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Theoretical and Experimental Optimization of a New Amino Phosphite Ligand Library for Asymmetric Palladium-Catalyzed Allylic Substitution

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A new library of modular amino phosphite ligands obtained in a few synthetic steps from enantiopure amino alcohols has been tested in asymmetric Pd-catalyzed allylic substitution. The modular ligand design is crucial to find highly selective catalysts for each substrate type using a wide range of C-, N-, and O-nucleophiles. A DFT study of the species responsible for the enantiocontrol was used to optimize the ligand structure. By selecting the ligand components, we were able to identify unprecedented catalytic systems that can create new chiral C–C, C–N, and C–O bonds in a variety of substrate types (hindered and unhindered) in high yields and enantioselectivities (*ee* values up to 99%). Further studies on the Pd-π-allyl intermediates provided a deep understanding of the effect of ligand structure in the origin of enantioselectivity. Potential applications of the new Pd/amino phosphite catalysts were demonstrated by the practical synthesis of a range of chiral carbocycles by simple tandem reactions, with no loss of enantioselectivity.

Introduction

The syntheses of chiral C–X bonds, in which X is C or a heteroatom, are the most significant processes in the preparation of complex chiral molecules from simple ones. Of the C–X bond-forming strategies, enantioselective Pd-catalyzed allylic substitution is among the most studied. Some advantages include a high functional group tolerance, mild reaction conditions, and high versatility of the alkene functionality of the substrate for further stereoselective functionalization.[1] Most of the best ligands reported to date for Pd-catalyzed allylic substitution use the capacity of the ligand to direct the nucleophilic attack to one of the allylic terminal atoms by either a secondary ligand–nucleophile interaction[2] or electronic discrimination.[1,3] The latter approach uses heterodonor ligands to differentiate electronically between the two allylic terminal C atoms because of the different *trans* influences of the donor groups. Mixed phosphine/phosphinite oxazoline ligands have played a dominant role as heterodonors.[1] Our group has contributed to Pd-catalyzed allylic substitution by the improved generation of ligands. We have shown that some common limitations of this process, such as low reaction rates and high substrate specificity, are overcome by the introduction of biaryl phosphite moieties into the ligand design.[4] As a result, increased reaction rates are achieved thanks to the higher π-acceptor ability of the phosphite groups and substrate versatility is increased because the flexibility of the phosphite moieties allows the catalyst chiral pocket to adapt to both hindered and unhindered substrates. Therefore, we have reported several phosphite oxazolines as extremely effective ligands for this process.[5] Despite the important advances, the application of phosphite oxazoline ligands is mainly limited to the use of a few nucleophiles, mainly dimethyl malonate and benzylamine. The use of functionalized malonates and alkyl alcohols is little reported.[1] In addition, only a few catalysts have been applied efficiently in the allylic substitution of several types of substrates with different electronic and steric proprieties using a broad range of nucleophiles.[6] Therefore, more effort should be made to expand this range of nucleophiles and substrates with the aim to synthesize more complex chiral organic molecules.

To expand the range of ligands and improve performance, we have moved our research towards the development of heterodonor ligands that contain groups more robust than oxazolines. In this context, we reported the application of Pd/phosphite pyridine/thioether catalytic systems in the allylic substitution of several substrate types using a large variety of nucleophiles.[7] Apart from this, the successful use in this process of other heterodonor P-X ligands, in which X is a more robust group than oxazoline, has not been reported yet, and a systematic study of the scope of this family of ligands is still missing.

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Although other researchers have developed heterodonor phosphine/phosphinite ligands that contain groups more robust than oxazoline (such as amine,[8] imine,[9] pyridine,[10] and thioether[11]), only a few of them have been applied successfully and these are limited in substrate and nucleophile scope (enantioselectivities are mainly high in the allylic substitution of the hindered standard substrate *rac*-1,3-diphenyl-3-acetoxyprop-1-ene (**S1**) using dimethyl malonate as the nucleophile). To be of practical interest, substantial improvements in terms of enantioselectivity, chemical yield, and substrate and nucleophile versatility are still needed.

To address this point, in this study we prepared and tested a new family of chiral ligands that are readily accessible, easy to handle, and expand the application range. We report a highly modular amino phosphite ligand library (Figure 1) for

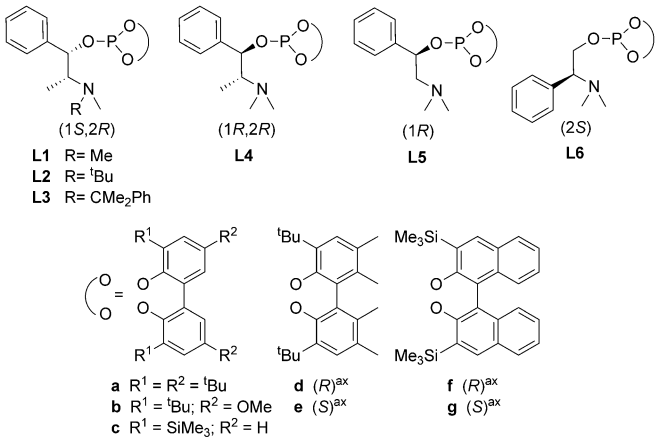
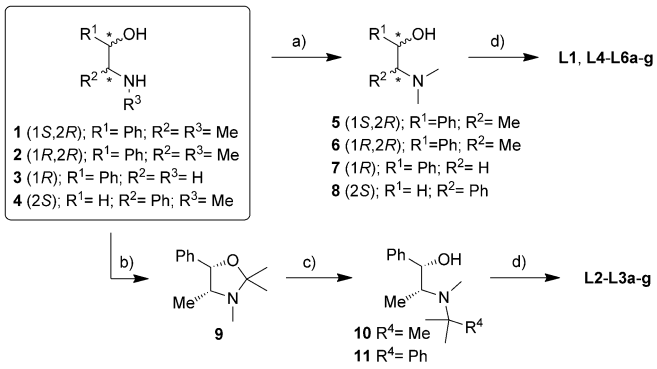


Figure 1. Amino phosphite ligand library **L1**–**L6a**–**g**.

the Pd-catalyzed allylic substitution of hindered and unhindered substrates with a large number of nucleophiles. These ligands are prepared easily in few steps from readily available enantiopure amino alcohols. They also incorporate the advantages of the robustness of the amine moiety and the additional control provided by either the adaptability of the chiral cavity because of the biaryl phosphite groups and the flexibility of the chiral pocket through a highly modular ligand scaffold. In a simple two- or three-step procedure (Scheme 1), several ligand parameters could be tuned easily to maximize the catalyst performance so that we could investigate the effect of the systematic change of the substituents (**L1**, **L5**, and **L6**) and configuration (**L1** and **L4**) at the ligand backbone, the amine substituents (**L1**–**L3**) and the substituents and configurations in the biaryl phosphite moiety (**a**–**g**). By a judicious choice of ligand components, we achieved high enantioselectivities and activities in a number of substrates using a wide range of C-, N-, and O-nucleophiles. The potential application of these new Pd/amino phosphite catalytic systems has been demonstrated by the practical synthesis of chiral carbocycles by simple sequential reactions with no loss of *ee*.

Despite the recent success of Pd/phosphite-nitrogen catalyst systems, the mechanistic aspects of these ligands are not sufficiently understood to predict, a priori, the type of ligand needed to obtain a high selectivity. To address this important point, in this study we performed DFT calculations and the synthesis and characterization of the Pd-π-allyl intermediates to explain the origin of enantioselectivity using these highly versatile catalytic systems. Notably, these DFT calculations have been crucial to the optimization of the ligand design.



Scheme 1. Synthesis of amino phosphites **L1**–**L6a**–**g**. a) Formic acid/paraformaldehyde/H_2O (yields 90–95%);[12] b) 2,2-dimethoxypropane/toluene (yield 72%);[13] c) MeMgBr/Et_2O or PhMgBr/THF (yields 87–93%),[14] and d) $ClP(OR)_2$; $(OR)_2$ = **a**–**g**/pyridine/toluene (yields 30–95%).

Results and Discussion

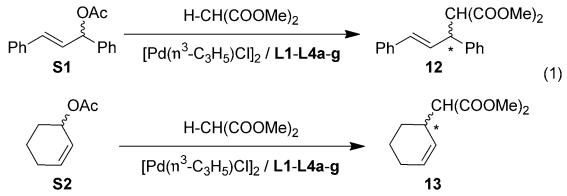
Synthesis of ligand library

Ligands **L1**–**L6a**–**g** were synthesized from the corresponding easily accessible enantiopure amino alcohols (**1**–**4**; Scheme 1). Amino alcohols **1**–**4** already incorporate the desired diversity in the substituents and in the configurations of the backbone. The diversity at the amino group was achieved by either direct methylation of **1**–**4** using formic acid and formaldehyde to afford **5**–**8**[12] (Scheme 1, step a) or by the formation of oxazolidine **9**[13] (Scheme 1, step b) from **1**, followed by ring-opening with the corresponding Grignard reagents (**10**–**11**, step c).[14] Finally, the reaction of amino alcohols **5**–**8**, **10**, and **11** with one equivalent of the desired phosphorochloridite formed in situ gave access to amino phosphite ligands **L1**–**L6a**–**g** (step d) with the desired substituents and configurations of the biaryl phosphite group (**a**–**g**). Ligands **L1**–**L6a**–**g** were isolated in moderate-to-good yields as white solids after purification on neutral alumina under an Ar atmosphere. Advantageously, they were stable in air and very stable to hydrolysis, so further manipulation/storage was performed in air. The ESI-HRMS spectra were in agreement with the assigned structures. Ligands **L1**–**L6a**–**g** were also characterized by ^1H, ^{13}C, and ^{31}P NMR spectroscopy. The spectral assignments, made using ^1H-^1H and ^{13}C-^1H correlation measurements, were as expected for these C_1-symmetric ligands. One singlet for each compound was observed in the ^{31}P NMR spectra. Rapid ring inversions (tropoisomerization) in the biphenyl phosphorus moieties (**a**–**c**) occurred on the NMR timescale because the expected diaste-

reoisomers were not detected by low-temperature ^{31}P NMR (in CD_2Cl_2 +35 to −85 °C).[15]

Allylic substitution of *rac*-1,3-diphenyl-3-acetoxyprop-1-ene (S1) and *rac*-3-acetoxycyclohexene (S2) with ephedrine-based ligands L1–L4 a–g: Computational study for ligand optimization

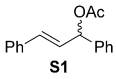
First, we tested the efficiency of the ephedrine-based amino phosphite ligands **L1**–**L4 a**–**g**. As mentioned previously, the asymmetric Pd-catalyzed allylic alkylation is highly dependent on the olefin geometry.[1] The effectiveness of the catalyst to transfer the chiral information to the alkylated product depends mainly on its ability to adapt to the variation of the steric demands of the substrate. To assess the performance of **L1**–**L4 a**–**g** in the allylic alkylation of substrates with different steric requirements, we evaluated them initially in the asymmetric Pd-catalyzed allylic alkylation of the model substrates **S1** and *rac*-3-acetoxycyclohexene (**S2**) [Eq. (1)]. As a result of the presence of less bulky *anti* substituents, the enantioselectivity for cyclic **S2** is more difficult to control.[1] There are, therefore, fewer successful catalysts for **S2**. In all cases, the catalysts were generated in situ from $[PdCl(\eta^3\text{-}C_3H_5)]_2$ and the corresponding ligand.



The results summarized in Table 1 indicate that the enantioselectivity is mainly affected by the substituents/configuration at the biaryl phosphite moiety (**a**–**g**) and by the amine substituents, whereas the configuration of the ephedrine backbone has less effect. Therefore, the enantioselectivity is controlled mostly by the biaryl phosphite moiety, regardless of the configuration of the ephedrine backbone. The effect of the substituents/configuration of the biaryl phosphite moiety was studied with **L1 a**–**g** (Table 1, entries 1–7). The results indicate that the presence of trimethylsilyl groups at the *ortho* positions of the biaryl phosphite moiety affects both the activity and the enantioselectivity negatively (entry 3 vs. 1–2 and entries 6–7 vs. 4–5). Also, if we compare the results of the use of **L1 a** with those of the related enantiopure biaryl ligands **L1 d** and **L1 e** (entry 1 vs. 4 and 5), we can conclude that the tropoisomeric biphenyl moiety in **L1 a**–**c** is not controlled when coordinated in the Pd-π-allyl intermediate species. The best enantioselectivities were obtained with ligands that contained enantiopure biaryl phosphite moieties with *tert*-butyl groups at the *ortho* positions (**d** and **e**; entries 4 and 5).

We then evaluated the effect of the amine substituents with **L1**–**L3**. In general, the use of **L1**, which have a dimethyl amine group, yielded higher enantioselectivities than the use of **L2** and **L3** (i.e., entry 4 vs. 9 and 12). A plausible explanation may be the formation of mixtures of diastereomeric amino complexes with **L2** and **L3** (the N atom in **L2** and **L3** becomes a stereogenic center upon coordination to the metal). In addition, **L1** have the advantage that they can be synthesized in fewer steps than **L2** and **L3** (Scheme 1).

Table 1. Pd-catalyzed allylic alkylation of **S1**–**S2** with dimethyl malonate as the nucleophile using ephedrine-based amino phosphite ligands **L1**–**L4 a**–**g**.[a]



Entry	Ligand	Conversion (yield) [%][b]	*ee* [%][c]	Conversion (yield) [%][d]	*ee* [%][e]
1	**L1 a**	100 (94)	31 (*R*)	100 (93)	9 (*R*)
2	**L1 b**	100 (92)	29 (*R*)	100 (94)	8 (*R*)
3	**L1 c**	51 (48)	11 (*R*)	98 (91)	3 (*R*)
4	**L1 d**	100 (94)	81 (*R*)	100 (90)	60 (*R*)
5	**L1 e**	100 (93)	75 (*S*)	100 (93)	60 (*S*)
6	**L1 f**	50 (45)	64 (*R*)	95 (89)	39 (*R*)
7	**L1 g**	36 (31)	27 (*S*)	97 (91)	58 (*S*)
8	**L2 a**	29 (24)	6 (*S*)	100 (92)	9 (*S*)
9	**L2 d**	100 (96)	42 (*R*)	100 (88)	36 (*R*)
10	**L2 e**	70 (66)	33 (*S*)	100 (93)	56 (*S*)
11	**L3 a**	56 (51)	0	100 (91)	9 (*S*)
12	**L3 d**	100 (93)	42 (*R*)	100 (92)	53 (*S*)
13	**L3 e**	84 (80)	29 (*S*)	100 (89)	68 (*S*)
14	**L4 a**	62 (57)	8 (*R*)	100 (93)	7 (*R*)
15	**L4 d**	100 (96)	81 (*R*)	100 (91)	45 (*R*)
16	**L4 e**	89 (85)	60 (*S*)	100 (93)	70 (*S*)

[a] Reactions were performed at 23 °C with $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (0.5 mol%), ligand (1 mol%), CH_2Cl_2 as solvent, bis(trimethylsilyl)acetamide (BSA, 3 equiv.), dimethyl malonate (3 equiv.), KOAc (3 mg). [b] Conversions and yields determined after 6 h. [c] *ee* determined by HPLC. [d] Conversions and yields determined after 18 h. [e] *ee* determined by GC.

