_2), δ: 0.85-0.95 (m, 6H, CH_3), 1.2-1.7 (36H, CH_3, *t*-Bu), 3.80 (m, 1H, CH terminal), 4.03 (m, 2H, H-6, H-6'), 4.09 (m, 2H, H-5, H-4), 4.51 (m, 1H, H-3), 4.67 (m,

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1H, H-2), 4.84 (m, 1H, CH terminal), 5.37 (m, 1H, CH central), 5.62 (s, 1H, H-7), 6.62 (m, 1H, H-1), 7.1-8.1 (m, 14H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 18.3 (CH_3), 18.7 (CH_3), 31.6-33.0 (CH_3, *t*-Bu), 35.0-36.5 (C, *t*-Bu), 62.3 (C-6), 65.2 (C-5), 67.5 (C-2), 75.3 (C-4), 76.2 (m, CH terminal), 81.3 (C-3), 101.8 (C-7), 103.9 (m, CH terminal), 105.2 (C-1), 123.2 (m, CH central), 125-152 (aromatic carbons), 170.1 (C=N). Anal. calcd (%) for $C_{53}H_{67}BF_4NO_7PPd$: C 60.38, H 6.41, N 1.33; found: C 60.45, H 6.52, N 1.36.

[Pd(η^3-1,3-dimethylallyl)(L3a)]BF$_4$ (20). Isomer **A** (54%): ^{31}P NMR (CD_2Cl_2), δ: 134.3 (s). ^{1}H NMR (CD_2Cl_2), δ: 1.00 (m, 3H, CH_3), 1.2-1.7 (36H, CH_3, *t*-Bu), 1.72 (m, 3H, CH_3), 3.65 (m, 1H, CH terminal), 3.82 (m, 2H, H-4, H-6’), 4.00 (m, 1H, H-5), 4.12 (m, 1H, H-3), 4.42 (m, 1H, H-6), 4.44 (m, 1H, H-2), 5.30 (m, 1H, CH central), 5.45 (m, 1H, CH terminal), 5.60 (m, 1H, H-7), 6.34 (m, 1H, H-1), 7.1-8.0 (m, 9H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 19.0 (CH_3), 19.7 (CH_3), 31.0-33.0 (CH_3, *t*-Bu), 35.0-36.5 (C, *t*-Bu), 65.2 (C-5), 66.8 (m, CH terminal), 67.1 (C-2), 68.5 (C-6), 75.1 (C-4), 81.5 (C-3), 101.6 (C-7), 104.7 (C-1), 110.4 (m, CH terminal), 122.1 (m, CH central), 122-151 (aromatic carbons), 181.7 (C=N). Isomer **B** (27%): ^{31}P NMR (CD_2Cl_2), δ: 134.0 (s). ^{1}H NMR (CD_2Cl_2), δ: 0.80 (m, 3H, CH_3), 1.2-1.7 (36H, CH_3, *t*-Bu), 1.8 (m, 3H, CH_3), 3.70 (m, 1H, CH terminal), 3.82 (m, 2H, H-4, H-6’), 4.00 (m, 2H, H-5, H-6), 4.19 (m, 1H, CH terminal), 4.12 (m, 1H, H-3), 4.62 (m, 1H, H-2), 5.60 (m, 2H, H-7, CH central), 6.40 (m, 1H, H-1), 7.1-8.0 (m, 9H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 17.9 (CH_3), 19.4 (CH_3), 31.0-33.0 (CH_3, *t*-Bu), 35.0-36.5 (C, *t*-Bu), 62.0 (C-6), 65.2 (C-5), 67.1 (C-2), 70.0 (m, CH terminal), 74.9 (m, CH terminal), 75.1 (C-4), 81.5 (C-3), 101.6 (C-7), 104.7 (C-1), 122.8 (m, CH central), 122-151 (aromatic carbons), 182.5 (C=N). Isomer **C** (14%): ^{31}P NMR (CD_2Cl_2), δ: 133.9 (s). ^{1}H NMR (CD_2Cl_2), δ: 0.62 (m, 3H, CH_3), 1.2-1.7 (39H, CH_3, *t*-Bu, CH_3), 3.65 (m, 1H, CH terminal), 3.82 (m, 2H, H-4, H-6’), 4.00 (m, 2H, H-5, H-6), 4.18 (m, 1H, CH terminal), 4.54 (m, 1H, H-2), 5.30 (m, 1H, CH central), 5.60 (m, 1H, H-7), 6.37 (m, 1H, H-1), 7.1-8.0 (m, 9H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 17.4 (CH_3), 19.1 (CH_3), 31.0-33.0 (CH_3, *t*-Bu), 35.0-36.5 (C, *t*-Bu), 61.6 (C-6), 65.1 (C-5), 65.2 (m, CH terminal), 67.1 (C-2), 75.1 (C-4), 81.5 (C-3), 95.8 (m, CH terminal), 101.6

