Modular Furanoside Diphosphite Ligands for Pd-Catalyzed Asymmetric Allylic Substitution Reactions: Scope and Limitations

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Abstract: We have synthesized a library of furanoside diphosphite ligands for the Pd-catalyzed allylic substitution reactions of acyclic and cyclic allylic esters. The library has been designed to rapidly screen the ligands to uncover their important structural features and to determine the scope of diphosphite ligands in these catalytic reactions. After the systematic variation of the sugar backbone, the substituent at C-5 and the phosphite moieties, the diphosphite ligand **4c** was found to be optimal in the Pd-catalyzed asymmetric allylic substitution of hindered (**S1**) and unhindered (**S2**–**S5**) substrates, yielding high activities [TOFs up to $>3000\ \mathrm{mol} \times (\mathrm{mol} \times \mathrm{h})^{-1}$] and enantioselectivities (ees up to 99%). In addition, the screening of the library enabled us to find other suitable ligands for hindered disubstituted linear substrate **S1** (ligands **1b**–**d**, **g** and **4b**, **d**, **g**) and for unhindered cyclic substrates **S3**–**S5 (**ligands **6c** and **7c**).

Keywords: allylic substitution; asymmetric catalysis; C–C bond formation, P ligands, palladium, phosphite ligands

Introduction

Palladium-catalyzed asymmetric allylic substitution is a versatile, widely used process in organic synthesis for the enantioselective formation of carbon-carbon and carbon-heteroatom bonds. In recent years, many chiral ligands, mainly P- and N-containing ligands, which possess either C_2 or C_1 symmetry, have provided high enantiomeric excesses.[1] However, these catalytic systems generally have two important limitations (Figure 1). Firstly, they have a high substrate specificity (i.e., high ees are obtained in hindered disubstituted linear substrates while low ees are obtained in cyclic substrates and unhindered linear substrates, or *vice versa*). Secondly, the reaction rates are usually low [i.e., TOFs = $100\ \mathrm{mol} \times (\mathrm{mol} \times \mathrm{h})^{-1}$].[1] In this context, the research into faster and more versatile ligand systems from readily available simple starting materials is nowadays of great importance in this reaction.

In 2001, we reported the first diphosphite furanoside ligands used for Pd-catalyzed asymmetric allylic alkylation. Results were only reported for the alkylation of 1,3-diphenyl-3-acetoxyprop-1-ene (**S1**).[2] In addition to the high enantiomeric excesses (ees up to 95%), the reaction rates were extremely fast [TOFs up to $1200\ \mathrm{mol} \times (\mathrm{mol} \times \mathrm{h})^{-1}$] in simple non-optimized reaction conditions.[2] Despite this success, the use of other diphosphite ligands has not yet been reported and a systematic study of the possibilities offered by diphosphites as new ligands for Pd-catalyzed allylic substitution reactions is still needed. To fully investigate these possibilities, in this paper we expand the previous study of 2001 to other diphosphite furanoside ligands (Figure 2) and also ex-

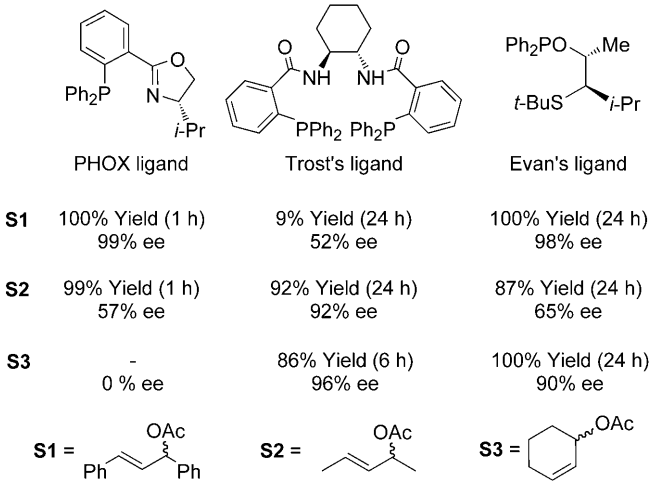

Figure 1. Summary of the best results with substrates **S1**–**S3** with three of the most representative ligands developed for the Pd-catalyzed allylic substitution reactions (reactions usually carried out with 2–4 mol % of Pd).

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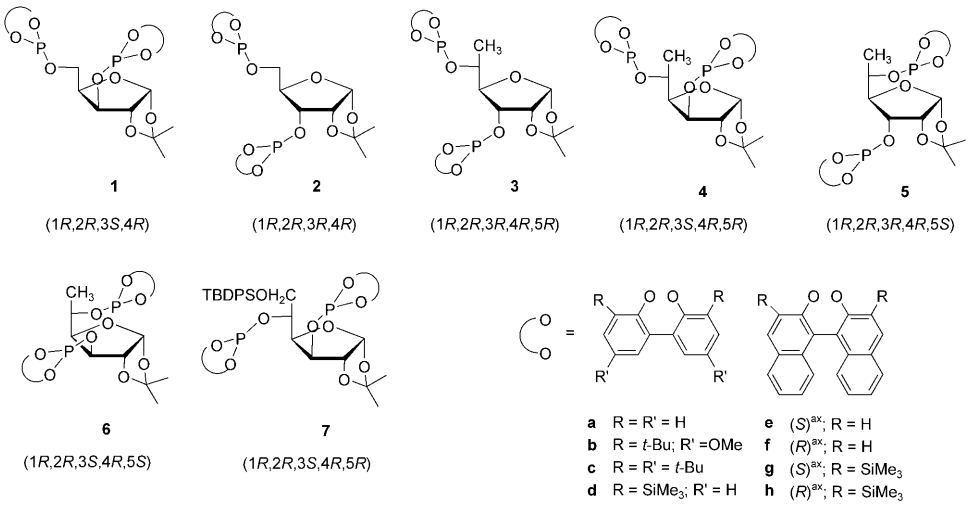


Figure 2. Diphosphite ligand library.