Finally, the configuration of the ephedrine backbone was studied by comparing **L1** and **L4**. A cooperative effect between the configurations of both the ephedrine backbone and the biaryl phosphite moiety was observed. Such a cooperative effect depends of the steric demands of the substrate. Although for **S1** the cooperative effect results in a matched combination for ligands **L1 d** and **L4 d** (81% *ee*, entries 4 and 15), which contains an *R*-biphenyl moiety, the matched combination for substrate **S2** was achieved using pseudoephedrine-based ligand **L4 e** (70% *ee*, entry 16), which contains an *S*-biphenyl phosphite moiety.

To identify which ligand parameters should be further modified to increase the enantioselectivity, we performed a DFT computational study of the key intermediates and transition states involved in the enantiocontrol of the Pd-catalyzed allylic substitution of **S1** using **L4 d** and **L4 e** as models. Previous mechanistic studies have shown that enantioselectivity is controlled in the effectively irreversible nucleophilic attack, but the transition state (TS) for this step can be either early or late depending on the nature of the nucleophile, ligands, and reaction conditions. In an early TS, the interactions that lead to ste-

reochemical differentiation can be understood from the structure of the Pd-allyl intermediate,[16] whereas the late TS is more reminiscent of the Pd-alkene product complex.[17] A sterically encumbered ligand can be employed to push the allyl group into a more product-like orientation, which affects the regiochemical preference in the nucleophilic attack strongly.[18] In our experience, a diffuse anion such as malonate or a neutral nucleophile such as amine would be expected to give relatively early TSs, whereas a highly concentrated charge such as a fluoride anion gives a late TS.[19]

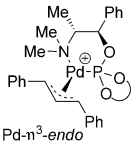
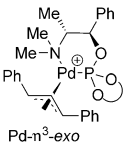
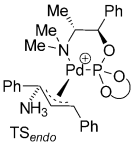
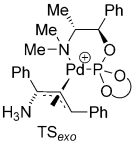
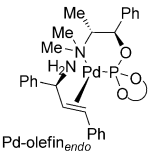
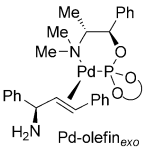
For the early TS case, the stereochemistry is governed by both the population of the Pd-η^3-allyl intermediates and the relative electrophilicity of the allylic carbon atoms, and an allyl terminus *trans* to a P atom is generally more reactive than one *trans* to a N atom. If the TS is late, the formation of the most stable Pd-olefin complex controls the enantioselectivity. Calculations were performed using the B3LYP functional, the 6-31G*/LANL2DZ basis set, and the polarizable continuum model (PCM) for the solvent with parameters for CH_2Cl_2 as implemented in Gaussian 09. The energies were further refined by performing single-point calculations at the 6-311+G** level and by dispersion correction with the DFT-D3 model. Previous experience has shown us that ammonia can be used as a good model nucleophile,[2b,20] which avoids the problems related to charge separation in conjunction with a continuum solvent model. Notably, the use of ammonia as the nucleophile instead of dimethyl malonate results in the inversion of the Cahn–Ingold–Prelog (CIP) descriptor in the 1,3-diphenylallyl case because of the change in the priority of the groups, although the stereoselectivity is maintained.

Initially, we calculated the relative stability of the Pd-η^3-diphenylallyl complexes. Only the two *syn-syn* η^3-allyl complexes (Pd-η^3-*endo* and Pd-η^3-*exo*, Table 2) were calculated. In accordance with that already described in the literature, the contribution of the other allylic species of higher energy (*anti-anti* and *syn-anti* Pd-η^3) was neglected.[1d] In line with the catalytic results (Table 1), the DFT results indicate that the configuration of the biaryl phosphite moiety controls the preferential formation of one of the *syn-syn* Pd-allyl intermediates. Thus, although the formation of Pd-η^3-*exo* is preferred for **L4d** ($\Delta G =$ 7.6 kJ mol^{-1}), the most stable Pd-allyl intermediate for **L4e** is Pd-η^3-*endo* ($\Delta G = 8.2$ kJ mol^{-1}). If we assume that the allyl intermediates are in rapid equilibrium[21] and that the nucleophile will always attack *trans* to the P atom, the preferred intermediate leads to the preferred product in this case.

We then calculated TS_{endo} and TS_{exo} using NH_3 as the nucleophile (Table 2). The energy differences of the calculated TSs agree with the catalytic results. The energy difference between the TSs of **L4d** ($\Delta G^{\#} = 4$ kJ mol^{-1}) is higher than that of **L4e** ($\Delta G^{\#} = 2$ kJ mol^{-1}). This is in good agreement with the higher enantioselectivities achieved using **L4d** (Table 1, 81% *ee* for **L4d** vs. 60% *ee* for **L4e**). In addition, the formation of the opposite enantiomers of the substituted product is predicted if **L4d** and **L4e** are used.

Finally, we calculated the Pd-olefin intermediates (Pd-olefin$_{endo}$ and Pd-olefin$_{exo}$). The results (Table 2) indicated that a higher energy difference of the Pd-olefin complexes is achieved with **L4e** ($\Delta G^{\#} = 5$ kJ mol^{-1} for **L4e** vs. 1.8 kJ mol^{-1} for **L4d**). Thus, in this case, the product complex energies do not correlate with the TS energies or with the experimental selectivities. The structural elucidation of the Pd-allyl intermediates and the determination of their relative reactivity towards the nucleophile are, therefore, crucial to understand their catalytic behavior (see below).

Table 2. Calculated energies [kJ mol^{-1}] for the *endo* and *exo* Pd-η^3-allyl intermediates, TSs, and Pd-π-olefin complexes using **S1** and NH_3 as nucleophile.[a]

	L4d	**L4e**
 Pd-η^3-*endo*	0	8.2
 Pd-η^3-*exo*	7.6	0
 TS_{endo}	0	2
 TS_{exo}	4	0
 Pd-olefin$_{endo}$	0	0
 Pd-olefin$_{exo}$	1.8	5

The calculated TSs for the major and the minor pathways with both ligands are shown in Figure 2. A special feature of all these TSs is that the methyl substituent of the ephedrine backbone points away from the coordination sphere. This suggests that the methyl group should have little impact on the enantioselectivity. To prove this, we recalculated the TSs by removing the methyl substituent of the ephedrine backbone (new ligand **L5e**; Figure 1). Surprisingly, the calculated energy difference between the two TSs for the formation of both enantiomers of the alkylated product (Figure 3a) was 8.5 kJ mol^{-1} (**L5e**), which surpasses the values for **L4d** and **L4e** (4 and 2 kJ mol^{-1}, respectively) and indicates that **L5e** should provide a higher enantioselectivity than the ephedrine-based ligands **L4d** and **L4e**.

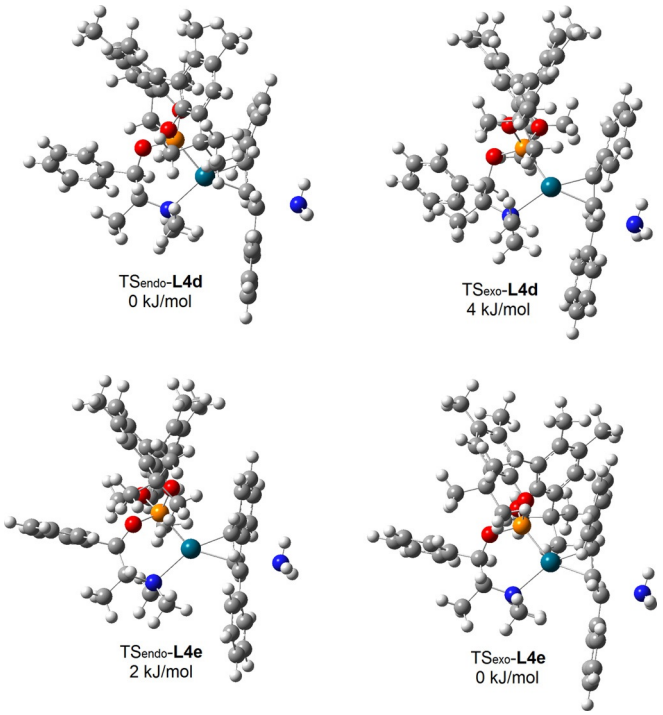


Figure 2. Calculated transition states using ephedrine-based **L4d** and **L4e**.

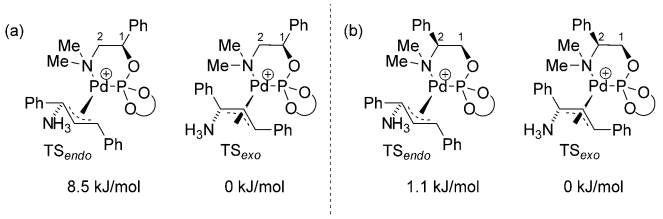


Figure 3. Calculated energies of TSs using a) **L5e** and b) **L6e**.

To study the effect of the other stereogenic center of the ephedrine backbone (C-2), the phenyl substituent was switched from C-1 to C-2 (**L6e**; Figure 1). A slightly lower energy difference between the TSs was achieved for Pd-**L6e** than Pd-**L4e** (Figure 3b), which suggests that this modification should provide lower enantioselectivities for **L6e** than **L4e**.

These theoretical results prompted us to prepare and screen amino phosphite ligands **L5**–**L6d**–**e** (Scheme 1) for the asymmetric allylic substitution of substrates **S1** and **S2** (Table 3). As predicted by the theoretical calculations, the use of **L5e**, which does not have the methyl substituent at the stereogenic C-2 position of the ephedrine backbone, in the allylic alkylation of **S1** provided the highest enantioselectivities (Table 3, entry 2, 94% (*S*) *ee*), whereas the use of **L6e** led to similar enantioselectivities as that of **L4e** (entry 4). The same behavior is observed in the allylic alkylation of cyclic **S2**. If we used **L5e**, we could, therefore, increase the enantioselectivity from 70 to 82% *ee* (Table 3, entry 2). Interestingly, for **S1**, ligand **L5d** provided similarly high enantioselectivities as **L5e** but in the opposite enantiomer of the substitution product (92% (*R*) *ee*, entry 1). Both enantiomers of the substitution products can, therefore, be obtained by simply changing the configuration of the biaryl phosphite moiety in **L5**. All these results show the importance of using a modular scaffold to build new ligand systems.

Table 3. Pd-catalyzed allylic alkylation of **S1** and **S2** with dimethyl malonate using amino phosphite ligands **L5**–**L6d**–**e**.[a]

Entry	Ligand	Conversion (yield) [%][b]	*ee* [%][c]	Conversion (yield) [%][d]	*ee* [%][e]
1	**L5d**	100 (94)	92 (*R*)	100 (90)	70 (*R*)
2	**L5e**	100 (96)	94 (*S*)	100 (89)	82 (*S*)
3	**L6d**	100 (92)	41 (*R*)	100 (91)	46 (*R*)
4	**L6e**	100 (93)	62 (*S*)	100 (92)	62 (*S*)
5[f]	**L5e**	100 (95)	97 (*S*)	100 (91)	86 (*S*)
6[g]	**L5e**	98 (91)	92 (*S*)	94 (87)	83 (*S*)
7[h]	**L5e**	38 (32)	89 (*S*)	56 (49)	74 (*S*)

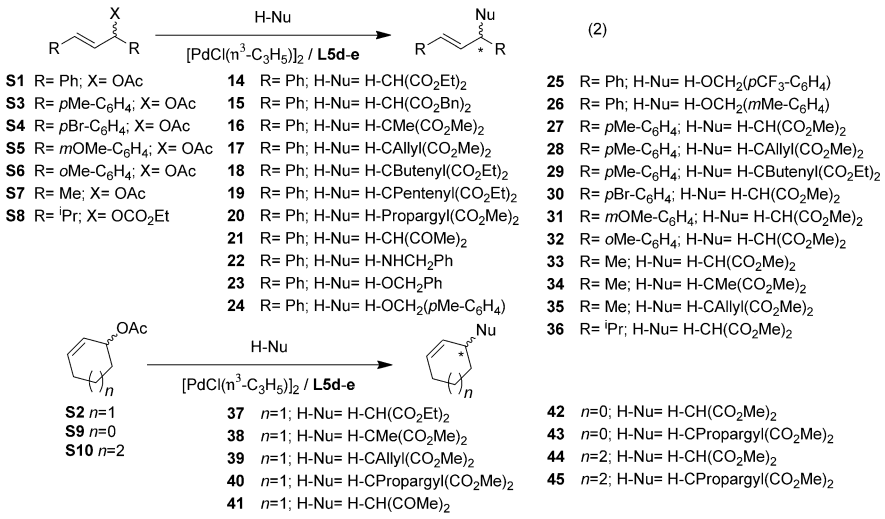
[a] Reactions were performed at 23 °C with $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (0.5 mol%), ligand (1 mol%), CH_2Cl_2 as solvent, BSA (3 equiv.), dimethyl malonate (3 equiv.), KOAc (3 mg). [b] Conversions and yields determined after 6 h. [c] *ee* determined by HPLC. [d] Conversions and yields determined after 18 h. [e] *ee* determined by GC. [f] Reactions performed at 5 °C for 18 h. [g] Reactions performed at 0 °C for 18 h. [h] Reactions performed at −15 °C for 18 h.

The enantioselectivity can be improved by controlling not only the structure but also the reaction parameters. Therefore, we studied these reactions at a low reaction temperature (entries 5–7). Enantioselectivity was further improved (*ee* values up to 97% for **S1** and 86% for **S2**) by decreasing the reaction temperature to 5 °C (Table 3, entry 5).

Allylic substitution of symmetrical 1,3-disubstituted allylic substrates S1–S10 with other C-, N-, and, O-nucleophiles: Scope and limitations

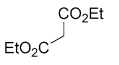
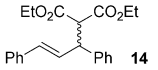
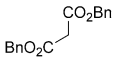
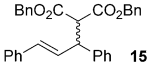
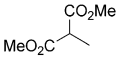
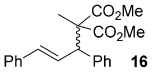
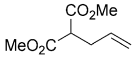
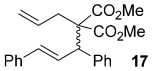
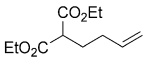
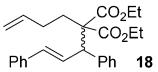
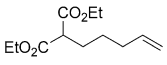
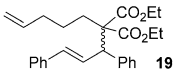
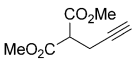
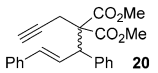
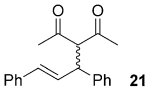
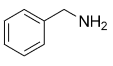
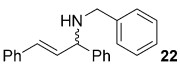
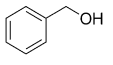
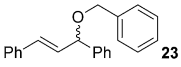
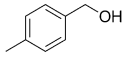
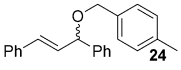
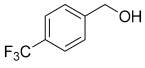
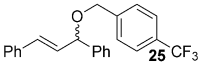
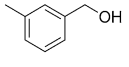
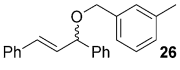
We investigated the substrate and nucleophile scope with the optimal amino phosphite ligands **L5e** and **L5d**. The following linear and cyclic disubstituted substrates with different steric properties were studied [Eq. (2)]: **S1**, **S2**, *rac*-1,3-di(4-tolyl)-3-acetoxyprop-1-ene (**S3**), *rac*-1,3-di(4-bromophenyl)-3-acetoxyprop-1-ene (**S4**), *rac*-1,3-di(3-methoxyphenyl)-3-acetoxyprop-1-ene (**S5**), *rac*-1,3-di(2-tolyl)-3-acetoxyprop-1-ene (**S6**), *rac*-1,3-dimethyl-3-acetoxyprop-1-ene (**S7**), *rac*-(*E*)-ethyl-2,5-dimethyl-3-hex-4-enylcarbonate (**S8**), *rac*-3-acetoxycyclopentene (**S9**), and *rac*-3-acetoxycycloheptene (**S10**). The range of nucleophiles was also expanded compared to that of previous work, with special attention paid to the more challenging and interesting from a synthetic point of view, such as functionalized malonates, β-diketones, and alkyl alcohols, which are seldom reported.