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(C-7), 104.7 (C-1), 122.0 (m, CH central), 122-151 (aromatic carbons), 181.7 (C=N). Isomer **D** (5%): ^{31}P NMR (CD_2Cl_2), δ: 135.0 (s). Anal. calcd (%) for $C_{51}H_{71}BF_4NO_7PPd \cdot 0.05C_{97}H_{133}BF_4N_2O_{14}P_2Pd$: C 59.48, H 6.94, N 1.36; found: C 59.52, H 7.01, N 1.41.

[Pd(η^3-1,3-dimethylallyl)(L1c)]BF_4 (21). Isomer **A** (25%): ^{31}P NMR (CD_2Cl_2), δ: 137.3 (s). ^{1}H NMR (CD_2Cl_2), δ: 0.40-0.65 (18H, CH_3-Si), 0.89 (m, 3H, CH_3), 1.31 (m, 3H, CH_3), 3.96 (m, 3H, CH terminal, H-6, H-6'), 4.07 (m, 1H, H-5), 4.29 (m, 1H, H-4), 4.56 (m, 1H, H-3), 4.83 (m, 1H, H-2), 4.95 (m, 1H, CH terminal), 5.53 (m, 1H, CH central), 5.60 (s, 1H, H-7), 6.83 (m, 1H, H-1), 7.4-8.2 (m, 16H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 0.2-0.6 (CH_3-Si), 17.3-18.9 (CH_3), 61.4 (C-6), 66.1 (C-5), 67.5 (C-2), 74.8 (C-4), 79.0 (m, CH terminal), 83.2 (C-3), 101.8 (C-7), 104.1 (m, CH terminal), 106.1 (C-1), 122.5 (m, CH central), 123-138 (aromatic carbons), 164.6 (C=N). Isomer **B** (25%): ^{31}P NMR (CD_2Cl_2), δ: 137.1 (s). ^{1}H NMR (CD_2Cl_2), δ: 0.40-0.65 (18H, CH_3-Si), 1.01 (m, 3H, CH_3), 1.45 (m, 3H, CH_3), 3.82 (m, 1H, CH terminal), 3.90 (m, 1H, CH terminal), 3.95 (m, 1H, H-6'), 4.07 (m, 1H, H-5), 4.29 (m, 1H, H-4), 4.44 (m, 2H, H-6, H-3), 4.63 (m, 1H, H-2), 5.43 (m, 1H, CH central), 5.60 (s, 1H, H-7), 6.62 (m, 1H, H-1), 7.4-8.2 (m, 16H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 0.2-0.6 (CH_3-Si), 17.3-18.9 (CH_3), 66.1 (C-5), 67.5 (C-2), 67.9 (C-6), 74.8 (C-4), 75.0 (m, CH terminal), 79.2 (m, CH terminal), 83.2 (C-3), 101.8 (C-7), 106.1 (C-1), 122.5 (m, CH central), 123-138 (aromatic carbons), 164.8 (C=N). Isomer **C** (50%): ^{31}P NMR (CD_2Cl_2), δ: 136.7 (s). ^{1}H NMR (CD_2Cl_2), δ: 0.40-0.65 (18H, CH_3-Si), 1.02 (m, 3H, CH_3), 1.45 (m, 3H, CH_3), 3.96 (m, 3H, CH terminal, H-6, H-6'), 4.07 (m, 1H, H-5), 4.22 (m, 1H, CH terminal), 4.29 (m, 1H, H-4), 4.43 (m, 1H, H-3), 4.72 (m, 1H, H-2), 5.53 (m, 1H, CH central), 5.60 (s, 1H, H-7), 6.67 (m, 1H, H-1), 7.4-8.2 (m, 16H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 0.2-0.6 (CH_3-Si), 17.3-18.9 (CH_3), 61.4 (C-6), 66.1 (C-5), 67.5 (C-2), 73.5 (m, CH terminal), 74.8 (C-4), 83.2 (C-3), 97.9 (m, CH terminal), 101.8 (C-7), 106.1 (C-1), 122.5 (m, CH central), 123-138 (aromatic carbons), 164.9 (C=N). Anal. calcd (%) for $C_{43}H_{51}BF_4NO_7PPdSi_2$: C 53.01, H 5.28, N 1.44; found: C 53.09, H 5.31, N 1.48.