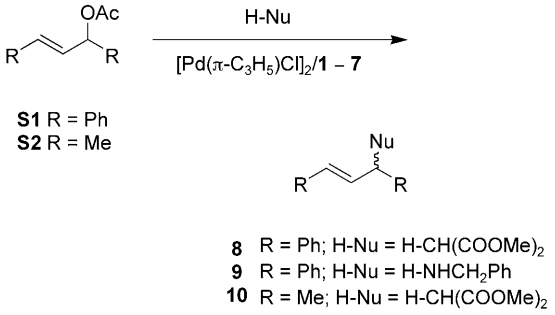
tend the study of this family of ligands to other types of substrates with different steric properties (Figure 3).

To do this, we have taken advantage of the high modularity of these ligands and have synthesized[3] and screened a library of 33 furanoside diphosphite ligands with the same underlying structure (Figure 2). The synthesis and screening of the library were performed in parallel using two parallel reactors each equipped with 24 different positions. With this library we fully investigated the effects of systematically varying the configurations at C-3 and C-5 of the ligand backbone (**1**–**6**), different substituents at C-5 [H, Me and $CH_2OTBDPS$ (TBDPS = *tert*-butyldiphenylsilyl); ligands **1** and **2**, **3**–**6** and **7**, respectively], and different substituents/configurations in the biaryl phosphite moieties (**a**–**h**). By carefully selecting these elements, we achieved high enantioselectivities and activities in different substrate types.

Results and Discussions

Allylic Substitution of Disubstituted Linear Substrates

In this section, we report the use of the chiral diphosphite ligands **1**–**7** in the Pd-catalyzed allylic substitution [Equation (1)] of two linear substrates with different steric properties: *rac*-1,3-diphenyl-3-acetoxyprop-1-ene (**S1**; widely used as a model substrate) and *rac*-1,3-dimethyl-3-acetoxyprop-1-ene (**S2**). Different nucleophiles were tested. In all the cases, the catalysts were generated *in situ* from π-allyl-palladium chloride dimer $[PdCl(\eta^3\text{-}C_3H_5)]_2$ and the corresponding ligand.



(1)

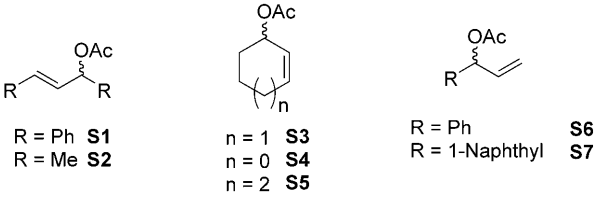


Figure 3. Substrates tested with diphosphite ligands **1a**–**h** to **7a**–**h**.

Allylic Alkylation of rac*-1,3-Diphenyl-3-acetoxyprop-1-ene (***S1***) using Dimethyl Malonate as Nucleophile [Equation (1)]*

We determined the optimal reaction conditions by conducting a series of experiments in which the solvent and the ligand-to-palladium ratio were varied.

We first studied the effect of the solvent. Four solvents [tetrahydrofuran (THF), dichloromethane (DCM), toluene and dimethylformamide (DMF)] and seven ligands (**1c**–**7c**) were tested. The best combination of activity and enantioselectivity was achieved with dichloromethane (Figures 4 and 5). The enantiomeric excesses obtained with tetrahydrofuran and toluene were comparable to those of dichloromethane, but the activities were the lowest. On the other hand, dimethylformamide yielded high relative conversions, similar to those of dichloromethane, but the ees were the lowest of the four

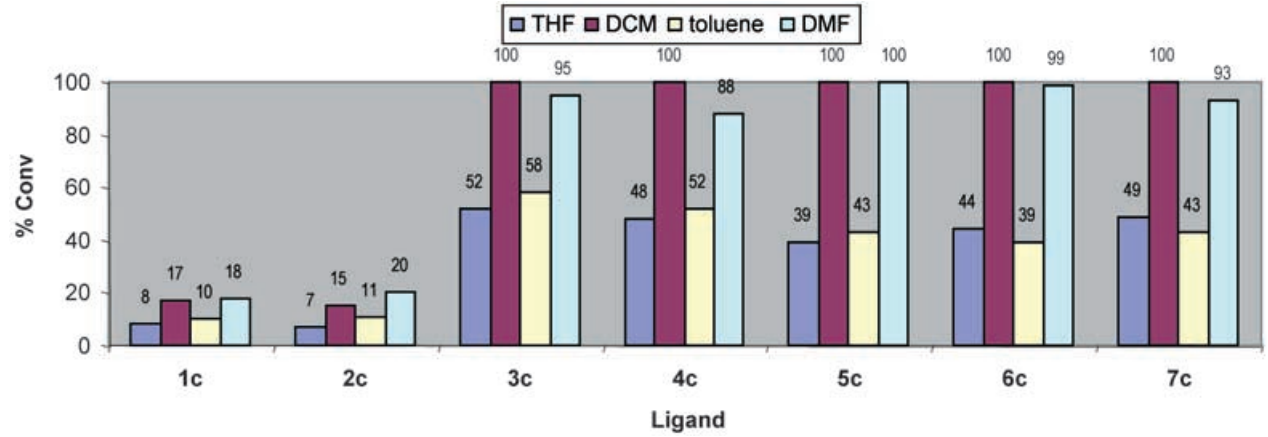


Figure 4. Conversions of **8** after 5 minutes using ligands **1c**–**7c** in different solvents (THF, DCM, toluene and DMF).