The results of Pd/**L5e** and Pd/**L5d** in the allylic substitution of **S1** using a wide range of C-, N-, and O-nucleophiles are shown in Table 4. The enantioselectivity was relatively unaffected by the change in the steric nature of the ester groups and in the substituents of the malonate nucleophiles (entries 1–13).



Therefore, a variety of malonates, which include those that are α-substituted, reacted cleanly with **S1** to afford products **14**–**20** in high yields and with enantioselectivities that were as high as or higher than those obtained with dimethyl malonate (*ee* values up to 99% *ee*; entries 1–13). Among these are the strikingly high enantioselectivities achieved using allyl-, butenyl, pentenyl-, and propargyl-substituted malonates (entries 7–13; 95–99% *ee*). This is advantageous because the resulting products are important precursors for more complex chiral

Table 4. Allylic substitution of **S1** with several C-, N-, and O-nucleophiles using Pd/**L5d**–**e** catalytic systems [see Eq. (2)].[a]

Entry	Nucleophile	Product	**L5d** Yield [%][b]	*ee* [%][c]	**L5e** Yield [%][b]	*ee* [%][c]
1			91	92 (*R*)	92	93 (*S*)
2[d]		**14**	88	94 (*R*)	87	95 (*S*)
3			93	92 (*R*)	91	94 (*S*)
4[d]		**15**	91	94 (*R*)	93	96 (*S*)
5			92	95 (*S*)	90	96 (*R*)
6[d]		**16**	91	98 (*S*)	92	99 (*R*)
7			94	96 (*S*)	93	97 (*R*)
8[d]		**17**	92	99 (*S*)	91	99 (*R*)
9[d]			95	94 (*S*)	92	95 (*R*)
		18				
10			93	95 (*S*)	94	97 (*R*)
11[d]		**19**	94	97 (*S*)	91	99 (*R*)
12			91	94 (*R*)	90	96 (*R*)
13[d]		**20**	92	97 (*R*)	93	98 (*R*)
14			93	96 (*R*)	94	96 (*S*)
15[d]		**21**	91	98 (*R*)	93	99 (*S*)
16			89	97 (*S*)	92	99 (*R*)
		22				
17[e]			92	53 (*S*)	95	56 (*R*)
		23				
18[e]			91	28 (+)	94	30 (−)
		24				
19[e]			92	91 (+)	94	94 (−)
		25				
20[e]			93	68 (+)	91	70 (−)
		26				

[a] Reactions were performed at 23 °C with $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (0.5 mol%), CH_2Cl_2 as solvent, ligand (1 mol%), BSA (3 equiv.), KOAc (3 mg). [b] Full conversions were achieved after 12 and 24 h for reactions performed at 23 and 5 °C, respectively. [c] *ee* determined by chiral HPLC or GC. [d] Reactions performed at 5 °C for 24 h. [e] Reactions performed using 2 mol% $[PdCl(\eta^3\text{-}C_3H_5)]_2$, 4 mol% ligand, Cs_2CO_3 (3 equiv.). Full conversions were achieved in all cases.

molecules (see below). Excellent enantiocontrol was also achieved if the β-diketone acetophenone and *N*-benzylamine were used as nucleophiles (*ee* values up to 99%; entries 14–16). Notably, the excellent results achieved using benzylamine validate the use of ammonia as a nucleophile for the computational model. In all cases, both enantiomers of the substituted product can be obtained in high yields and enantioselectivities.

We then went on to study the allylic substitution of **S1** using alkyl alcohols as a challenging class of O-nucleophiles. The stereoselective construction of compounds with ether groups next to a chiral carbon atom is important for the preparation of biologically active compounds.[22] Although the enantioselective Pd-catalyzed allylic etherification is currently studied by several research groups, few successful examples have been reported. Among them phenols have been the most studied,[23] whereas aliphatic alcohols have been explored less.[11f,24] The reaction of Pd/**L5e** and Pd/**L5d** with several substituted benzylic alcohols proceeded smoothly to afford both enantiomers of the desired products in high yields (Table 4, entries 17–20). Furthermore, the enantioselectivity was influenced by the electronic nature of the substituted benzylic alcohol. The highest enantioselectivity (*ee* values up to 94%; entry 19) was obtained if the benzylic alcohol contained an electron-deficient *para*-CF_3 substituent, and the selectivity diminished gradually as the substituent became more electron rich. This behavior is the opposite to that observed in the etherification reaction with the Pd/(*S*,*Rp*)-FerroNPS ((*S*)-*N*-methyl-*N*-diphenylphosphino-1-[(*R*)-2-cyclohexylthio)ferrocenyl]ethylamine) catalytic system,[24c] which is one of the few Pd catalysts that has been designed especially for this purpose and applied successfully. The Hammett plot of this electronic effect shows a linear free-energy relationship between the enantioselectivity and the electronic character of the substituent (Figure 4; $\rho = 1.78$).[25] This plot could, therefore, be used to predict the enantioselectivity of an asymmetric allylic substitution if *para*-substituted benzylic alcohols are used.

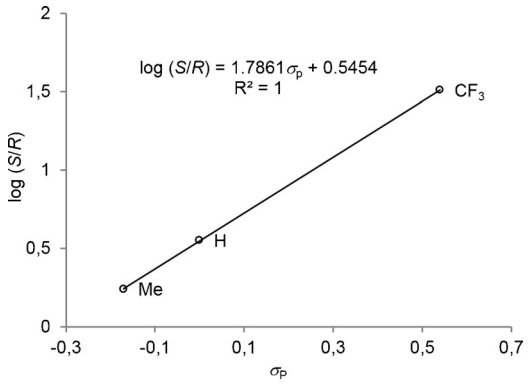


Figure 4. Hammett plot of the Pd-catalyzed allylic etherification of **S1** with **L5e**.

The scope of the Pd/**L5d** and Pd/**L5e** catalytic systems was further studied by using other linear substrates [Eq. (2)] that have different electronic (**S3**–**S5**) and steric requirements (**S6**–**S8**) to substrate **S1** (Figure 5; **27**–**36**). The results obtained using **S3** followed the same trend as the use of **S1**. High enantioselectivities in both enantiomers of the substituted product were obtained in the alkylation of **S3** using several malonates, which include those α-substituted with allyl and butenyl groups (*ee* values up to 99%, **27**–**29**). In addition, the catalytic performance is unaffected by the presence of electron-withdrawing groups at the *para* position as well as by the introduction of *meta* and *ortho* substituents at the phenyl groups. Thus, high enantioselectivities were also achieved for the allylic alkylation of **S4**–**S6** (Figure 5; *ee* values up to 94%, **30**–**32**). The allylic substitution of **S7**, which is less sterically demanding and is substituted much less enantioselectively than **S1**,[26] also proceeded smoothly (**33**–**35**). Although the enantioselectivity depended on the steric properties of the nucleophile, we were pleased to see that the enantioselectivities were higher for the more challenging α-substituted malonates (**34**–**35**, *ee* values up to 81%) than for the standard dimethyl malonate. Finally, we were pleased to find that Pd/**L5d**–**e** also provided high enantioselectivity, in both enantiomers of the alkylated product, of the more demanding substrate **S8** (95% *ee*), which usually reacts with lower yields and enantioselectivities than model substrate **S1**.

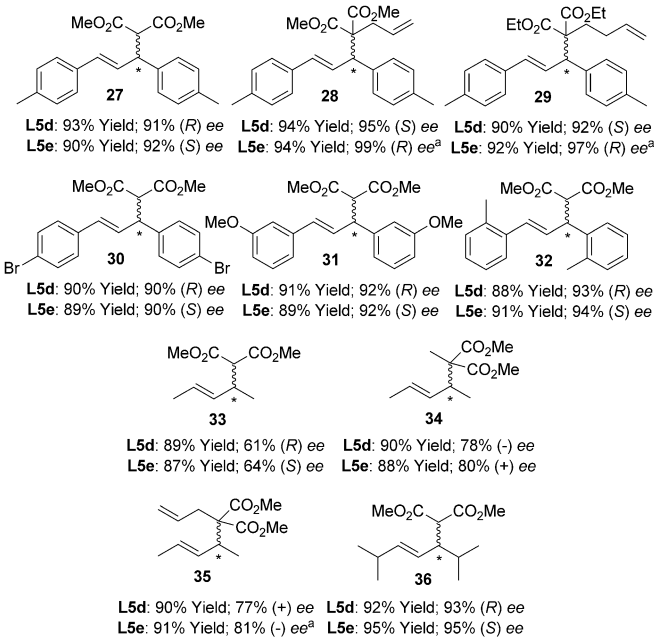
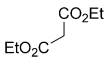
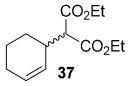
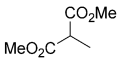
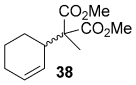
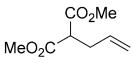
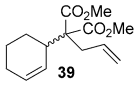
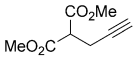
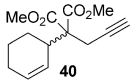
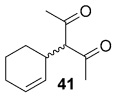
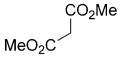
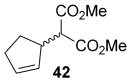
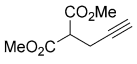
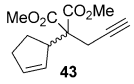
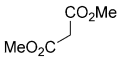
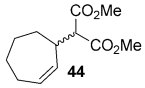
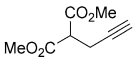
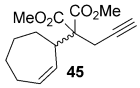


Figure 5. Pd-catalyzed allylic substitution of **S3**–**S8** using several C-nucleophiles. Full conversions were achieved in all cases. $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (0.5 mol%), CH_2Cl_2 as solvent, ligand (1 mol%), 23 °C, 18 h. [a] Reaction performed at 5 °C for 24 h.

Finally, the good performance of Pd/**L5e** was also seen in the allylic substitution of cyclic substrates using a range of C-nucleophiles, which included the less studied α-substituted malonates and β-diketones. For **S2**, the enantioselectivities were as high as those obtained with dimethyl malonate (Table 5; entries 1–5, **37**–**41**). Even more interesting is the high enantioselectivity achieved using other cyclic substrates with a different ring size (**S9** and **S10**). The enantiocontrol was high

Table 5. Allylic substitution of cyclic **S2**, **S6**, and **S7** with several C-nucleophiles using the Pd/**L5e** catalytic system.[a]

Entry	Substrate	Nucleophile	Product	Yield [%][b]	*ee* [%][c]
1	**S2**		 **37**	89	83 (*S*)
2	**S2**		 **38**	91	86 (+)
3	**S2**		 **39**	94	90 (−)
4	**S2**		 **40**	93	87 (*S*)
5	**S2**		 **41**	92	76 (−)
6	**S6**		 **42**	88	75 (−)
7	**S6**		 **43**	92	84 (*S*)
8	**S7**		 **44**	93	91 (*S*)
9	**S7**		 **45**	94	93 (*S*)

[a] Reactions were performed at 5 °C with $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (0.5 mol%), CH_2Cl_2 as solvent, ligand (1 mol%), BSA (3 equiv.), KOAc (3 mg). [b] Full conversions were achieved after 24 h. [c] *ee* determined by chiral HPLC or GC.

in both cases, even in the allylic substitution of **S9** (**42** and **43**), which is usually alkylated much less enantioselectively than six- and seven-membered cyclic substrates.

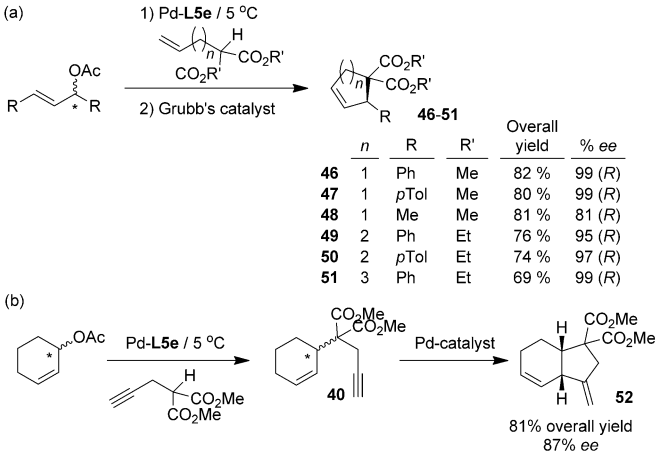
In summary, by the theoretically guided optimization of the crucial stereodefining moieties in this new modular amino phosphite ligand library, we have been able to identify one of the very few catalytic systems that can create new C–C, C–N, and C–O bonds with high activities and enantioselectivities in a number of substrate types, which have different electronic and steric proprieties, using a wide range of nucleophiles.

Synthetic applications of the allylic substitution compounds: Preparation of chiral carbocycles

Asymmetric allylic alkylation (AAA) is a relevant method for the creation of chiral C–C and C–heteroatom bonds. Furthermore, functionalized substrates (e.g., **17**–**19**, **28**–**29**, and **35** formed by Pd-AAA with nucleophiles that contain allyl, butenyl, and pentenyl groups) open up new pathways to build more complex molecules easily. To illustrate these aspects, we have prepared a range of chiral carbocycles (**46**–**51**) by simple tandem reactions that involve the allylic substitution of the substrate and ring-closing metathesis reactions (Scheme 2a) or the sequential allylic substitution and cycloisomerization of the 1,6-enyne (Scheme 2b). Thus, allyl-substituted compounds [**17**–**19**, **28**–**29**, and **35**; Eq. (2)] that bear a terminal alkene can undergo clean ring-closing metathesis with no loss in enantiomeric excess. A range of five-, six-, and seven-membered carbocycles with different substituents (R = Me, Ph, *p*Tol) were prepared in good yields and high enantioselectivities (**46**–**51**; Scheme 2a). Also, the carbobicycle hydrindane **52** is obtained by cycloisomerization of the 1,6-enyne **40**, which is produced from the AAA of **S2** with dimethyl propargylmalonate, using the methodology described by Uozumi and coworkers (Scheme 2b).

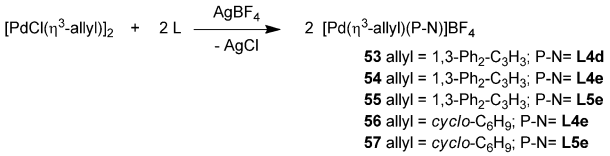
NMR spectroscopy of key Pd-η^3-allyl intermediates

Our DFT studies have shown that enantioselectivity is determined during the nucleophilic attack (see above). Consequently, the structural elucidation of the Pd-allyl intermediates and the determination of their relative reactivity towards the nucleophile are essential to understand their catalytic behavior. For this purpose, we studied the Pd-η^3-allyl compounds **53**–**57** ($[Pd(\eta^3\text{-allyl})(P\text{-}N)]BF_4$; P-N = **L4**–**L6d**–**e**) to obtain further insight into how the ligand parameters affect catalytic performance (Scheme 3). These ionic Pd complexes, which contain 1,3-diphenyl or cyclohexenyl allyl groups, were prepared using the method from the corresponding Pd-allyl dimer reported previously and the appropriate ligand in the presence of silver tetrafluoroborate (Scheme 3).[27] The complexes were characterized by elemental analysis and ^1H, ^{13}C, and ^{31}P NMR spectroscopy. The spectral assignments were based on information from ^1H-^1H, ^{31}P-^1H, and ^{13}C-^1H correlation measurements in combination with ^1H-^1H NOESY experiments. Unfortunately, we were unable to



	n	R	R'	Overall yield	% *ee*
46	1	Ph	Me	82 %	99 (*R*)
47	1	*p*Tol	Me	80 %	99 (*R*)
48	1	Me	Me	81 %	81 (*R*)
49	2	Ph	Et	76 %	95 (*R*)
50	2	*p*Tol	Et	74 %	97 (*R*)
51	3	Ph	Et	69 %	99 (*R*)

Scheme 2. Preparation of chiral carbocycles by the sequential allylic substitution of functionalized olefins/cyclization reactions.