[Pd(η^3-1,3-cyclohexenylallyl)(L1a)]BF_4 (22). Isomer **A** (89%): ^{31}P NMR (CD_2Cl_2), δ: 136.2 (s). ^{1}H NMR (CD_2Cl_2), δ: 1.06 (m, 2H, CH_2), 1.34 (s, 9H, CH_3, *t*-Bu), 1.42 (s, 9H, CH_3, *t*-Bu), 1.55 (s, 9H, CH_3, *t*-Bu), 1.57 (s, 9H, CH_3, *t*-Bu), 1.70 (m, 2H, CH_2), 1.87 (m, 2H, CH_2), 3.95 (m, 1H, H-6'), 4.02 (m, 1H, CH terminal), 4.14 (m, 1H, H-5), 4.46 (m, 2H, H-4, H-6), 4.64 (m, 1H, H-3), 4.79 (m, 1H, H-2), 5.26 (m, 1H, CH central), 5.36 (m, 1H, CH terminal), 5.66 (s, 1H, H-7), 6.77 (d, 1H, H-1, $^{3}J_{1\text{-}2}$= 3.6 Hz), 7.1-7.9 (m, 14H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 19.8 (m, CH_2), 27.9 (m, CH_2), 29.0 (m, CH_2), 31.5-32.1 (CH_3, *t*-Bu), 35.1-36.3 (C, *t*-Bu), 65.8 (C-5), 68.0 (C-2), 68.6 (C-6), 71.1 (d, CH terminal, $J_{C\text{-}P}$= 8.2 Hz), 81.8 (m, C-3), 84.5 (C-4), 101.6 (C-7), 104.4 (d, CH terminal, $J_{C\text{-}P}$= 36.4 Hz), 105.5 (C-1), 111.5 (m, CH central), 125-150 (aromatic carbons), 171.4 (C=N). Isomer **B** (11%): ^{31}P NMR (CD_2Cl_2), δ: 137.0 (s). ^{1}H NMR (CD_2Cl_2), δ: 0.94 (m, 2H, CH_2), 1.35 (s, 9H, CH_3, *t*-Bu), 1.40 (s, 9H, CH_3, *t*-Bu), 1.49 (s, 9H, CH_3, *t*-Bu), 1.53 (s, 9H, CH_3, *t*-Bu), 1.70 (m, 2H, CH_2), 1.87 (m, 2H, CH_2), 3.95 (m, 1H, H-6'), 4.14 (m, 2H, H-5, H-6), 4.36 (m, 1H, CH terminal), 4.46 (m, 1H, H-4), 4.55 (m, 1H, H-2), 4.64 (m, 1H, H-3), 5.26 (m, 1H, CH central), 5.36 (m, 1H, CH terminal), 5.64 (s, 1H, H-7), 6.71 (d, 1H, H-1, $^{3}J_{1\text{-}2}$= 3.6 Hz), 7.1-7.9 (m, 14H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 19.8 (m, CH_2), 27.9 (m, CH_2), 29.0 (m, CH_2), 31.5-32.1 (CH_3, *t*-Bu), 35.1-36.3 (C, *t*-Bu), 62.0 (C-6), 65.8 (C-5), 68.0 (C-2), 71.8 (d, CH terminal, $J_{C\text{-}P}$= 6 Hz), 81.8 (m, C-3), 84.5 (C-4), 101.6 (C-7), 103.1 (d, CH terminal, $J_{C\text{-}P}$= 37.5 Hz), 105.5 (C-1), 111.5 (m, CH central), 125-150 (aromatic carbons), 171.7 (C=N). Anal. calcd (%) for $C_{54}H_{67}BF_4NO_7PPd$: C 60.82, H 6.33, N 1.31; found: C 60.96, H 6.37, N 1.30.