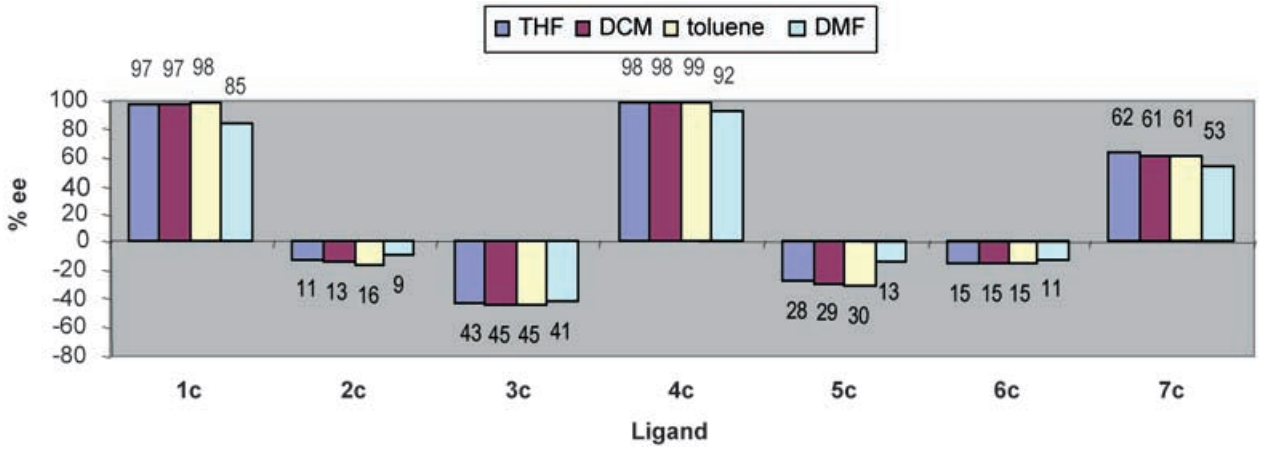


Figure 5. Enantiomeric excess of **8** obtained using ligands **1c**–**7c** in four solvents. The positive numbers refer to the formation of the *S*-isomer in excess and the negative numbers refer to the formation of the *R*-isomer.

solvents. In conclusion, we choose dichloromethane as our solvent.

We next studied the effect of varying the ligand-to-palladium ratio. The conversion and enantioselectivity when dichloromethane was used as a solvent are shown in Table 1 (similar trends were observed for the other solvents). These results show that excess ligand is not needed to obtain high enantioselectivities.

In conclusion, the trade-off between enantioselectivities and reaction rates was optimum with dichloromethane and a ligand-to-palladium ratio of 1.1 : 1. These optimal conditions were then used to test the catalytic performance of the complete series of ligands. The activities and enantiomeric excesses obtained are plotted in Figure 6. Note the high activities obtained with these catalytic systems (e.g., 100% conversion is usually reached after 5 minutes) and the excellent enantioselectivities obtained with ligands **1b**–**d, g** and **4b**–**d, g** (ees up to 98%).

From Figure 6 (*left*) we can conclude that activities were affected by the substituent at C-5 and the phos-

Table 1. Selected results for the Pd-catalyzed allylic alkylation of **S1** using ligands **1c**, **3c** and **4c**. Effect of the ligand-to-palladium ratio.[a]

Entry	Ligand	L/Pd	% Conversion (t/min)[b]	% ee[c]
1	**1c**	0.9	100 (30)	97 (*S*)
2	**1c**	1.1	100 (30)	97 (*S*)
3	**1c**	2	100 (30)	97 (*S*)
4	**3c**	0.9	100 (5)	45 (*R*)
5	**3c**	1.1	100 (5)	45 (*R*)
6	**3c**	2	100 (5)	44 (*R*)
7	**4c**	0.9	100 (5)	98 (*S*)
8	**4c**	1.1	100 (5)	98 (*S*)
9	**4c**	2	100 (5)	98 (*S*)

[a] All reactions were run at room temperature: 0.5 mol % $[PdCl(\eta^3\text{-}C_3H_5)]_2$; CH_2Cl_2 as solvent.

[b] Conversion percentage of acetate **8** determined by ^{1}H-NMR.

[c] Enantiomeric excesses determined by HPLC on a Chiralcel-OD column. Absolute configuration given in parentheses.