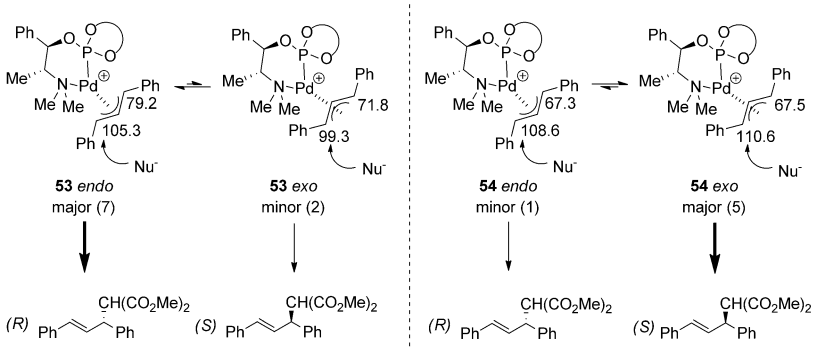


Scheme 3. Preparation of [Pd(η^3-allyl)(P-N)]BF_4 (**53**–**57**).

obtain crystals of sufficient quality to perform XRD measurements.

Palladium 1,3-diphenyl allyl complexes

The variable-temperature (VT) NMR spectra (30 to −80 °C) of Pd-allyl intermediates **53** and **54**, which contain ephedrine-based **L4d** and **L4e**, respectively, showed a mixture of two isomers in equilibrium at a ratio of 7:2 and 1:5, respectively.[28] Both isomers were assigned unambiguously by NMR spectroscopy to the two *syn*/*syn* Pd-η^3-*endo* and *exo* isomers (Scheme 4).



Scheme 4. Diastereoisomer Pd-allyl intermediates for **S1** with **L4d** and **L4e**. The relative amounts of each isomer are shown in parentheses. The chemical shifts [ppm] of the allylic terminal carbon atoms are also shown.

In all cases, the NOE indicated interactions between the two terminal protons of the allyl group, which indicates a *syn*/*syn* disposition (Figure 6). In addition, for the major isomer of **53** and the minor isomer of **54**, one of the methyl substituents of the amino group (the one that shows a NOE interaction with the H atom attached to C-2) showed a NOE interaction between the terminal allyl proton *trans* to the phosphite moiety, whereas this interaction appeared with the central allyl proton in the minor isomer **53** and major isomer of **54** (Figure 6). Moreover, the other methyl substituent of the amino group (the one that shows a NOE interaction with the H atom attached to C-1) also shows a NOE interaction with the central allyl proton in the major isomer **53** and the minor isomer of **54**, whereas this interaction appears with the terminal allyl proton *trans* to the phosphite moiety for the minor and major isomers of **54** and **54**, respectively. Finally, the minor isomer of **53** and major isomer of **54** showed NOE interactions between the terminal allyl proton *trans* to the amino group with one of the *tert*-butyl substituents at the biaryl phosphite moiety (the one that shows NOE contacts with the H atom attached to C-1). These interactions can be explained by assuming a *syn*/*syn endo* disposition for the major and minor isomers of **53** and **54** and a *syn*/*syn exo* disposition for the minor and major isomers of **53** and **54** (Scheme 4). Although the population of the Pd-allyl intermediates obtained by DFT calculations is different to that found by NMR spectroscopy, the general trend is reproduced well. Thus, although for Pd/**L4d** the major isomer is Pd-η^3-*endo*, for Pd-**L4e** the major isomer is Pd-η^3-*exo*.

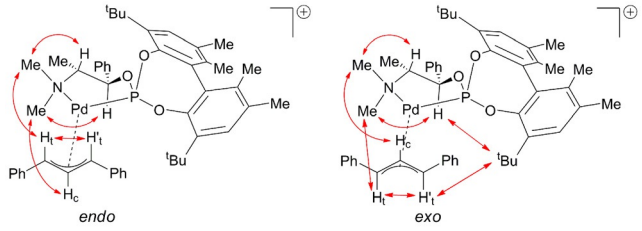
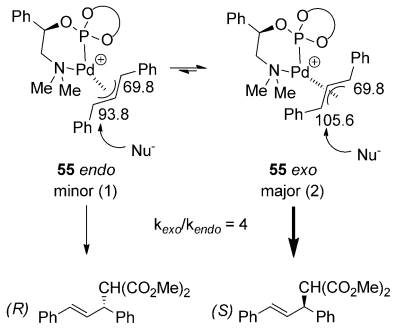


Figure 6. Relevant NOE contacts from the NOESY experiment of [Pd(η^3-1,3-diphenylallyl)(**L4d**)]BF_4 (**53**) isomers are shown as an example. The same NOE contacts were observed for the isomers of [Pd(η^3-1,3-diphenylallyl)-(**L4e**)]BF_4 (**54**).

In all isomers, the chemical shifts in the ^{13}C NMR spectra indicate that the most electrophilic allyl C terminus is *trans* to the phosphite moiety (Scheme 4). If we assume that the nucleophilic attack takes place at the more electrophilic allyl C terminus,[1] which is in line with the DFT calculations, the stereochemical outcome of the reaction is not controlled fully by the population of the Pd-allyl intermediates (note that the diastereomeric excesses differ from the *ee* values). So, the relative electrophilicity of the terminal allylic C atoms of each isomer plays an important role and has to been taken into account. In this respect, the Pd/**L4d** catalyst shows a higher electronic difference between the more electrophilic allylic terminal C atoms of both isomers ($\Delta(\delta^{13}C) = 6$ ppm) than Pd/**L4e** ($\Delta(\delta^{13}C) = 2$ ppm). This higher electronic difference makes the major isomer of Pd/**L4d** react faster than the major isomer of Pd/**L4e** and accounts fully for the higher enantioselectivity achieved with Pd/**L4d** than Pd/**L4e**.

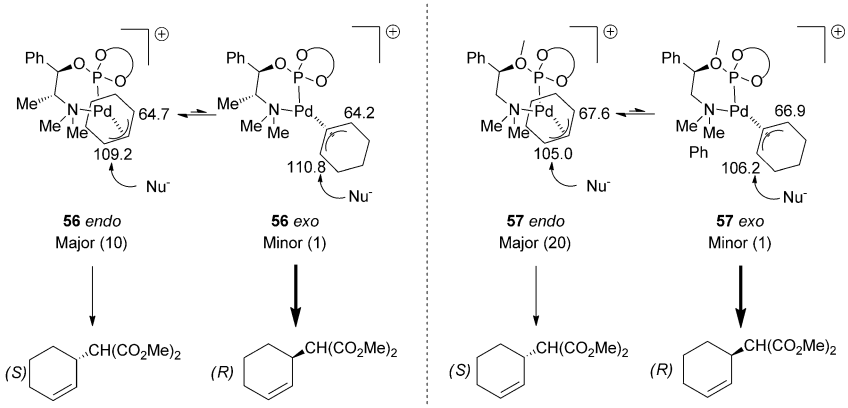
The VT-NMR spectra of Pd-allyl intermediate **55**, which contains **L5e** and differs from the previous Pd/**L4d**–**e** catalysts in that the methyl substituent of the ephedrine ligand backbone has been removed, also had a mixture of two *syn*/*syn* Pd-η^3-*endo* and *exo* isomers in a ratio of 1:2 (Scheme 5).

Furthermore, the most electrophilic allyl C terminus was *trans* to the phosphite moiety. However, an important difference between **53** and **54** is the higher electronic differentiation between the more electrophilic allylic terminal C atoms of both isomers in **55** ($\Delta(\delta^{13}C) = 11$ ppm) than in **53** and **54**



Scheme 5. Diastereoisomer Pd-allyl intermediates for **S1** with **L5e**. The relative amounts of each isomer are shown in parentheses. The chemical shifts [ppm] of the allylic terminal carbon atoms are also shown.

1,3-cyclohexenyl-allyl intermediate **56**, which contains ephedrine-based amino phosphite ligand **L4e**, and compared it with its related amino phosphite counterpart Pd/**L5e**. The VT-NMR spectra (35 to −80 °C) of Pd intermediates **56** and **57** showed a mixture of the two possible isomers at a ratio of 10:1 and 20:1, respectively (Scheme 6). The major isomers were assigned unambiguously by NOE to Pd-η^3-*endo* isomers (Figure 8). In both cases, the NOE indicates interactions between the central allyl proton and one of the methyl substituents of the amino group (the one that shows a NOE interaction with the H atom attached to C-1 of the ligand backbone) and with one of the *tert*-butyl substituents at the biaryl phosphite moiety (the one that also shows a NOE contact with the H atom attached to C-1; Figure 8). The chemical shifts of the ($\Delta(\delta^{13}C) = 6$ and 2 ppm, respectively). This higher electronic differentiation may explain the higher enantioselectivity obtained with Pd/**L5e** than that with Pd/**L4d–e**. Accordingly, the reactivity of the Pd intermediates with sodium malonate at low temperature studied by in situ NMR spectroscopy indicates that the major Pd-η^3-*exo* isomer reacts four times faster than the minor Pd-η^3-*endo* isomer (Figure 7), which agrees fully with the *ee* obtained experimentally.



Scheme 6. Diastereoisomer Pd-allyl intermediates for **S2** with **L4e** and **L5e**. The relative amounts of each isomer are shown in parentheses. The chemical shifts [ppm] of the allylic terminal carbons are also shown.

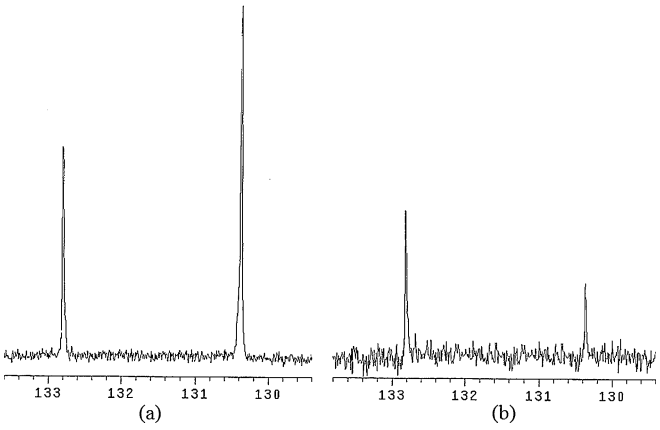


Figure 7. ^{31}P-{^1H} NMR spectra of [Pd(η^3-1,3-diphenylallyl)(**L5e**)]BF_4 (**55**) in CD_2Cl_2 at −80 °C a) before the addition of sodium malonate and b) after the addition of sodium malonate.

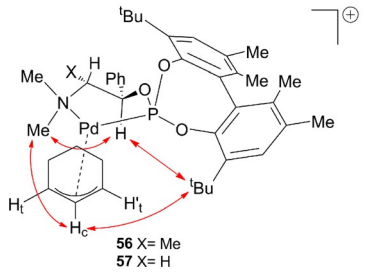


Figure 8. Relevant NOE contacts from the NOESY experiments for the major isomers of [Pd(η^3-1,3-cyclohexenylallyl)(L)]BF_4 (**56** and **57**; L = **L4e** and **L5e**, respectively).

Palladium 1,3-cyclohexenyl allyl complexes

Finally, in an attempt to provide further information about the positive effect on the enantioselectivity observed in the allylic substitution of unhindered cyclic **S2** if the methyl substituent of the ephedrine backbone was removed, we studied the Pd-

^{13}C NMR spectra indicated that the most electrophilic allylic C terminus is *trans* to the phosphite moiety. If we assume that the nucleophilic attack takes place at the most electrophilic allyl C terminus and if we take into account the observed stereochemical outcome of the reaction (70% *S* for **56** and 82% *S* for **57**) and that the *ee* values of the alkylation product **13** are different from the diastereoisomeric excesses (*de*) of the Pd intermediates (*de* = 81% *S* for **56** and 90% *S* for **57**), the minor isomers must react slightly faster than the major isomers. This is in agreement with the slightly higher electrophilicity of the allylic terminal C atom *trans* to the phosphite moiety located

at the minor isomers (i.e., $\Delta(\delta^{13}C)$ around 1 ppm for Pd/**L4e**). The lower enantioselectivities obtained with Pd/ephedrine-based amino phosphite **L4e** than with the related Pd/**L5e** catalytic system can, therefore, be attributed to the increase in the relative amount of the fast-reacting *exo* isomer with respect to the *endo* isomer compared with the population of the *endo* and *exo* isomers in Pd/**L5e**.

Conclusions

A new library of modular amino phosphite ligands has been tested successfully in the asymmetric Pd-catalyzed allylic substitution of substrates with different steric and electronic requirements with a large variety of nucleophiles. These ligands, which are prepared in a few steps from readily available enantiopure amino alcohols, include the benefits of a high stability of the amine moiety and the additional control provided by both the adaptability of the chiral cavity caused by the biaryl phosphite groups and the flexibility of the chiral pocket through a highly modular ligand scaffold. Other advantages of these ligands are that they are solid, stable to air and other oxidizing agents and are, therefore, easy to handle and can be manipulated and stored in air. In two or three simple steps, several ligand parameters have been tuned to maximize the catalyst performance. Enantioselectivity is controlled mainly by the substituents/configuration at the biaryl phosphite moiety and by the amine substituents, whereas the configuration of the ephedrine backbone has less effect. Theoretically guided optimization based on DFT studies allowed us to rationalize the modifications required in the ligand to improve selectivity. These results led to the identification of one of the very few catalytic systems that can create C–C, C–N, and C–O bonds in substrates with a variety of electronic and steric proprieties in high yields and enantioselectivities (*ee* values up to 99%) using a wide range of nucleophiles. Further studies on the Pd-π-allyl intermediates provided a deep understanding of the effect of the ligand parameters on the origin of the enantioselectivity. Potential applications of the new Pd/amino phosphite catalysts were demonstrated by the synthesis of a range of chiral five-, six-, and seven-membered carbocycles by simple tandem reactions with no loss of enantioselectivity. These results open up the asymmetric Pd-catalyzed allylic substitution of several substrate types with a wide range of nucleophiles to the potential effective use of readily available and highly modular amino phosphite ligands.

Experimental Section

General considerations

All reactions were performed using standard Schlenk techniques under an Ar atmosphere. Solvents were purified and dried by standard procedures. Phosphorochloridites were prepared in one step from the corresponding biaryls.[29] Enantiopure amino alcohols **5**–**8**[12] and oxazolidine **9**[13] were prepared as described previously. Racemic substrates **S1**–**S10** were prepared as reported previously.[30] $[Pd(\eta^3\text{-}1,3\text{-}Ph_2\text{-}C_3H_3)(\mu\text{-}Cl)]$[31] and $[Pd(\eta^3\text{-cyclohexenyl})(\mu\text{-}Cl)]_2$[32] were prepared as described previously. Carbocycle **49** was prepared following the methodology described by Uozumi et al.[33] ^1H, $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR spectra were recorded by using a 400 MHz spectrometer. Chemical shifts are relative to that of $SiMe_4$ (^1H and ^{13}C) as the internal standard or H_3PO_4 (^{31}P) as the external standard. ^1H, ^{13}C, and ^{31}P assignments were made based on ^1H-^1H gCOSY, ^1H-^{13}C gHSQC and ^1H-^{31}P gHMBC experiments.