[Pd(η^3-1,3-cyclohexenylallyl)(L1b)]BF_4 (23). Isomer **A** (10%): ^{31}P NMR (CD_2Cl_2), δ: 136.7 (s). ^{1}H NMR (CD_2Cl_2), δ: 1.11 (m, 2H, CH_2), 1.52 (s, 9H, CH_3, *t*-Bu), 1.56 (s, 9H, CH_3, *t*-Bu), 1.68 (m, 2H, CH_2), 1.91 (m, 2H, CH_2), 3.81 (s, 3H, CH_3O), 3.89 (s, 3H, CH_3O), 3.92 (m, 1H, H-6'), 4.02 (m, 2H, H-4, H-5), 4.35 (m, 1H, H-3), 4.46 (m, 2H, H-6, CH terminal), 4.85 (m, 1H, H-2), 5.33 (m, 1H, CH central), 5.45 (m, 1H, CH terminal), 5.60 (s, 1H, H-7), 6.72 (d, 1H, H-1, $^{3}J_{1\text{-}2}$= 3.6 Hz), 6.8-8.0 (m, 14H, CH=).

^{13}C NMR (CD_2Cl_2), δ: 19.9 (m, CH_2), 27.8 (m, CH_2), 29.0 (m, CH_2), 31.5-32.0 (CH_3, *t*-Bu), 35.9-36.4 (C, *t*-Bu), 56.2 (CH_3O), 56.3 (CH_3O), 65.6 (C-5), 68.2 (C-6), 68.5 (m, C-2), 71.5 (m, C-3), 74.9 (C-4), 82.0 (m, CH terminal), 102.1 (C-7), 104.5 (d, CH terminal, J_{C-P}= 36.4 Hz), 105.6 (C-1), 111.4 (m, CH central), 114-157 (aromatic carbons), 171.4 (C=N). Isomer **B** (90%): ^{31}P NMR (CD_2Cl_2), δ: 137.3 (s). ^{1}H NMR (CD_2Cl_2), δ: 1.11 (m, 2H, CH_2), 1.47 (s, 9H, CH_3, *t*-Bu), 1.53 (s, 9H, CH_3, *t*-Bu), 1.68 (m, 2H, CH_2), 1.91 (m, 2H, CH_2), 3.85 (s, 3H, CH_3O), 3.89 (s, 3H, CH_3O), 3.92 (m, 1H, H-6'), 4.02 (m, 3H, H-4, H-5, H-6), 4.35 (m, 2H, H-3, CH terminal), 4.69 (m, 1H, H-2), 5.33 (m, 1H, CH central), 5.45 (m, 1H, CH terminal), 5.56 (s, 1H, H-7), 6.68 (d, 1H, H-1, $^{3}J_{1-2}$= 3.6 Hz), 6.8-8.0 (m, 14H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 19.9 (m, CH_2), 27.8 (m, CH_2), 29.0 (m, CH_2), 31.5-32.0 (CH_3, *t*-Bu), 35.9-36.4 (C, *t*-Bu), 56.2 (CH_3O), 56.3 (CH_3O), 61.6 (C-6), 65.5 (C-5), 68.5 (m, C-2), 71.5 (m, C-3), 75.6 (C-4), 85.2 (m, CH terminal), 102.1 (C-7), 103.3 (d, CH terminal, J_{C-P}= 35.2 Hz), 105.9 (C-1), 111.4 (m, CH central), 114-157 (aromatic carbons), 171.2 (C=N). Anal. calcd (%) for $C_{48}H_{55}BF_4NO_9PPd$: C 56.85, H 5.47, N 1.38; found: C 56.79, H 5.40, N 1.29.