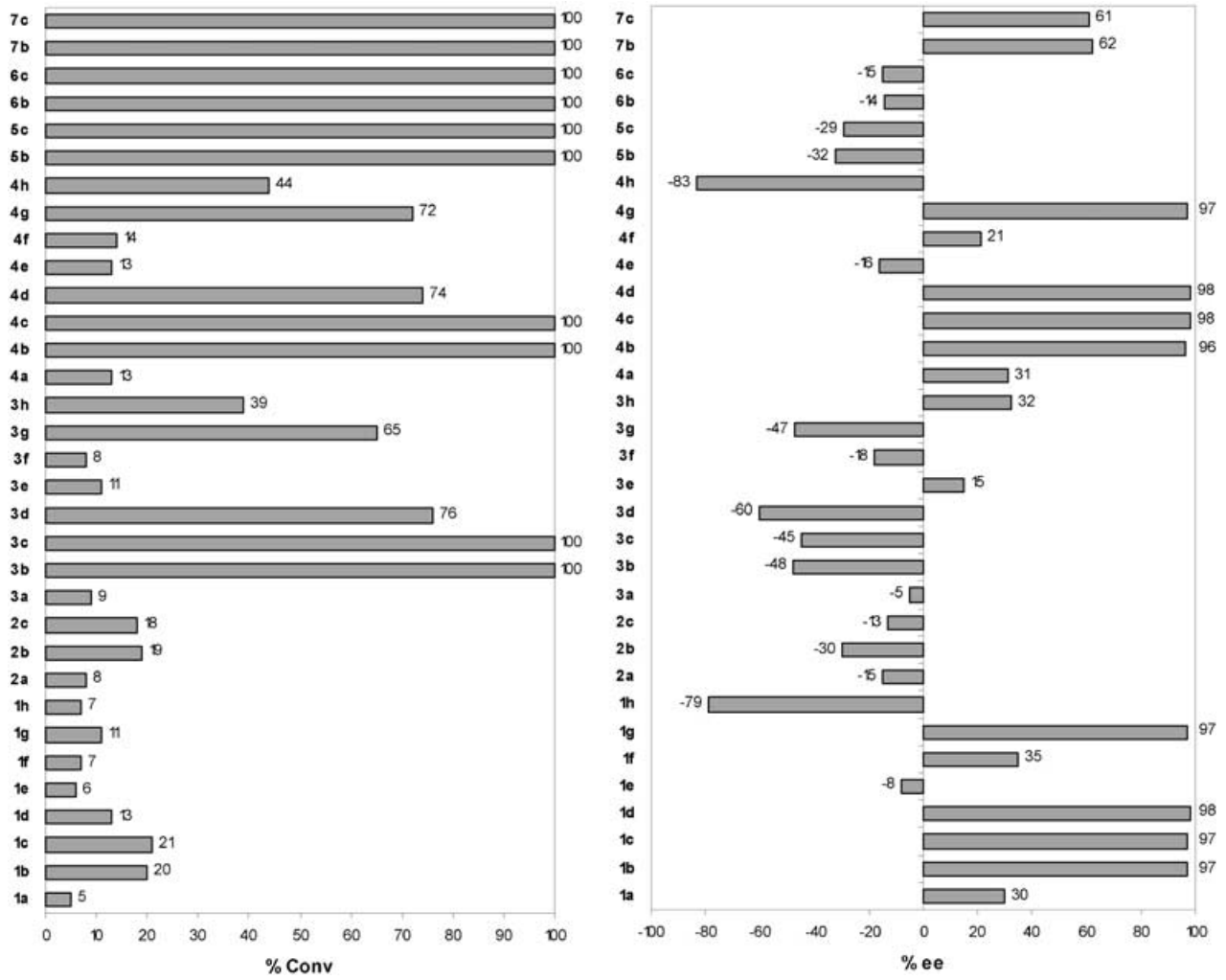


Figure 6. *Left*: Conversion of **8** after 5 minutes using the library presented in Figure 2. *Right*: Enantiomeric excess of **8** using the different ligands. The positive numbers refer to the formation of the *S*-isomer in excess and the negative numbers refer to the formation of the *R*-isomer.

phite moiety. When the substituent at C-5 was Me or $CH_2OTBDPS$ (ligands **3**–**7**), activities were better than when the substituent was H (ligands **1** and **2**). Activities were also better when the ligand contained bulky substituents at the *ortho* positions and electron-donating substituents at the *para* position of the biphenyl moieties (i.e., $\mathbf{b} \sim \mathbf{c} > \mathbf{d} > \mathbf{a}$).

Like activities, enantioselectivities (Figure 6, *right*) were affected by the substituent at C-5 and the phosphite moiety but they were also affected by the configuration of carbon atoms C-3 and C-5 and the configurations of the biaryl moieties. Since each of these parameters interacted with the others, we could not assign a certain effect on the enantiomeric excess to each individual parameter. However, we found that enantioselectivities were best (ees up to 98%) with the following specific combination: *xylo*- (**1b**–**d, g**) and *gluco*-furanoside (**4b**–**d, g**) ligands containing bulky substituents at the *ortho* positions of the biaryl moieties. Moreover, by considering ligands **3**–**6**, which contemplate the four possible combinations of stereocenters C-3 and C-5, we found a cooperative effect between C-3 and C-5. [*The opportunity provided by this ligand library to study all the possible combinations of stereocenters C-3 and C-5 complements the preliminary results (Ref.[2]) that erroneously indicated that enantioselectivities were mainly affected by the configuration of C-3.*] Specifically, the best results were obtained when the configuration of C-3 was *S* and the configuration of C-5 was *R* (ligands **4b**–**d, g**). The excellent ees obtained with ligands **1**, which do not have a stereocenter in C-5, suggest that the spatial arrangement around C-5 adopted by these ligands in the Pd-allyl intermediate must be similar to that of ligands **4**. A second cooperative effect between the stereogenic centers of the ligand backbone and the configuration of the binaphthyl phosphite moieties was observed when binaphthyl-based ligands (**e**–**h**) were used. This cooperative effect, and the previously ob-

served cooperative effect between the backbone stereocenters C-3 and C-5, control the enantioselectivity.