Preparation of (1*S*,2*R*)-2-[*tert*-butyl(methyl)amino]-1-phenylpropan-1-ol (10)

Compound **9** (1 g, 4.88 mmol) was dissolved in dry ether (20 mL). The solution was stirred in an ice-bath for 5 min, and MeMgBr (3 M in diethyl ether, 4.96 mL, 14.64 mmol) was added dropwise. The solution was warmed to reflux, and the reaction was kept at that temperature for 8 h. The reaction was quenched with saturated NH_4Cl (20 mL), and the aqueous layer was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were dried over $MgSO_4$, and the removal of solvents provided **10** as a pale-yellow solid. Yield: 1.0 g (93%); ^1H NMR ($CDCl_3$): $\delta = 0.94$ (d, 3H, CH_3, $^3J_{H-H} = 7.2$ Hz), 1.06 (s, 9H, *t*Bu), 2.0 (s, 3H, CH_3–N), 3.35 (m, 1H, CH–N), 4.50 (m, 1H, CH–O), 7.21–7.32 ppm (m, 4H, CH=); ^{13}C NMR ($CDCl_3$): $\delta = 12.9$ (CH_3), 27.1 (CH_3, *t*Bu), 30.9 (CH_3, NMe), 55.1 (C, *t*Bu), 55.2 (CH–N), 75.3 (CH–O), 126.7 (CH=), 126.8 (CH=), 127.5 (CH=), 143.1 ppm (C).

Preparation of (1*S*,2*R*)-2-[methyl(2-phenylpropan-2-yl)amino]-1-phenylpropan-1-ol (11)

Compound **9** (1 g, 4.88 mmol) was dissolved in dry THF (20 mL). The solution was stirred in an ice-bath for 5 min, and PhMgBr (1 M in THF, 14.7 mL, 14.64 mmol) was added dropwise. Then, the reaction was warmed to reflux and kept at that temperature for 8 h. The reaction was quenched with saturated NH_4Cl (20 mL), and the aqueous layer was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were dried over $MgSO_4$. The organic solvents were removed, and the crude was purified by silica flash chromatography (AcOEt/light petroleum/NEt_3 6:2:0.1) to afford **11** as a white solid. Yield: 1.2 g (87%); ^1H NMR ($CDCl_3$): $\delta = 0.95$ (d, 3H, CH_3, $^3J_{H-H} = 7.1$ Hz), 1.34 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 2.13 (s, 3H, CH_3–N), 3.20 (m, 1H, CH–N), 4.50 (d, 1H, CH–O, $^3J_{H-H} = 4.8$ Hz), 7.10–7.38 ppm (m, 10H, CH=); ^{13}C NMR ($CDCl_3$): $\delta = 11.7$ (CH_3), 24.8 (CH_3), 25.6 (CH_3), 30.9 (CH_3, NMe), 56.4 (C, CMe_2Ph), 61.0 (CH–N), 77.6 (CH–O), 126.2 (CH=), 126.3 (CH=), 126.4 (CH=), 126.8 (CH=), 127.7 (CH=), 127.9 (CH=), 143.3 (C), 149.0 ppm (C).

General procedure for the preparation of amino phosphite ligands L1–L6a–g

Phosphorochloridite (1.1 mmol) produced in situ was dissolved in toluene (5 mL), and pyridine (0.18 mL, 2.3 mmol) was added. Amino alcohol (1 mmol) was dried azeotropically with toluene (3×1 mL) and then dissolved in toluene (5 mL), to which pyridine (0.18 mL, 2.3 mmol) was added. The phosphorochloridite solution was transferred slowly to the solution of amino alcohol. The reaction mixture was stirred at RT for 90 h (**L1**, **L4**–**L6a**–**g**) or 15 h (ligands **L2**, **L3a**–**g**), 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.

L1a: Yield: 303 mg (49%); ^{31}P NMR (C_6D_6): $\delta = 150.5$ ppm (s); ^1H NMR (C_6D_6): $\delta = 0.98$ (d, 3H, CH_3, $^3J_{H-H} = 6.8$ Hz), 1.29 (s, 9H, CH_3, *t*Bu), 1.3 (s, 9H, CH_3, *t*Bu), 1.48 (s, 9H, CH_3, *t*Bu), 1.62 (s, 9H, CH_3,

*t*Bu), 2.14 (s, 6H, CH_3, NMe_2), 2.59 (m, 1H, CH–N), 5.55 (dd, 1H, CH–O, $^3J_{H-P}=8$ Hz, $^3J_{H-H}=4$ Hz,), 7.03–7.25 (m, 7H, CH=), 7.33 (d, 1H, CH=, $^4J_{H-H}=2.4$ Hz), 7.37 (d, 1H, CH=, $^4J_{H-H}=2.4$ Hz), 7.58 (d, 1H, CH=, $^4J_{H-H}=2.0$ Hz), 7.61 ppm (d, 1H, CH=, $^4J_{H-H}=2.8$ Hz); ^{13}C NMR (C_6D_6): $\delta=8.4$ (CH_3), 28.8 (CH_3,*t*Bu), 28.9 (CH_3, *t*Bu), 29.9 (CH_3,*t*Bu), 30.2 (CH_3,*t*Bu), 33.2 (C, *t*Bu), 34.1 (C, *t*Bu), 34.3 (C, *t*Bu), 40.9 (CH_3, NMe), 41.0 (CH_3, NMe), 64.7 (d, CH–N, $^3J_{C-P}=9.2$ Hz), 76.6 (d, CH–O, $^2J_{C-P}=9.2$ Hz), 122.6–145.4 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{39}H_{56}NO_3P$: 618.4101 $[M+H]^+$; found 618.4071.

L1 b: Yield: 170 mg (30%); ^{31}P NMR (C_6D_6): $\delta=150.2$ ppm (s); ^{1}H NMR (C_6D_6): $\delta=1.00$ (d, 3H, CH_3, $^3J_{H-H}=6.4$ Hz), 1.38 (s, 9H, CH_3, *t*Bu), 1.56 (s, 9H, CH_3, *t*Bu), 2.14 (s, 6H, CH_3, NMe_2), 2.57 (m, 1H, CH–N), 3.33 (s, 3H, CH_3, OMe), 3.34 (s, 3H, CH_3, OMe), 5.5 (dd, 1H, CH–O, $^3J_{H-P}=8.0$ Hz, $^3J_{H-H}=4.0$ Hz), 6.67 (d, 1H, CH=, $^4J_{H-H}=2.8$ Hz), 6.72 (d, 1H, CH=, $^4J_{H-H}=3.2$ Hz), 7.01–7.26 ppm (m, 7H, CH=); ^{13}C NMR (C_6D_6): $\delta=9.5$ (CH_3), 30.6 (CH_3,*t*Bu), 30.7 (CH_3, *t*Bu), 35.1(C, *t*Bu), 35.2 (C, *t*Bu), 41.9 (CH_3, NMe), 42.1 (CH_3, NMe), 54.7 (CH_3, OMe), 65.8 (CH–N), 77.6 (d, CH–O, $^2J_{C-P}=9.9$ Hz), 112.6–155.9 (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{33}H_{44}NO_5P$: 566.3028 $[M+H]^+$; found 566.3030.

L1 c: Yield: 194 mg (32%); ^{31}P NMR (C_6D_6): $\delta=152.4$ ppm (s); ^{1}H NMR (C_6D_6): $\delta=0.33$ (s, 9H, CH_3–Si), 0.44 (s, 9H, CH_3–Si), 0.95 (d, 3H, CH_3, $^3J_{H-H}=6.8$ Hz), 2.10 (s, 6H, CH_3, NMe_2), 2.68 (m, 1H, CH–N), 5.45 (dd, 1H, CH–O, $^3J_{H-P}=8.8$ Hz, $^3J_{H-H}=5.6$ Hz), 7.03–7.46 ppm (m, 11H, CH=); ^{13}C NMR (C_6D_6): $\delta=0.0$ (CH_3–Si), 0.1 (CH_3–Si), 9.7 (CH_3), 42.1 (CH_3, NMe_2), 65.8 (d, CH–N, $^3J_{C-P}=2.3$ Hz), 78.1 (d, CH–O, $^2J_{C-P}=4.8$ Hz), 124.7–155.2 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{29}H_{40}NO_3PSi_2$: 538.2354 $[M+H]^+$; found 538.2357.

L1 d: Yield: 188 mg (32%); ^{31}P NMR (C_6D_6): $\delta=141.1$ ppm (s); ^{1}H NMR (C_6D_6): $\delta=1.12$ (d, 3H, CH_3, $^3J_{H-H}=7.2$ Hz), 1.46 (s, 9H, CH_3, *t*Bu), 1.63 (s, 9H, CH_3, *t*Bu), 1.69 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 2.16 (s, 6H, CH_3, NMe_2), 2.82 (m, 1H, CH–N), 5.4 (dd, 1H, CH–O, $^3J_{H-P}=8.0$ Hz, $^3J_{H-H}=5.6$ Hz), 7.0–7.3 ppm (m, 7H, CH=); ^{13}C NMR (C_6D_6): $\delta=8.1$ (CH_3), 15.1 (CH_3), 15.3 (CH_3), 19.0 (CH_3), 19.1 (CH_3), 29.9 (d, CH_3, *t*Bu, $J_{C-P}=5.4$ Hz), 30.4 (CH_3, *t*Bu), 33.2 (C, *t*Bu), 33.7 (C, *t*Bu), 40.5 (CH_3, NMe), 40.6 (CH_3, NMe), 63.9 (d, CH–N, $^3J_{C-P}=6.1$ Hz), 77.3 (d, CH–O, $^2J_{C-P}=6.2$ Hz), 124.3–144.6 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{35}H_{48}NO_3P$: 562.3452 $[M+H]^+$; found 562.3445.

L1 e: Yield: 182 mg (31%); ^{31}P NMR (C_6D_6): $\delta=144.9$ (s); ^{1}H NMR (C_6D_6): $\delta=0.78$ (d, CH_3, 3H, $^3J_{H-H}=6.4$ Hz), 1.41 (s, 9H, CH_3, *t*Bu), 1.59 (s, 9H, CH_3, *t*Bu), 1.66 (s, 3H, CH_3), 1.72 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 2.11 (s, 6H, CH_3, NMe_2), 2.37 (m, 1H, CH–N), 5.41 (dd, 1H, CH–O, $^3J_{H-P}=8.0$ Hz, $^3J_{H-H}=4.0$ Hz), 6.95–7.22 ppm (m, 7H, CH=); ^{13}C NMR (C_6D_6): $\delta=9.7$ (CH_3), 16.2 (CH_3), 16.4 (CH_3), 20.0 (CH_3), 20.1(CH_3), 30.9 (d, CH_3, *t*Bu, $J_{C-P}=4.6$ Hz), 31.2 (CH_3, *t*Bu), 34.5 (C, *t*Bu), 34.7 (C, *t*Bu), 42.0 (CH_3, NMe), 42.3 (CH_3, NMe), 62.2 (CH–N), 77.2 (d, CH–O, $^2J_{C-P}=10.7$ Hz), 125.3–146.2 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{35}H_{48}NO_3P$: 562.3448 $[M+H]^+$; found 562.3445.

L1 f: Yield: 439 mg (69%); ^{31}P NMR (C_6D_6): $\delta=155.8$ (s); ^{1}H NMR (C_6D_6): $\delta=0.40$ (s, 9H, CH_3, $SiMe_3$), 0.51 (s, 9H, CH_3, $SiMe_3$), 0.72 (d, CH_3, 3H, $^3J_{H-H}=6.8$ Hz), 1.96 (s, 6H, CH_3, NMe_2), 2.50 (m, 1H, CH–N), 5.43 (dd, 1H, CH–O, $^3J_{H-P}=8.4$ Hz, $^3J_{H-H}=4.8$ Hz), 6.82–7.4 (m, 5H, CH=), 7.4 (d, 1H, CH=, $^3J_{H-H}=8.4$ Hz), 7.70 (d, 1H, CH=, $^3J_{H-H}=8.0$ Hz), 7.8 (d, 1H, CH=, $^3J_{H-H}=8.4$ Hz), 8.1 (s, 1H, CH=), 7.9 ppm (s, 1H, CH=); ^{13}C NMR (C_6D_6): $\delta=-0.4$ (d, CH_3, $SiMe_3$, $J_{C-P}=4.6$ Hz), −0.1 (CH_3, $SiMe_3$), 9.3 (CH_3), 41.8 (CH_3, NMe_2), 66.0 (CH–N), 77.5 (d, CH–O, $^2J_{C-P}=5.3$ Hz), 122.8–152.6 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{37}H_{44}NO_3PSi_2$: 638.2673 $[M+H]^+$; found 638.2670.

L1 g: Yield: 400 mg (63%); ^{31}P NMR (C_6D_6): $\delta=148.5$ ppm (s); ^{1}H NMR (C_6D_6): $\delta=0.51$ (s, 9H, CH_3, $SiMe_3$), 0.52 (s, 9H, CH_3, $SiMe_3$), 1.09 (d, 3H, CH_3, $^3J_{H-H}=6.4$ Hz), 2.05 (s, 6H, CH_3, NMe_2), 2.87 (m, 1H, CH–N), 5.35 (dd, 1H, CH–O, $^3J_{H-P}=8.4$ Hz, $^3J_{H-H}=6.5$ Hz), 6.7–7.3 (m, 6H, CH=), 7.68 (m, 2H, CH=), 7.95 (s, 1H; CH=), 8.05 ppm (s, 1H, CH=); ^{13}C NMR (C_6D_6): $\delta=-0.2$ (d, CH_3, $SiMe_3$, $J_{C-P}=4.6$ Hz), −0.1 (CH_3, $SiMe_3$), 9.2 (CH_3), 41.3 (CH_3, NMe_2), 64.3 (d, CH–N, $^3J_{C-P}=4.6$ Hz), 78.9 (d, CH–O, $^2J_{C-P}=2.3$ Hz), 122.4–152.3 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{37}H_{44}NO_3PSi_2$: 638.2669 $[M+H]^+$; found 638.2670.

L2 a: Yield: 330 mg (50%); ^{31}P NMR (C_6D_6): $\delta=148.4$ ppm (s); ^{1}H NMR (C_6D_6): $\delta=0.83$ (s, 9H, CH_3, *t*Bu, N*t*Bu), 1.21 (d, 3H, CH_3, $^3J_{H-H}=6.4$ Hz), 1.31 (s, 9H, CH_3, *t*Bu), 1.33 (s, 9H,CH_3, *t*Bu), 1.56 (s, 9H, CH_3, *t*Bu), 1.61 (s, 9H, CH_3, *t*Bu), 2.11 (s, 3H, NMe), 3.4 (m, 1H, CH–N), 5.25 (m, 1H, CH–O), 7.0–7.2 (m, 6H, CH=), 7.37 (m, 2H, CH=), 7.60 ppm (d, 1H, CH=, $^4J_{H-H}=2$ Hz); ^{13}C NMR (C_6D_6): $\delta=12.8$ (CH_3), 26.8 (CH_3, *t*Bu), 29.3 (NMe), 31.0 (CH_3, *t*Bu), 31.1 (CH_3, *t*Bu), 31.2 (CH_3, *t*Bu), 31.3 (CH_3, *t*Bu), 34.3 (C, *t*Bu), 35.2 (C, *t*Bu), 35.3 (C, *t*Bu), 54.1 (C, *t*Bu, N*t*Bu), 56.6 (d, CH–N, $^3J_{C-P}=3.1$ Hz), 81.3 (d, CH–O, $^2J_{C-P}=5.43$ Hz), 123.8–146.7 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{42}H_{62}NO_3P$: 660.5438 $[M+H]^+$; found 660.4540.