[Pd(η^3-1,3-cyclohexenylallyl)(L4a)]BF_4 (24). Isomer **A** (28%): ^{31}P NMR (CD_2Cl_2), δ: 135.3 (s). ^{1}H NMR (CD_2Cl_2), δ: 1.11 (m, 2H, CH_2), 1.35 (s, 9H, CH_3, *t*-Bu), 1.43 (s, 9H, CH_3, *t*-Bu), 1.45 (s, 9H, CH_3, *t*-Bu), 1.53 (s, 9H, CH_3, *t*-Bu), 1.62 (m, 2H, CH_2), 1.98 (m, 2H, CH_2), 2.25 (CH_3-N), 3.95 (m, 3H, H-6', H-5, CH terminal), 4.14 (m, 2H, H-3, H-6), 4.46 (m, 1H, H-2), 4.79 (m, 1H, H-4), 5.33 (m, 1H, CH central), 5.62 (s, 1H, H-7), 6.22 (m, 1H, CH terminal), 6.40 (d, 1H, H-1, $^{3}J_{1-2}$= 3.6 Hz), 7.2-7.9 (m, 9H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 19.7 (m, CH_2), 28.4 (m, CH_2), 29.0 (m, CH_2), 31.5-32.0 (CH_3, *t*-Bu), 35.9-36.4 (C, *t*-Bu), 62.6 (C-6), 65.2 (C-5), 73.6 (m, C-3), 81.1 (C-4), 84.1 (C-2), 84.3 (m, CH terminal), 100.3 (d, CH terminal, J_{C-P}= 38.7 Hz), 102.1 (C-7), 104.6 (C-1), 112.1 (m, CH central), 125-1507 (aromatic carbons), 171.5 (C=N). Isomer **B** (72%): ^{31}P NMR (CD_2Cl_2), δ: 136.9 (s). ^{1}H NMR (CD_2Cl_2), δ: 1.11 (m, 2H, CH_2), 1.33 (s, 9H, CH_3, *t*-Bu), 1.41 (s, 9H, CH_3, *t*-Bu), 1.45 (s, 9H, CH_3, *t*-Bu), 1.49 (s, 9H, CH_3, *t*-Bu), 1.62 (m, 2H, CH_2), 1.98 (m, 2H, CH_2), 2.27 (CH_3-N), 3.85 (m, 2H, H-6', CH terminal),

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4.14 (m, 3H, H-3, H-5, H-6), 4.46 (m, 1H, H-2), 4.79 (m, 1H, H-4), 5.33 (m, 1H, CH central), 5.62 (s, 1H, H-7), 6.26 (m, 1H, CH terminal), 6.44 (d, 1H, H-1, $^3J_{1\text{-}2}$= 3.6 Hz), 7.2-7.9 (m, 9H, CH=). ^{13}C NMR (CD_2Cl_2), δ: 19.7 (m, CH_2), 28.4 (m, CH_2), 29.0 (m, CH_2), 31.5-32.0 (CH_3, *t*-Bu), 35.9-36.4 (C, *t*-Bu), 65.2 (C-5), 68.3 (C-6), 73.6 (m, C-3), 81.1 (C-4), 81.9 (C-2), 84.1 (m, CH terminal), 98.8 (d, CH terminal, $J_{C\text{-}P}$= 41 Hz), 102.1 (C-7), 104.6 (C-1), 111.2 (m, CH central), 125-1507 (aromatic carbons), 171.0 (C=N). Anal. calcd (%) for $C_{49}H_{65}BF_4NO_7PPd$: C 58.60, H 6.52, N 1.39; found: C 58.82, H 6.61, N 1.42.