In addition to the effect of structural parameters on enantioselectivity, reaction parameters can also be controlled to further improve enantioselectivity. In this case, ees were further improved by lowering the reaction temperature to 5 °C. For example, enantioselectivities up to > 99% were obtained with ligands **1c** and **4c** while activity was almost unaffected (100% conversion after 35 and 7 minutes using ligands **1c** and **4c**, respectively). We also performed the reaction at a low catalyst concentration (**S1**/Pd = 2000) using ligand **4c**. In this way, excellent enantioselectivity [98% (*S*) ee] and activity [100% conversion after 40 min at room temperature, TOF > 3000 mol $(mol \cdot h)^{-1}$] were obtained.

Allylic Amination of rac-*1,3-Diphenyl-3-acetoxyprop-1-ene (***S1***) using Benzylamine as Nucleophile*

We also evaluated the ligand library in the allylic substitution process of **S1** using benzylamine as nucleophile [Equation (1)]. This situation is different from that described before for the alkylation of **S1** because a new stereogenic C–N bond is created rather than a C–C bond. The most remarkable results are shown in Table 2. In general, they follow the same trends as for the allylic alkylation of **S1**. However, the enantiomeric excesses were higher (ees up to 99% at room temperature). Although, as expected, the activities were lower than in the alkylation reaction of **S1**, they were much higher than those obtained with other homodonor ligands.[1c] Again, the catalyst precursor containing the diphosphite ligands **1b**–**d**, **g** and **4b**–**d**, **g** provided the best trade-off between activity and enantioselectivity (entries 1–4 and 7). The stereoselectivity of the amination was the same as for the alkylation reaction, though the CIP descriptor was inverted due to the change in priority of the groups.

Table 2. Selected results for the Pd-catalyzed allylic amination of **S1**.[a]

Entry	Ligand	% Conversion (t/h)[b]	% ee[c]
1	**1b**	100 (1)	98 (*R*)
2	**1c**	92 (1)	98 (*R*)
3	**1d**	95 (1)	98 (*R*)
4	**1g**	53 (1)	98 (*R*)
5	**2c**	81 (1)	16 (*S*)
6	**3c**	100 (0.75)	61 (*S*)
7	**4c**	100 (0.75)	99 (*R*)
8	**5c**	100 (0.75)	13 (*S*)
9	**6c**	100 (0.75)	55 (*S*)
10	**7c**	67 (1)	81 (*R*)

[a] All reactions were run at room temperature: 1 mol % $[PdCl(\eta^3\text{-}C_3H_5)]_2$; CH_2Cl_2 as solvent.
[b] Conversion percentage of **9** determined by ^{1}H-NMR.
[c] Enantiomeric excesses determined by HPLC on a Chiralcel-OJ column. Absolute configuration given in parentheses.

Allylic Alkylation of rac-*1,3-Dimethyl-3-acetoxyprop-1-ene (***S2***) using Dimethyl Malonate as Nucleophile*

We also screened the ligand library in the allylic alkylation of the linear substrate **S2** [Equation (1)]. This substrate is less sterically demanding than the previously used substrate **S1**. Enantioselectivity for **S2** is therefore more difficult to control than with hindered substrates such as **S1**. To obtain high ees, the ligand must create a small chiral pocket (the chiral cavity where the allyl is embedded) around the metal center, mainly because of the presence of less sterically methyl *syn* substituents.[1]

The results of using the diphosphite ligand library under the optimized conditions are summarized in Table 3. Activities followed the same trends as for the alkylation of substrate **S1**. The best reaction rates were obtained with ligands **3b** and **c** to **7b** and **c**, which contained Me or CH_2OTBDPS groups at C-5, and bulky *tert*-butyl substituents at the *ortho* positions and electron-donating substituents at the *para* position of the biphenyl moieties [TOF > 300 mol $(mol \cdot h)^{-1}$]. However, the general trends that controlled enantioselectivity were different from those that controlled **S1**, and only ligand **4c** reached high enantioselectivities for this substrate (entry 15). This result is amongst the best reported for this type of unhindered substrates.[4] Note also that these li-

Table 3. Selected results for the Pd-catalyzed allylic substitution of **S2**.[a]

Entry	Ligand	% Conversion (t/min)[b]	% ee[c]
1	**1c**	100 (30)	59 (*R*)
2	**2c**	100 (30)	52 (*S*)
3	**3c**	100 (10)	45 (*S*)
4	**4a**	100 (30)	4 (*R*)
5	**4b**	100 (10)	67 (*R*)
6	**4c**	100 (10)	78 (*R*)
7	**4d**	90 (30)	71 (*R*)
8	**4e**	54 (30)	8 (*R*)
9	**4f**	61 (30)	4 (*S*)
10	**4g**	51 (30)	72 (*R*)
11	**4h**	49 (30)	21 (*S*)
12	**5c**	100 (10)	34 (*S*)
13	**6c**	100 (10)	43 (*S*)
14	**7c**	100 (15)	58 (*R*)
15[d]	**4c**	12 (60)	85 (*R*)

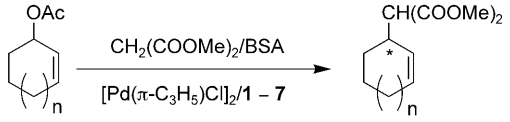
[a] All reactions were run at room temperature: 1 mol % $[PdCl(\eta^3\text{-}C_3H_5)]_2$; CH_2Cl_2 as solvent.
[b] Conversion percentage of **10** determined by ^{1}H-NMR.
[c] Enantiomeric excesses determined by GC. Absolute configuration given in parentheses.
[d] Reaction carried out at −20 °C.

gands provided higher activities [TOFs up to >300 mol $\times$ (mol $\times$ h)$^{-1}$] than those for other successful ligands for this substrate.[4]