L2 d: Yield: 422.6 mg (70%); ^{31}P NMR (C_6D_6): $\delta=141.1$ ppm (s); ^{1}H NMR (C_6D_6): $\delta=0.84$ (s, 9H, CH_3, *t*Bu, N*t*Bu), 2.15 (d, 3H, CH_3, $^3J_{H-H}=6.4$ Hz), 1.51 (s, 9H, CH_3, *t*Bu), 1.63 (s, 9H,CH_3, *t*Bu), 1.69 (s, 3H, CH_3), 1.71 (s, 3H, CH_3,), 2.04 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.16 (s, 3H, NMe), 3.4 (m, 1H, CH–N), 5.1 (m, 1H, CH–O), 7.0–7.3 ppm (m, 7H, CH=); ^{13}C NMR (C_6D_6): $\delta=12.7$ (CH_3), 16.1 (CH_3), 16.3 (CH_3), 20.0 (CH_3), 20.1 (CH_3), 26.8 (CH_3, *t*Bu), 29.4 (NMe), 31.1 (d, CH_3, *t*Bu, $J_{C-P}=5.3$ Hz), 31.4 (CH_3, *t*Bu), 34.4(C, *t*Bu), 34.7 (C, *t*Bu), 54.2 (C, *t*Bu, N*t*Bu), 56.4 (d, CH–N, $^3J_{C-P}=5.6$ Hz), 81.6 (d, CH–O, $^2J_{C-P}=3.0$ Hz), 125.3–145.6 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{39}H_{56}NO_3P$: 604.3917 $[M+H]^+$; found 604.3914.

L2 e: Yield: 392 mg (65%); ^{31}P NMR (C_6D_6): $\delta=142.9$ ppm (s); ^{1}H NMR (C_6D_6): $\delta=0.60$ (s, 9H, CH_3, *t*Bu, N*t*Bu), 1.0 (d, 3H, CH_3, $^3J_{H-H}=6.8$ Hz), 1.51 (s, 9H, CH_3, *t*Bu), 1.60 (s, 9H,CH_3, *t*Bu), 1.66 (s, 3H, CH_3), 1.75 (s, 3H, CH_3,), 1.95 (s, 3H, NMe), 2.0 (s, 3H, CH_3), 2.1 (s, 3H, CH_3), 3.2 (m, 1H, CH–N), 5.0 (m, 1H, CH–O), 7.0–7.45 ppm (m, 7H, CH=); ^{13}C NMR (C_6D_6): $\delta=13.8$ (CH_3), 16.2 (CH_3), 16.4 (CH_3), 20.0 (CH_3), 20.1 (CH_3), 26.8 (CH_3, *t*Bu), 28.7 (NMe), 31.2 (d, CH_3, *t*Bu, $J_{C-P}=5.4$ Hz), 31.6 (CH_3, *t*Bu), 34.5 (C, *t*Bu), 34.8 (C, *t*Bu), 53.7 (C, *t*Bu, N*t*Bu), 56.7 (d, CH–N, $^3J_{C-P}=2.3$ Hz), 80.3 (d, CH–O, $^2J_{C-P}=5.3$ Hz), 125.9–145.6 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{39}H_{56}NO_3P$: 604.3912 $[M+H]^+$; found 604.3914.

L3 a: Yield: 262 mg (37%); ^{31}P NMR (C_6D_6): $\delta=148.90$ ppm (s); ^{1}H NMR (C_6D_6): $\delta=1.01$ (d, 3H, CH_3, $^3J_{H-H}=6.8$ Hz), 1.09 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 1.28 (s, 9H, CH_3, *t*Bu), 1.39 (s, 9H, CH_3, *t*Bu), 1.55 (s, 9H, CH_3, *t*Bu), 1.86 (s, 9H, CH_3, *t*Bu), 2.2 (s, 3H, NMe), 3.2 (m, 1H, CH–N), 5.4 (dd, 1H, CH–O, $^3J_{H-P}=9.6$ Hz, $^3J_{H-H}=4.4$ Hz), 7.0–7.4 (m, 12H, CH=), 7.58 (d, 1H, CH=, $^4J_{H-H}=2.8$ Hz), 7.62 ppm (d, 1H, CH=, $^4J_{H-H}=2.8$ Hz); ^{13}C NMR (C_6D_6): $\delta=9.9$ (CH_3), 22.3 (CH_3), 25.2 (CH_3), 28.9 (NMe), 29.9 (CH_3, *t*Bu), 30.0 (CH_3, *t*Bu), 30.1 (CH_3, *t*Bu), 30.2 (CH_3, *t*Bu), 33.2 (C, *t*Bu), 34.2(C, *t*Bu), 34.3 (C, *t*Bu), 56.4 (d, CH–N, $^3J_{C-P}=3.8$ Hz), 59.8 (C, N-CMe_2Ph), 81.2 (d, CH–O, $^2J_{C-P}=6.9$ Hz), 122.7–148.7 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{47}H_{64}NO_3P$: 722.4694 $[M+H]^+$; found 722.4697.

L3 d: Yield: 244 mg (37%); ^{31}P NMR (C_6D_6): $\delta=143.4$ ppm (s); ^{1}H NMR (C_6D_6): $\delta=1.01$ (d, 3H, CH_3, $^3J_{H-H}=6.9$ Hz), 1.03, (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.59 (s, 9H, CH_3, *t*Bu), 1.65 (s, 9H, CH_3, *t*Bu),

1.71 (s, 3H, CH_3), 1.8 (s, 3H, CH_3), 1.91 (s, 3H, NMe), 2.06 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 3.3 (m, 1H, CH–N), 5.3 (m, 1H, CH–O), 7.0–7.3 ppm (m, 12H, CH=); ^{13}C NMR (C_6D_6): δ = 10.9 (CH_3), 15.2 (CH_3), 15.4 (CH_3), 19.0 (CH_3) 23.4 (CH_3), 24.7 (CH_3), 28.2 (NMe), 30.2 (d, CH_3, *t*Bu, J_{C-P} = 5.3 Hz), 30.5 (CH_3, *t*Bu), 33.4 (C, *t*Bu), 33.7 (C, *t*Bu), 56.3 (d, CH–N, $^3J_{C-P}$ = 2.3 Hz), 59.4 (C, N-CMe_2Ph), 80.7 (d, CH–O, $^2J_{C-P}$ = 6.1 Hz), 124.3–148.8 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{43}H_{56}NO_3P$: 666.4068 $[M+H]^+$; found 666.4071.

L3e: Yield: 331.0 mg (50%); ^{31}P NMR (C_6D_6): δ = 148.90 ppm (s); ^{1}H NMR (C_6D_6): δ = 1.02 (d, 3H, CH_3, $^3J_{H-H}$ = 6.8 Hz), 1.03 (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 1.59 (s, 9H, CH_3, *t*Bu), 1.65 (s, 9H, CH_3, *t*Bu), 1.71 (s, 3H, CH_3), 1.79 (s, 3H, CH_3), 2.01 (s, 3H, CH_3, NMe), 2.06 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 3.31 (m, 1H, CH–N), 5.3 (m, 1H, CH–O), 7.0–7.4 ppm (m, 12H, CH=); ^{13}C NMR (C_6D_6): δ = 11.9 (CH_3), 16.2 (CH_3), 16.5 (CH_3), 20.1 (CH_3) 24.6 (CH_3), 25.7 (CH_3), 29.2 (NMe), 31.2 (d, CH_3, *t*Bu, J_{C-P} = 5.3 Hz), 31.5 (CH_3, *t*Bu), 34.5 (C, *t*Bu), 34.8(C, *t*Bu), 57.3 (CH–N), 60.5 (C, N-CMe_2Ph), 81.7 (d, CH–O, $^2J_{C-P}$ = 6.1 Hz), 125.3–149.9 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{43}H_{56}NO_3P$: 666.4072 $[M+H]^+$; found 666.4071.

L4a: Yield: 276 mg (43%); ^{31}P NMR (C_6D_6): δ = 148.4 ppm (s); ^{1}H NMR (C_6D_6): δ = 0.47 (d, 3H, CH_3, $^3J_{H-H}$ = 6.8 Hz), 1.24 (s, 9H, CH_3, *t*Bu), 1.25 (s, 9H, CH_3, *t*Bu), 1.35 (s, 9H, CH_3, *t*Bu), 1.62 (s, 9H, CH_3, *t*Bu), 2.09 (s, 6H, CH_3, NMe_2), 2.78 (m, 1H, CH–N), 5.06 (dd, 1H, CH–O, $^3J_{H-P}$ = 8 Hz, $^3J_{H-H}$ = 4 Hz), 6.9–7.1 (m, 7H, CH=), 7.27 (d, 1H, CH=, $^4J_{H-H}$ = 2.4 Hz), 7.33 (d, 1H, CH=, $^4J_{H-H}$ = 2.8 Hz), 7.46 (d, 1H, CH=, $^4J_{H-H}$ = 2.4 Hz), 7.57 ppm (d, 1H, CH=, $^4J_{H-H}$ = 2.4 Hz); ^{13}C NMR (C_6D_6): δ = 7.9 (CH_3), 30.9 (CH_3,*t*Bu), 31.1 (CH_3, *t*Bu), 31.2 (CH_3, *t*Bu), 31.3 (CH_3, *t*Bu), 33.2 (C, *t*Bu), 34.3 (C, *t*Bu), 40.9 (CH_3, NMe), 41.0 (CH_3, NMe), 64.7 (d, CH–N, $^3J_{C-P}$ = 1.5 Hz), 76.6 (d, CH–O, $^2J_{C-P}$ = 9.2 Hz), 123.6–145.8 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{39}H_{56}NO_3P$: 618.4070 $[M+H]^+$; found 618.4071.

L4d: Yield: 344 mg (61%); ^{31}P NMR (C_6D_6): δ = 139.0 ppm (s); ^{1}H NMR (C_6D_6): δ = 0.62 (d, 3H, CH_3, $^3J_{H-H}$ = 7.2 Hz), 1.48 (s, 9H, CH_3, *t*Bu), 1.6 (s, 9H, CH_3, *t*Bu), 1.66 (s, 3H, CH_3), 1.67 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.1 (s, 3H, CH_3), 2.15 (s, 6H, CH_3, NMe_2), 3.0 (m, 1H, CH–N), 5.1 (dd, 1H, CH–O, $^3J_{H-H}$ = 5.6 Hz, $^3J_{H-P}$ = 8.0 Hz), 6.9–7.2 ppm (m, 7H, CH=); ^{13}C NMR (C_6D_6): δ = 7.4 (CH_3), 15.1 (CH_3), 15.3 (CH_3), 19.0 (CH_3), 30.0 (d, CH_3, *t*Bu, J_{C-P} = 5.4 Hz), 30.4 (CH_3, *t*Bu), 33.3 (C, *t*Bu), 33.7 (C, *t*Bu), 40.1 (CH_3, NMe), 40.2 (CH_3, NMe), 63.9 (d, CH–N, $^3J_{C-P}$ = 3.8 Hz), 77.6 (d, CH–O, $^2J_{C-P}$ = 10.7 Hz), 126.3–144.6 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{35}H_{48}NO_3P$: 562.3440 $[M+H]^+$; found 562.3445.

L4e: Yield: 324 mg (58%); ^{31}P NMR (C_6D_6): δ = 144.7 ppm (s); ^{1}H NMR (C_6D_6): δ = 0.4 (d, 3H, CH_3, $^3J_{H-H}$ = 7.2 Hz), 1.29 (s, 9H, CH_3, *t*Bu), 1.67 (s, 9H, CH_3, *t*Bu), 1.68 (s, 3H, CH_3), 1.72 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.11 (s, 6H, CH_3, NMe_2), 2.65 (m, 1H, CH–N), 4.95 (m, 1H, CH–O), 7.05–7.25 ppm (m, 7H, CH=); ^{13}C NMR (C_6D_6): δ = 7.5 (CH_3), 16.2 (CH_3), 16.3 (CH_3), 19.9 (CH_3), 20.1 (CH_3), 30.9 (d, CH_3, *t*Bu, J_{C-P} = 4.6 Hz), 31.4 (CH_3, *t*Bu), 34.5 (C, *t*Bu), 34.6 (C, *t*Bu), 42.0 (CH_3, NMe), 42.3 (CH_3, NMe), 64.8 (CH–N), 78.7 (d, CH–O, $^2J_{C-P}$ = 13.9 Hz), 127.3–146.7 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{35}H_{48}NO_3P$: 562.3442 $[M+H]^+$; found 562.3445.

L4f: Yield: 467 mg (73%); ^{31}P NMR (C_6D_6): δ = 143.7 ppm (s); ^{1}H NMR (C_6D_6): δ = 0.47 (s, 9H, CH_3, $SiMe_3$), 0.52 (s, 9H, CH_3, $SiMe_3$), 0.64 (d, 3H, CH_3, $^3J_{H-H}$ = 6.8 Hz), 2.02 (s, 6H, CH_3, NMe_2), 3.0 (m, 1H, CH–N), 5.1 (dd, 1H, CH–O, $^3J_{H-H}$ = 6.8 Hz; $^3J_{H-P}$ = 10.4 Hz), 6.82–7.27 (m, 5H, CH=), 7.7 (m, 2H, CH=), 8.0 (s, 1H, CH=), 8.1 ppm (s, 1H, CH=); ^{13}C NMR (C_6D_6): δ = −0.0 (CH_3, $SiMe_3$), 9.11 (CH_3), 41.4 (CH_3, NMe_2), 63.9 (d, CH–N, $^3J_{C-P}$ = 3.1 Hz), 78.7 (CH–O), 122.0–152.8 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{37}H_{44}NO_3PSi_2$: 638.2665 $[M+H]^+$; found 638.2670.

L4g: Yield: 666 mg (95%); ^{31}P NMR (C_6D_6): δ = 151 ppm. (s); ^{1}H NMR (C_6D_6): δ = 0.4 (s, 9H, CH_3, $SiMe_3$), 0.47 (s, 9H, CH_3, $SiMe_3$), 0.55 (d, 3H, CH_3, $^3J_{H-H}$ = 6.8 Hz), 1.85 (s, 6H, CH_3, NMe_2), 2.57 (m, 1H, CH–N), 5.2 (m, 1H, CH–O), 6.79–7.16 (m, 9H, CH=), 7.19 (d, 1H, CH=, $^4J_{H-H}$ = 8 Hz), 7.32 (d, 1H, CH=, $^4J_{H-H}$ = 8 Hz), 7.66 (d, 1H, CH=, $^4J_{H-H}$ = 8.8 Hz), 7.73 (d, 1H, CH=, $^4J_{H-H}$ = 8.4 Hz), 8.0 ppm (s, 2H, CH=); ^{13}C NMR (C_6D_6): δ = −0.3 (d, 9H, CH_3, $SiMe_3$, J_{C-P} = 4.6 Hz), −0.1 ($SiMe_3$), 9.1 (CH_3), 41.2 (CH_3, NMe_2), 64.2 (CH–N), 78.4 (d, CH–O, $^2J_{C-P}$ = 2.3 Hz), 122.6–152.9 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{37}H_{44}NO_3PSi_2$: 638.2669 $[M+H]^+$; found 638.2670.