3.2.4.4. Typical procedure of allylic alkylation of *rac*-1,3-diphenyl-3-acetoxyprop-1-ene S1

A degassed solution of $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (0.9 mg, 0.0025 mmol) and the corresponding phosphite-oxazoline (0.0045 mmol) in dichloromethane (0.5 mL) was stirred for 30 min. Subsequently, a solution of **S1** (126 mg, 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 NH_4Cl (aq) (25 mL) was added. The mixture was extracted with Et_2O (3 x 10 mL) and the extract dried over $MgSO_4$. 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), a sample was filtered over basic alumina using dichloromethane as the eluent.[26]

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3.2.4.5. Typical procedure of allylic alkylation of *rac*-1,3-dimethyl-3-acetoxyprop-1-ene S2

A degassed solution of $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (0.9 mg, 0.0025 mmol) and the corresponding phosphite-oxazoline (0.0045 mmol) in dichloromethane (0.5 mL) was stirred for 30 min. Subsequently, a solution of **S2** (64 mg, 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. The reaction mixture was stirred at room temperature. After 30 min the reaction mixture was diluted with Et_2O (5 mL) and saturated NH_4Cl (aq) (25 mL) was added. The mixture was extracted with Et_2O (3 x 10 mL) and the extract dried over $MgSO_4$. Conversion and enantiomeric excess was determined by GC.[16]

3.2.4.6. Typical procedure of allylic alkylation of *rac*-3-acetoxycyclohexene S3 and *rac*-3-acetoxycycloheptene S4

A degassed solution of $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (1.8 mg, 0.005 mmol) and the corresponding phosphite-oxazoline (0.009 mmol) in dichloromethane (0.5 mL) was stirred. After 30 minutes the solution was kept to the desired temperature and subsequently, a solution of racemic substrate (0.5 mmol) in dichloromethane (1.5 mL) at the desired temperature, dimethyl malonate (171 μL, 1.5 mmol), *N*,*O*-bis(trimethylsilyl)-acetamide (370 μL, 1.5 mmol) and a pinch of KOAc were added. The reaction mixture was stirred at the desired temperature. After 24 hours the reaction mixture was diluted with Et_2O (5 mL) and saturated NH_4Cl (aq) (25 mL) was added. The mixture was extracted with Et_2O (3 x 10 mL) and the extract dried over $MgSO_4$. Conversion and enantiomeric excess was determined by GC.[16]

3.2.4.7. Typical procedure of allylic alkylation of 1-(1-naphthyl)allyl acetate S5 and 1-(1-naphthyl)-3-acetoxyprop-1-ene S6

A degassed solution of $[PdCl(\eta^3-C_3H_5)]_2$ (1.8 mg, 0.005 mmol) and the corresponding phosphite-oxazoline (0.009 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 hours the reaction mixture was diluted with Et_2O (5 mL) and saturated NH_4Cl (aq) (25 mL) was added. The mixture was extracted with Et_2O (3 x 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), a sample was filtered over basic alumina using dichloromethane as the eluent.[27]

3.2.4.8.Typical procedure of allylic amination of *rac*-1,3-diphenyl-3-acetoxyprop-1-ene S1

A degassed solution of $[PdCl(\eta^3-C_3H_5)]_2$ (1.8 mg, 0.005 mmol) and the corresponding phosphite-oxazoline (0.009 mmol) in dichloromethane (0.5 mL) was stirred for 30 min. Subsequently, a solution of **S1** (126 mg, 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 24 hours the reaction mixture was diluted with Et_2O (5 mL) and saturated NH_4Cl (aq) (25 mL) was added. The mixture was extracted with Et_2O (3 x 10 mL) and the extract dried over $MgSO_4$. 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), a sample was filtered over silica using 10% Et_2O/hexane mixture as the eluent.[26]

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3.2.5. Acknowledgements

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3.2.6. References

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