Allylic Alkylation of Cyclic Substrates

As for the unhindered substrate **S2**, enantioselectivity in cyclic substrates is difficult to control. Although high enantioselective catalysts have been developed for cyclic substrates, they generally provide low enantiocontrol in hindered linear substrates.[1] Presumably this lack of generality is derived from different ligand structural requirements for both types of substrates (see above). Therefore, the development of enantioselective catalysts for both unhindered (**S2**–**S5**, Figure 3) and hindered substrates (**S1**) is still a challenge.[5]

This section reports that the chiral diphosphite ligands **1**–**7** applied in the previous section to the Pd-catalyzed allylic alkylation of linear substrates, can also be used for cyclic substrates. In this case, three cyclic substrates were tested [Equation (2)]: *rac*-3-acetoxycyclohexene (**S3**; which is widely used as a model substrate), *rac*-3-acetoxycyclopentene (**S4**) and *rac*-3-acetoxycycloheptene (**S5**).



(2)

S3 n = 1
S4 n = 0
S5 n = 2

11 n = 1
12 n = 0
13 n = 2

Allylic Alkylation of rac-*3-Acetoxycyclohexene (***S3***) [Equation (2)]*

Preliminary investigations into the solvent effect and ligand-to-palladium ratio provided the same trends as those with the previously tested linear substrate **S1**. The trade-off between enantioselectivities and reaction rates was optimum with dichloromethane and a ligand-to-palladium ratio of 1.1:1. The results of using the diphosphite ligand library under the optimized conditions are shown in Figure 7.

Activities (Figure 7, *left*) followed the already observed trends for the alkylation of substrates **S1** and **S2**. The best reaction rates, therefore, were obtained with ligands **3b** and **c** to **7b** and **c**, which contain Me or $CH_2OTBDPS$ groups at C-5, and bulky *tert*-butyl substituents at the *ortho* positions and electron-donating substituents at the *para* position of the biphenyl moieties [TOF >200 mol (mol$\cdot$h)$^{-1}$]. As expected, the activities were lower than in the alkylation reaction of **S1**.[4a,6]

Again, enantioselectivities (Figure 7, *right*) were highly affected by the substituent at C-5, the configuration of carbon atoms C-3 and C-5 and the phosphite moieties. However, the effect of these parameters was different from those observed in the alkylation of **S1** and **S2**. Enantioselectivity was best with ligands **4c**, **6c** and **7c**. To obtain high enantioselectivities, therefore, the ligand must have a substituent at C-5, bulky *tert*-butyl groups at both the *ortho* and *para* positions and an *S* configuration at C-3. These results also indicate that the configuration at C-5 controls the sense of the enantioselectivity. Therefore, the *R* enantiomer of **11** was obtained using ligand **6c** and the *S* enantiomer of **11** was obtained using ligand **4c**, both with excellent enantioselectivities and activities. For these two ligands, enantioselectivities up to 95% were obtained by lowering the reaction temperature to $-20\,^{\circ}$C (24% conversion after 12 hours using ligand **4c** and 26% conversion after 12 hours using ligand **6c**). These results are amongst the best reported for cyclic substrates.[4a,6]

Allylic Alkylation of rac-*3-Acetoxycyclopentene (***S4***) and* rac-*3-Acetoxycycloheptene (***S5***) [Equation (2)]*

To further study the potential of ligand **4c** (the only ligand that reaches excellent values of enantioselectivities for both linear and cyclic substrates), we also tested it in the allylic alkylation of 5- and 7-membered cyclic substrates **S4** and **S5**, respectively (Table 4). Interestingly, for these sterically undemanding substrates, high reaction rates [TOFs up to >200 mol $\times$ (mol $\times$ h)$^{-1}$] and enantioselectivities (ees up to 96%) were also obtained.

Allylic Substitution of Monosubstituted Linear Substrates

Encouraged by the excellent results obtained for disubstituted linear substrates and for cyclic substrates, we examined the regio- and stereoselective allylic alkylation of 1-phenylallyl acetate (**S6**) and 1-(1-naphthyl)allyl acetate (**S7**) with dimethyl malonate. For both substrates, the development of highly regio- and enantioselective Pd-catalysts is still a challenge.[7] The results obtained with the diphosphite ligand library are summarized in Table 5. Unfortunately, the regioselectivity for the branched products was not high in this case. However, high enantioselectivities can be obtained by increasing the size of the substrate substituent. Ligand **4c** provided 95% ee for substrate **S7** but only 29% ee for substrate **S6** (entry 10 *vs.* 6). Note also, the high activities [TOFs up to >600 mol $\times$ (mol $\times$ h)$^{-1}$] observed for these substrates.