L5d: Yield: 362 mg (64%); ^{31}P NMR (C_6D_6): δ = 143.7 ppm (s); ^{1}H NMR (C_6D_6): δ = 1.51 (s, 9H, CH_3, *t*Bu), 1.76 (s, 9H, CH_3, *t*Bu), 1.82 (s, 3H, CH_3), 1.89 (s, 3H, CH_3), 2.17 (s, 6H, CH_3, NMe_2), 2.23 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 2.30 (dd, 1H, CH_2, $^2J_{H-H}$ = 12.4 Hz,$^3J_{H-H}$ = 5.6 Hz), 2.73 (dd, 1H, CH_2, $^2J_{H-H}$ = 12.4 Hz,$^3J_{H-H}$ = 6 Hz), 5.33 (m, 1H, CH–O), 7.13–7.4 ppm (m, 7H, CH=); ^{13}C NMR (C_6D_6): δ = 16.1 (CH_3), 16.4 (CH_3), 20.0 (CH_3), 20.1 (CH_3), 30.9 (d, CH_3,*t*Bu, J_{C-P} = 4.6 Hz), 31.3 (CH_3, *t*Bu), 34.5 (C, *t*Bu), 34.6 (C, *t*Bu), 45.5 (CH_3, NMe), 45.6 (CH_3, NMe), 67.6 (CH_2–N), 75.2 (d, CH–O, $^2J_{C-P}$ = 13.6 Hz), 125.3–146.3 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{34}H_{46}NO_3P$: 548.3287 $[M+H]^+$; found 548.3288.

L5e: Yield: 362 mg (64%); ^{31}P NMR (C_6D_6): δ = 138.1 ppm (s); ^{1}H NMR (C_6D_6): δ = 1.44 (s, 9H, CH_3, *t*Bu), 1.46 (s, 9H, CH_3, *t*Bu), 1.65 (s, 3H, CH_3), 1.72 (s, 3H, CH_3), 1.98 (s, 6H, CH_3, NMe_2), 2.07 (s, 3H, CH_3), 2.1(s, 3H, CH_3), 2.43 (dd, 1H, CH_2, $^2J_{H-H}$ = 12.4 Hz,$^3J_{H-H}$ = 5.6 Hz), 2.85 (dd, 1H, CH_2, $^2J_{H-H}$ = 12.4 Hz, $^3J_{H-H}$ = 6 Hz), 5.1 (m, 1H, CH–O), 6.95–7.19 ppm (m, 7H, CH=); ^{13}C NMR (C_6D_6): δ = 16.1 (CH_3), 16.3 (CH_3), 20.0 (CH_3), 20.1 (CH_3), 30.9 (d, CH_3, *t*Bu, J_{C-P} = 5.3 Hz), 31.3 (CH_3, *t*Bu), 34.3 (C, *t*Bu), 34.6 (C, *t*Bu), 45.6 (CH_3, NMe_2), 66.7 (d, CH_2–N, $^2J_{C-P}$ = 3.8 Hz), 75.2 (d, CH–O, $^2J_{C-P}$ = 8.4 Hz), 125.3–145.8 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{34}H_{46}NO_3P$: 548.3287 $[M+H]^+$; found 548.3288.

L6d: Yield: 362 mg (64%); ^{31}P NMR (C_6D_6): δ = 129.7 ppm (s); ^{1}H NMR (C_6D_6): δ = 1.48 (s, 9H, CH_3, *t*Bu), 1.53 (s, 9H, CH_3, *t*Bu), 1.64 (s, 3H, CH_3), 1.72 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 2.04 (s, 6H, CH_3, NMe_2), 3.4 (m, 1H, CH–N), 3.6 (m, 1H, CH_2–O), 4.3 (m, 1H, CH_2–O), 6.95–7.2 ppm (m, 7H, CH=); ^{13}C NMR (C_6D_6): δ = 16.1 (CH_3), 16.3 (CH_3), 20.0 (CH_3), 20.1 (CH_3), 30.9 (CH_3, *t*Bu), 31.2 (d, CH_3,*t*Bu, J_{C-P} = 5.3 Hz), 34.4 (C, *t*Bu), 34.5 (C, *t*Bu), 42.9 (CH_3, NMe_2), 66.4 (CH_2–O), 70.6 (d, CH–N, $^2J_{C-P}$ = 3.0 Hz), 125.3–146.1 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{34}H_{46}NO_3P$: 548.3489 $[M+H]^+$; found 548.3288.

L6e: Yield: 362 mg (64%); ^{31}P NMR (C_6D_6): δ = 131.1 ppm (s); ^{1}H NMR (C_6D_6): δ = 1.46 (s, 9H, CH_3, *t*Bu), 1.55 (s, 9H, CH_3, *t*Bu), 1.64 (s, 3H, CH_3), 1.71 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.06 (s, 6H, CH_3, NMe_2), 3.6 (m, 1H, CH–N), 3.8 (m, 1H, CH_2–O), 4.0 (m, 1H, CH_2–O), 6.95–7.2 ppm (m, 7H, CH=); ^{13}C NMR (C_6D_6): δ = 16.1 (CH_3), 16.3 (CH_3), 20.0 (CH_3), 20.1 (CH_3), 30.9 (CH_3, *t*Bu), 31.2 (d, CH_3,*t*Bu, J_{C-P} = 5.3 Hz), 34.5 (C, *t*Bu), 34.6 (C, *t*Bu), 42.9 (CH_3, NMe_2), 66.1 (CH_2–O), 70.6 (d, CH–N, $^2J_{C-P}$ = 2.3 Hz), 125.3–146.1 ppm (aromatic C); TOF-MS (ESI+): *m/z*: calcd for $C_{34}H_{46}NO_3P$: 548.3287 $[M+H]^+$; found 548.3288.

General procedure for the preparation of [Pd(η^3-allyl)-(P-S)]BF_4 (53–57)

The 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 RT under Ar. $AgBF_4$ (9.8 mg, 0.05 mmol) was added after 30 min, and the mixture was stirred for 30 min. The mixture was then filtered through

Celite under Ar, and the resulting solutions were analyzed by NMR spectroscopy. The complexes were precipitated as pale yellow solids by adding hexane.

[Pd(η^3-1,3-diphenylallyl)(L4 d)]BF_4 (53): *endo* isomer (77%): ^{31}P NMR (CD_2Cl_2, 298 K): δ = 136.8 ppm (s, 1P); ^{1}H NMR (CD_2Cl_2, 298 K): δ = 0.50 (d, 3H, CH_3, $^3J_{H-H}$ = 6.8 Hz), 1.22 (s, 9H, CH_3, *t*Bu), 1.47 (s, 3H, CH_3–Ar), 1.66 (s, 3H, CH_3–Ar), 1.71 (s, 9H, CH_3, *t*Bu), 2.13 (s, 3H, CH_3–Ar), 2.29 (s, 3H, CH_3–Ar), 2.75 (s, 3H, CH_3–N), 2.76 (s, 3H, CH_3–N), 3.19 (m, 1H, CH–N), 5.35 (dd, 1H, CH allyl *trans* to N, $^3J_{H-H}$ = 12.0 Hz, $^3J_{H-P}$ = 4.4 Hz), 5.64 (dd, 1H, CH allyl *trans* to P, $^3J_{H-H}$ = 12.0 Hz, $^3J_{H-P}$ = 16.4 Hz), 5.79 (dd, 1H, CH–O, $^3J_{H-H}$ = 4.8 Hz, J_{C-P} = 7.2 Hz), 6.68 (m, 1H, CH allyl central), 6.9–7.8 ppm (m, 17H, CH=); ^{13}C NMR (C_6D_6, 298 K): δ = 10.4 (CH_3), 16.7 (CH_3, Ar), 16.8 (CH_3, Ar), 20.5 (CH_3, Ar), 20.7 (CH_3, Ar), 32.0 (CH_3, *t*Bu), 32.3 (CH_3, *t*Bu), 35.0–35.8 (C, *t*Bu), 42.9 (CH_3–N), 48.6 (CH_3–N), 73.5 (CH–N), 79.2 (d, CH allyl *trans* to N, J_{C-P} = 8.3 Hz), 84.6 (d, CH–O, J_{C-P} = 11.5 Hz), 105.3 (d, CH allyl *trans* to P, J_{C-P} = 33.8 Hz), 114.8 (d, CH allyl central, J_{C-P} = 12.2 Hz), 123–145 ppm (aromatic C). *exo* isomer (23%): ^{31}P NMR (CD_2Cl_2, 298 K): δ = 132.9 ppm (s, 1P); ^{1}H NMR (CD_2Cl_2, 298 K): δ = 0.50 (d, 3H, CH_3, $^3J_{H-H}$ = 6.8 Hz), 0.91 (s, 9H, CH_3, *t*Bu), 1.59 (s, 3H, CH_3–Ar), 1.74 (s, 3H, CH_3–Ar), 1.79 (s, 9H, CH_3, *t*Bu), 2.17 (s, 6H, CH_3–N and CH_3–Ar), 2.21 (s, 3H, CH_3–N), 2.43 (s, 3H, CH_3–Ar), 3.10 (m, 1H, CH–N), 4.50 (m, 1H, CH allyl *trans* to N), 5.22 (m, 1H, CH–O), 5.45 (m, 1H, CH allyl *trans* to P), 6.59 (m, 1H, CH allyl central), 6.9–7.8 ppm (m, 17H, CH=); ^{13}C NMR (C_6D_6, 298 K): δ = 10.1 (CH_3), 17.1 (CH_3, Ar), 17.3 (CH_3, Ar), 20.4 (CH_3, Ar), 20.8 (CH_3, Ar), 31.9 (CH_3, *t*Bu), 32.8 (CH_3, *t*Bu), 35.0–35.8 (C, *t*Bu), 38.8 (CH_3–N), 50.5 (CH_3–N), 71.8 (d, CH allyl *trans* to N, J_{C-P} = 9.2 Hz), 72.1 (CH–N), 84.0 (d, CH–O, J_{C-P} = 9.1 Hz), 99.3 (d, CH allyl *trans* to P, J_{C-P} = 33.0 Hz), 113.4 (d, CH allyl central, J_{C-P} = 14.0 Hz), 123–145 ppm (aromatic C); elemental analysis calcd (%) for $C_{50}H_{61}BF_4NO_3PPd$ (947.3453): C 63.33, H 6.48, N 1.48; found: C 63.12, H 6.43, N 1.45.

[Pd(η^3-1,3-diphenylallyl)(L4 e)]BF_4 (54): *endo* isomer (17%): ^{31}P NMR (CD_2Cl_2, 298 K): δ = 129.8 ppm (s, 1P); ^{1}H NMR (CD_2Cl_2, 298 K): δ = 0.43 (d, 3H, CH_3, $^3J_{H-H}$ = 6.8 Hz), 1.33 (s, 9H, CH_3, *t*Bu), 1.66 (s, 3H, CH_3–Ar), 1.74 (s, 9H, CH_3, *t*Bu), 1.84 (s, 3H, CH_3–N), 2.14 (s, 3H, CH_3–Ar), 2.23 (s, 3H, CH_3–Ar), 2.26 (s, 3H, CH_3–N), 2.40 (s, 3H, CH_3–Ar), 3.40 (m, 1H, CH–N), 3.72 (dd, 1H, CH allyl *trans* to N, $^3J_{H-H}$ = 10.2 Hz, $^3J_{H-P}$ = 6.8 Hz), 4.40 (m, 1H, CH allyl *trans* to P), 5.54 (m, 1H, CH–O), 6.60 (m, 1H, CH allyl central), 6.8–7.8 ppm (m, 17H, CH=); ^{13}C NMR (C_6D_6, 298 K): δ = 10.8 (CH_3), 16.7 (CH_3, Ar), 17.0 (CH_3, Ar), 20.5 (CH_3, Ar), 20.6 (CH_3, Ar), 32.2 (d, CH_3, *t*Bu, J_{C-P} = 6.3 Hz), 32.5 (CH_3, *t*Bu), 35.0–35.8 (C, *t*Bu), 43.0 (CH_3–N), 49.1 (CH_3–N), 67.3 (d, CH allyl *trans* to N, J_{C-P} = 12.8 Hz), 68.7 (CH–N), 84.9 (CH–O), 108.6 (d, CH allyl *trans* to P, J_{C-P} = 32.4 Hz), 114.5 (d, CH allyl central, J_{C-P} = 12.4 Hz), 127–145 ppm (aromatic C). *exo* isomer (83%): ^{31}P NMR (CD_2Cl_2, 298 K): δ = 128.7 ppm (s, 1P); ^{1}H NMR (CD_2Cl_2, 298 K): δ = 0.54 (d, 3H, CH_3, $^3J_{H-H}$ = 7.2 Hz), 1.34 (s, 9H, CH_3, *t*Bu), 1.62 (s, 3H, CH_3–Ar), 1.78 (s, 9H, CH_3, *t*Bu), 2.11 (s, 3H, CH_3–Ar), 2.19 (s, 3H, CH_3–Ar), 2.40 (s, 3H, CH_3–N), 2.42 (s, 3H, CH_3–Ar), 2.61 (s, 3H, CH_3–N), 3.16 (m, 1H, CH–N), 4.40 (m, 1H, CH allyl *trans* to N), 5.03 (m, 1H, CH–O), 5.73 (m, 1H, CH allyl *trans* to P), 6.60 (m, 1H, CH allyl central), 6.9–7.8 ppm (m, 17H, CH=); ^{13}C NMR (C_6D_6, 298 K): δ = 9.7 (CH_3), 16.9 (CH_3, Ar), 17.3 (CH_3, Ar), 20.5 (CH_3, Ar), 20.7 (CH_3, Ar), 32.0 (CH_3, *t*Bu), 32.6 (CH_3, *t*Bu), 35.0–35.8 (C, *t*Bu), 42.9 (CH_3–N), 48.8 (CH_3–N), 67.5 (d, CH allyl *trans* to N, J_{C-P} = 12.6 Hz), 69.4 (CH–N), 81.4 (CH–O), 110.6 (d, CH allyl *trans* to P, J_{C-P} = 30.6 Hz), 113.5 (d, CH allyl central, J_{C-P} = 13.8 Hz), 123–145 ppm (aromatic C); elemental analysis calcd (%) for $C_{50}H_{61}BF_4NO_3PPd$ (947.3453): C 63.33, H 6.48, N 1.48; found: C 63.02, H 6.43, N 1.44.