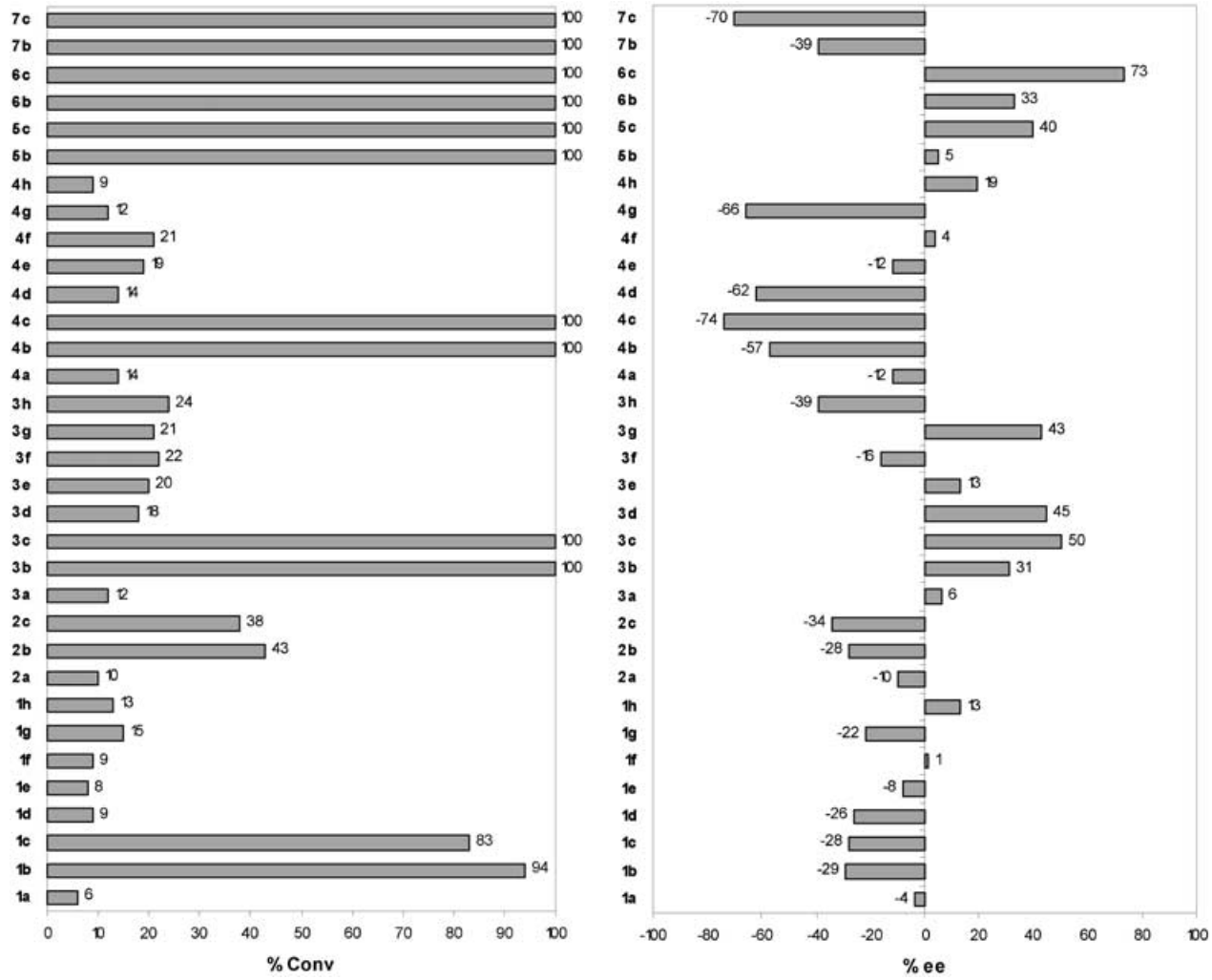


Figure 7. *Left*: Conversion of **11** after 30 minutes. Enantiomeric excess of **11** using the library presented in Figure 2. *Right*: Enantiomeric excess of **11** using the different ligands. The positive numbers refer to the formation of the *R*-isomer in excess, and the negative numbers refer to the formation of the *S*-isomer.

Table 4. Pd-catalyzed allylic alkylation of **S4** and **S5** using ligand **4c**.[a]

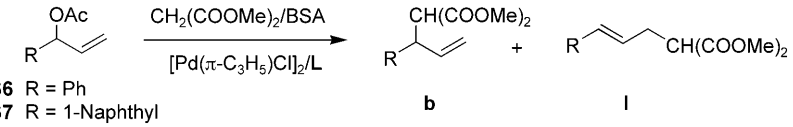
Entry	Substrate	T [°C]	% Conversion (t/min)[b]	% ee[c]
1	**S4**	20	100 (30)	68 (*R*)
2	**S5**	20	100 (30)	87 (*S*)
3	**S4**	−20	12 (90)	81 (*S*)
4	**S5**	−20	13 (90)	96 (*R*)

[a] All reactions were run at room temperature: 0.5 mol % $[PdCl(\eta^3\text{-}C_3H_5)]_2$; CH_2Cl_2 as solvent.
[b] Conversion percentage of **12** and **13** determined by ^{1}H-NMR.
[c] Enantiomeric excesses determined by ^{1}H-NMR using $Eu(hfc)_3$.

Conclusion

A library of readily available diphosphite ligands has been synthesized for the Pd-catalyzed allylic substitution reactions of several substrate types. By carefully designing this library we were able to systematically investigate the effects of varying the configurations at C-3 and C-5 of the ligand backbone, the type of substituents at C-5 (H, Me and CH_2OTBDPS) and the type of substituents/configurations in the biaryl phosphite moieties. Particularly, for the hindered disubstituted acyclic substrate **S1**, we found that activities and enantioselectivities were highest with glucofuranoside ligands **4b** and **c**, which have an *S* configuration of C-3 and an *R* configuration of C-5, a methyl substituent at C-5 and bulky *tert*-butyl substituents in the *ortho* positions of the biphenyl phosphite moieties. By screening the library we were able to find other suitable ligands for this substrate **S1** (ligands **1b**–**d**, **g** and **4d**, **g**). For the unhindered cyclic substrate **S3**–**S5**, activities followed the same trends as those for the alkylation of substrate **S1**, but enantioselectivities were highest with ligands **4c**, **6c** and **7c**. Remarkably, ligands **4c** and **6c** offer the *S* and *R* enantiomers of the product, respectively, in high enantiomeric ex-