[Pd(η^3-1,3-diphenylallyl)(L5 e)]BF_4 (55): *endo* isomer (33%): ^{31}P NMR (CD_2Cl_2, 298 K): δ = 132.7 ppm (s, 1P); ^{1}H NMR (CD_2Cl_2, 298 K): δ = 1.45 (s, 9H, CH_3, *t*Bu), 1.68 (s, 3H, CH_3–Ar), 1.71 (s, 3H, CH_3–Ar), 1.73 (s, 9H, CH_3, *t*Bu), 2.11 (s, 3H, CH_3–Ar), 2.30 (s, 3H, CH_3–Ar), 2.32 (s, 3H, CH_3–N), 2.42 (m, 1H, CH_2), 2.70 (s, 3H, CH_3–N), 3.56 (dd, 1H, CH_2, $^3J_{H-H}$ = 10.0 Hz, $^3J_{H-P}$ = 14.4 Hz), 4.49 (m, 1H, CH allyl *trans* to N), 4.84 (m, 1H, CH allyl *trans* to P), 5.23 (m, 1H, CH–O), 6.19 (m, 1H, CH allyl central), 6.7–7.8 ppm (m, 17H, CH=); ^{13}C NMR (C_6D_6, 298 K): δ = 16.5 (CH_3, Ar), 16.7 (CH_3, Ar), 20.0 (CH_3, Ar), 20.1 (CH_3, Ar), 31.9 (CH_3, *t*Bu), 32.4 (d, CH_3, *t*Bu, J_{C-P} = 4.6 Hz), 34.4–35.3 (C, *t*Bu), 48.7 (CH_3–N), 54.3 (CH_3–N), 69.8 (m, CH allyl *trans* to N), 70.9 (CH_2), 74.8 (CH–O), 93.8 (d, CH allyl *trans* to P, J_{C-P} = 39.7 Hz), 114.1 (d, CH allyl central, J_{C-P} = 12.2 Hz), 125–146 ppm (aromatic C). *exo* isomer (67%): ^{31}P NMR (CD_2Cl_2, 298 K): δ = 130.3 ppm (s, 1P); ^{1}H NMR (CD_2Cl_2, 298 K): δ = 1.31 (s, 9H, CH_3, *t*Bu), 1.60 (s, 9H, CH_3, *t*Bu), 1.62 (s, 3H, CH_3–Ar), 1.74 (s, 3H, CH_3–Ar), 2.16 (s, 6H, CH_3-Ar and CH_3–N), 2.45 (s, 3H, CH_3–Ar), 2.52 (m, 1H, CH_2), 2.75 (s, 3H, CH_3–N), 3.19 (dd, 1H, CH_2, $^3J_{H-H}$ = 9.6 Hz, $^3J_{H-P}$ = 14.4 Hz), 4.52 (m, 1H, CH allyl *trans* to N), 5.30 (m, 1H, CH–O), 5.61 (m, 1H, CH allyl *trans* to P), 6.54 (m, 1H, CH allyl central), 6.7–7.8 ppm (m, 17H, CH=); ^{13}C NMR (C_6D_6, 298 K): δ = 16.2 (CH_3, Ar), 16.7 (CH_3, Ar), 20.0 (CH_3, Ar), 20.2 (CH_3, Ar), 31.6 (CH_3, *t*Bu), 32.1 (CH_3, *t*Bu), 34.4–35.3 (C, *t*Bu), 49.9 (CH_3–N), 51.6 (CH_3–N), 69.8 (m, CH allyl *trans* to N), 71.2 (CH_2), 75.6 (CH–O), 105.6 (d, CH allyl *trans* to P, J_{C-P} = 32.0 Hz), 112.3 (d, CH allyl central, J_{C-P} = 10.7 Hz), 125–146 ppm (aromatic C); elemental analysis calcd (%) for $C_{49}H_{59}BF_4NO_3PPd$ (933.3297): C 63.00, H 6.37, N 1.50; found: C 59.61, H 6.31, N 1.46.

[Pd(η^3-1,3-cyclohexenylallyl)(L4 e)]BF_4 (56): *endo* isomer (91%): ^{31}P NMR (CD_2Cl_2, 298 K): δ = 134.4 ppm (s, 1P); ^{1}H NMR (CD_2Cl_2, 298 K): δ = 0.74 (d, 3H, CH_3, $^3J_{H-H}$ = 6.8 Hz), 1.2–1.6 (m, 4H, CH_2), 1.46 (s, 9H, CH_3, *t*Bu), 1.54 (s, 9H, CH_3, *t*Bu), 1.69 (s, 3H, CH_3–Ar), 1.80 (m, 1H, CH_2), 1.87 (s, 3H, CH_3–Ar), 2.21 (m, 1H, CH_2), 2.23 (s, 3H, CH_3–Ar), 2.34 (s, 3H, CH_3–Ar), 2.82 (s, 3H, CH_3–N), 3.24 (s, 3H, CH_3–N), 3.31 (m, 1H, CH allyl *trans* to N), 3.38 (m, 1H, CH–N), 4.97 (dd, 1H, CH–O, $^3J_{H-H}$ = 7.2 Hz, $^3J_{H-P}$ = 12 Hz), 5.49 (m, 1H, CH allyl central), 5.96 (m, 1H, CH allyl *trans* to P), 7.2–7.5 ppm (m, 7H, CH=);^{13}C NMR (C_6D_6, 298 K): δ = 9.9 (CH_3), 16.7 (CH_3, Ar), 20.5 (CH_3, Ar), 20.6 (CH_3, Ar), 21.4 (b, CH_2), 27.4 (b, CH_2), 21.4 (d, CH_2, J_{C-P} = 8.4 Hz), 31.7 (CH_3, *t*Bu), 32.0 (CH_3, *t*Bu), 35.2–35.4 (C, *t*Bu), 44.8 (CH_3–N), 53.4 (CH_3–N), 64.7 (d, CH allyl *trans* to N, J_{C-P} = 10 Hz), 69.7 (CH–N), 82.7 (d, CH–O, J_{C-P} = 6.1 Hz), 109.2 (d, CH allyl *trans* to P, J_{C-P} = 40 Hz), 113.5 (d, CH allyl central, J_{C-P} = 10.7 Hz), 127–145 ppm (aromatic C). *exo* isomer (9%): ^{31}P NMR (CD_2Cl_2, 298 K): δ = 133.0 ppm (s, 1P); ^{1}H NMR (CD_2Cl_2, 298 K): δ = 0.72 (d, 3H, CH_3, $^3J_{H-H}$ = 6.8 Hz), 1.2–1.6 (m, 4H, CH_2), 1.45 (s, 9H, CH_3, *t*Bu), 1.54 (s, 9H, CH_3, *t*Bu), 1.62 (s, 3H, CH_3–Ar), 1.80 (m, 1H, CH_2), 1.89 (s, 3H, CH_3–Ar), 2.21 (m, 1H, CH_2), 2.27 (s, 3H, CH_3–Ar), 2.29 (s, 3H, CH_3–Ar), 2.68 (s, 3H, CH_3–N), 3.20 (s, 3H, CH_3–N), 3.36 (m, 1H, CH allyl *trans* to N), 3.42 (m, 1H, CH–N), 5.21 (m, 1H, CH–O), 5.68 (m, 1H, CH allyl central), 6.08 (m, 1H, CH allyl *trans* to P), 7.2–7.5 ppm (m, 7H, CH=); ^{13}C NMR (C_6D_6, 298 K): δ = 9.2 (CH_3), 16.7 (CH_3, Ar), 16.8 (CH_3, Ar), 20.4 (CH_3, Ar), 20.6 (CH_3, Ar), 21.4 (b, CH_2), 27.4 (b, CH_2), 21.4 (d, CH_2, J_{C-P} = 8.4 Hz), 31.5 (CH_3, *t*Bu), 31.6 (CH_3, *t*Bu), 35.2–35.4 (C, *t*Bu), 45 (CH_3–N), 52.8 (CH_3–N), 64.2 (d, CH allyl *trans* to N, J_{C-P} = 9.2 Hz), 69.7 (CH–N), 81.9 (d, CH–O, J_{C-P} = 7.3 Hz), 110.8 (d, CH allyl *trans* to P, J_{C-P} = 38.6 Hz), 113.2 (d, CH allyl central, J_{C-P} = 9.6 Hz), 127–145 ppm (aromatic C); elemental analysis calcd (%) for $C_{41}H_{57}BF_4NO_3PPd$ (835.3140): C 58.90, H 6.87, N 1.68; found: C 58.21, H 6.84, N 1.65.

[Pd(η^3-1,3-cyclohexenylallyl)(L5 e)]BF_4 (57):[34] *endo* isomer (96%): ^{31}P NMR (CD_2Cl_2, 298 K): δ = 135.2 ppm (s, 1P); ^{1}H NMR (CD_2Cl_2,

298 K): $\delta = 1.25$ (m, 1H, CH_2), 1.43 (m, 2H, CH_2), 1.45 (s, 9H, CH_3, *t*Bu), 1.54 (s, 9H, CH_3, *t*Bu), 1.70 (m, 1H, CH_2), 1.73 (s, 3H, CH_3–Ar), 1.88 (s, 3H, CH_3–Ar), 1.90 (m, 1H, CH_2), 2.16 (m, 1H, CH_2), 2.24 (s, 3H, CH_3–Ar), 2.35 (s, 3H, CH_3–Ar), 2.71 (d, 1H, CH_2–N, $^3J_{H-H} = 14.4$ Hz), 2.90 (s, 3H, CH_3–N), 3.12 (s, 3H, CH_3–N), 3.42 (dd, 1H, CH_2–N, $^3J_{H-H} = 14.4$ Hz, $^3J_{H-P} = 9.6$ Hz), 3.49 (m, 1H, CH allyl *trans* to N), 5.23 (m, 1H, CH–O), 5.44 (m, 1H, CH allyl central), 6.03 (m, 1H, CH allyl *trans* to P), 7.2–7.5 ppm (m, 7H, CH=); ^{13}C NMR (C_6D_6, 298 K): $\delta = 16.7$ (CH_3, Ar), 16.8 (CH_3, Ar), 20.5 (CH_3, Ar), 20.6 (CH_3, Ar),), 20.9 (d, CH_2, $J_{C-P} = 2.3$ Hz), 27.6 (b, CH_2), 28.5 (d, CH_2, $J_{C-P} = 7.6$ Hz),31.8 (CH_3, *t*Bu), 32.0 (d, CH_3, *t*Bu, $J_{C-P} = 1.5$ Hz)), 35.2 (C, *t*Bu), 35.5 (C, *t*Bu), 51.8 (CH_3–N), 56.7 (CH_3–N), 67.6 (d, CH allyl *trans* to N, $J_{C-P} = 9.1$ Hz), 71.8 (CH–N), 77.9 (d, CH–O, $J_{C-P} = 6.8$ Hz), 105.0 (d, CH allyl *trans* to P, $J_{C-P} = 40.3$ Hz), 113.5 (d, CH allyl central, $J_{C-P} = 10.6$ Hz), 126–146 ppm (aromatic C). *exo* isomer (4%): ^{31}P NMR (CD_2Cl_2, 298 K): $\delta = 134.2$ ppm (s, 1P); ^{1}H NMR (CD_2Cl_2, 298 K): $\delta = 1.25$ (m, 1H, CH_2), 1.43 (m, 2H, CH_2), 1.47 (s, 9H, CH_3, *t*Bu), 1.54 (s, 9H, CH_3, *t*Bu), 1.70 (m, 1H, CH_2), 1.74 (s, 3H, CH_3–Ar), 1.90 (bs, 4H, CH_3-Ar and CH_2), 2.16 (m, 1H, CH_2), 2.24 (s, 3H, CH_3–Ar), 2.35 (s, 3H, CH_3–Ar), 2.81 (d, 1H, CH_2–N, $^3J_{H-H} = 14.0$ Hz), 2.91 (s, 3H, CH_3–N), 3.09 (s, 3H, CH_3–N), 3.27 (dd, 1H, CH_2–N, $^3J_{H-H} = 14.0$ Hz, $^3J_{H-P} = 8.4$ Hz), 3.39 (m, 1H, CH allyl *trans* to N), 5.39 (m, 1H, CH–O), 5.54 (m, 1H, CH allyl central), 5.84 (m, 1H, CH allyl *trans* to P), 7.2–7.5 ppm (m, 7H, CH=); elemental analysis calcd (%) for $C_{40}H_{55}BF_4NO_3PPd$ (821.2984): C 58.44, H 6.74, N 1.70; found: C 58.06, H 6.70, N 1.67.

Study of the reactivity of the [Pd(η³-allyl)(L)]BF_4 with sodium malonate by in situ NMR spectroscopy[35]

A solution of in situ prepared [Pd(η³-allyl)(L)]BF_4 (L = phosphite pyridine, 0.05 mmol) in CD_2Cl_2 (1 mL) was cooled in the NMR spectrometer to −80 °C. At this temperature, a solution of cooled sodium malonate (0.1 mmol) was added. The reaction was then followed by ^{31}P NMR spectroscopy. The relative reaction rates were calculated using a capillary that contained a solution of triphenylphosphine in CD_2Cl_2 as the external standard.

Typical procedure for the allylic alkylation of linear (S1 and S3–S8) and cyclic (S2, S9, and S10) substrates

A degassed solution of [PdCl(η³-C_3H_5)]$_2$ (0.9 mg, 0.0025 mmol) and the corresponding amino phosphite (0.0055 mmol) in dichloromethane (0.5 mL) was stirred for 30 min. Subsequently, a solution of the corresponding substrate (0.5 mmol) in dichloromethane (1.5 mL), nucleophile (1.5 mmol), *N*,*O*-bis(trimethylsilyl)acetamide (370 μL, 1.5 mmol), and KOAc (3 mg, 0.03 mmol) was added. The reaction mixture was stirred at RT. 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 (3×10 mL), and the extract was dried over $MgSO_4$. For **12**, **14**–**21**, **27**–**32**, **35**, **37**–**39**, and **45**, the solvent was removed, conversions were measured by ^{1}H NMR spectroscopy, and *ee* values were determined by HPLC. For **13**, **33**–**34**, **40**–**41**, and **43**–**44**, the conversion and *ee* were determined by GC. For **36** and **42**, conversion were measured by ^{1}H NMR spectroscopy and the *ee* was determined by ^{1}H NMR spectroscopy using [Eu(hfc)$_3$], hfc = [3-(heptafluoropropylhydroxymethylene)-(+)-camphorate]. For details of the characterization and determination of *ee* see Supporting Information.

Typical procedure for the allylic amination of S1

A degassed solution of [PdCl(η³-C_3H_5)]$_2$ (0.9 mg, 0.0025 mmol) and the corresponding amino phosphite ligand (0.0055 mmol) in dichloromethane (0.5 mL) was stirred for 30 min. Subsequently, a solution of **S1** (0.5 mmol) in dichloromethane (1.5 mL) and benzylamine (131 μL, 1.5 mmol) were added. The reaction mixture was stirred at RT. 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 (3×10 mL), and the extract was dried over $MgSO_4$. The conversion was measured by ^{1}H NMR spectroscopy, and the *ee* was determined by HPLC. For details of the characterization and determination of *ee* see Supporting Information.

Typical procedure for the allylic etherification of S1

A degassed solution of [PdCl(η³-C_3H_5)]$_2$ (0.9 mg, 0.0025 mmol) and the corresponding amino phosphite ligand (0.0055 mmol) in dichloromethane (0.5 mL) was stirred for 30 min. Subsequently, a solution of the corresponding substrate (31.5 mg, 0.125 mmol) in dichloromethane (1.5 mL) was added. After 10 min, Cs_2CO_3 (122 mg, 0.375 mmol) and alkyl alcohol (0.375 mmol) were added. The reaction mixture was stirred at RT. 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× 10 mL), and the extract was dried over $MgSO_4$. The conversion was measured by ^{1}H NMR spectroscopy. HPLC was used to determine the *ee*. For details of the characterization and determination of *ee* see Supporting Information.

Typical procedure for the preparation of carbocycles 46–51

A solution of Grubbs II catalyst (5 mg, 0.006 mmol) and the corresponding alkylated product (0.12 mmol) in CH_2Cl_2 (3 mL) was stirred for 16 h. The solution was purified directly by flash chromatography (95:5; Hex/EtOAc) to obtain the desired carbocycle. For details of the characterization and determination of *ee* see Supporting Information.

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Keywords: allylic compounds · asymmetric catalysis · ligand design · ligand effects · palladium

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