Table 5. Selected results for the Pd-catalyzed allylic alkylation of **S6** and **S7**.[a]



Entry	Substrate	Ligand	% Conversion (t/min)[b]	Branched to linear ratio (**b/l**)[b]	% ee[c]
1	**S6**	**1a**	42 (30)	7/93	15 (*S*)
2	**S6**	**1b**	100 (30)	24/76	23 (*S*)
3	**S6**	**1c**	100 (30)	14/86	7 (*S*)
4	**S6**	**2c**	26 (30)	29/71	33 (*R*)
5	**S6**	**3c**	100 (5)	30/70	5 (*R*)
6	**S6**	**4c**	100 (5)	24/76	29 (*S*)
7	**S6**	**5c**	100 (5)	29/71	16 (*S*)
8	**S6**	**6c**	100 (5)	24/76	9 (*R*)
9	**S6**	**7c**	80 (5)	17/83	19 (*S*)
10	**S7**	**4c**	100 (10)	34/66	95 (*S*)

[a] All reactions were run at room temperature: 1 mol % $[PdCl(\eta^3\text{-}C_3H_5)]_2$; CH_2Cl_2 as solvent.
[b] Conversion percentage and linear-to-branched ratio determined by ^{1}H-NMR.
[c] Enantiomeric excesses determined by HPLC on a Chiralcel-OJ column. Absolute configuration given in parentheses.

cesses. For the monosubstituted acyclic substrate **S6** and **S7**, this ligand library proved to be inadequate in terms of regioselectivities. However, we obtained high enantioselectivities by increasing the size of the substrate substituent. In this way, ligand **4c** provided 95% ee for substrate **S7**.

To sum up, by carefully selecting the ligand components we obtained high enantioselectivities (ees up to 99%) and high activities [TOFs up to $>3000\ mol \times (mol \times h)^{-1}$] in substrates with different steric properties. We highlight the excellent activities and enantioselectivities obtained with ligand **4c** for disubstituted acyclic and cyclic substrates with dimethyl malonate or benzylamine as nucleophiles. This is therefore an exceptional ligand that competes favorably with the few other ligands that also provide high ees for both types of substrates.[5] Mechanistic and computational studies are currently under way.

Experimental Section

General Considerations

All reactions were carried out using standard Schlenk techniques under an atmosphere of argon. Solvents were purified and dried by standard procedures. Diphosphite ligands **1**–**6** were prepared using previously described methods.[3,8] 1,2-*O*-Isopropylidene-6-*tert*-butyldiphenylsilyl-glucofuranose was prepared as previously reported.[9] Racemic substrates **S1**–**S7** were prepared as previously reported.[10–12] ^{1}H, ^{13}C{^{1}H}, and ^{31}P{^{1}H} NMR spectra were recorded using a 400 MHz spectrometer. Chemical shifts are relative to that of $SiMe_4$ (^{1}H and ^{13}C) as internal standard or H_3PO_4 (^{31}P) as external standard.

3,5-Bis[(3,3′-bis-*tert*-butyl-5,5′-dimethoxy-1,1′-biphenyl-2,2′-diyl)phosphite]-1,2-*O*-isopropylidene-6-*tert*-butyldiphenylsilyl-glucofuranose (7b)

Phosphorochloridite[13] (2.2 mmol) produced *in situ* was dissolved in toluene (5 mL) and pyridine (0.36 mL, 4.6 mmol) was added. 1,2-*O*-Isopropylidene-6-*tert*-butyldiphenylsilyl-glucofuranose (0.46 g, 1 mmol) was azeotropically dried with toluene (3 × 1 mL) and then dissolved in toluene (10 mL), to which pyridine (0.18 mL, 2.3 mmol) has been added. The diol solution was transferred slowly over 30 minutes at room temperature to the solution of phosphorochloridite. The reaction mixture was stirred overnight at 80 °C, and the pyridine salts were removed by filtration. Evaporation of the solvent gave a white foam, which was purified by flash chromatography (toluene, $R_f = 0.42$) to produce a white powder. Yield: 0.52 g (42%); ^{31}P NMR: δ = 145.3 (d, $J_{P\text{-}P}$ = 38 Hz), 147.3 (bd, $J_{P\text{-}P}$ = 38 Hz); ^{1}H NMR: δ = 0.85 (s, 9H, CH_3, *t*-Bu-Si), 1.13 (s, 3H, CH_3), 1.32 (s, 9H, CH_3, *t*-Bu), 1.33 (s, 9H, CH_3, *t*-Bu), 1.36 (s, 18H, CH_3, *t*-Bu), 1.40 (s, 28H, CH_3, *t*-Bu), 1.43 (s, 3H, CH_3), 1.53 (s, 9H, CH_3, *t*-Bu), 1.57 (s, 9H, CH_3, *t*-Bu), 3.81 (s, 3H, OMe), 3.84 (b, 9H, OMe), 4.10 (m, 2H, H-6′, H-6), 4.24 (d, 1H, H-2, $^3J_{H\text{-}H}$ = 3.6 Hz), 4.55 (m, 1H, H-5), 4.85 (m, 1H, H-4), 5.01 (m, 1H, H-3), 5.53 (d, 1H, H-1, $^3J_{H\text{-}H}$ = 3.6 Hz), 7.0–7.8 (m, 18H, CH=); ^{13}C NMR: δ = 26.9 (CH_3, *t*-Bu-Si), 27.0 (CH_3), 27.2 (CH_3), 31.4 (CH_3, *t*-Bu), 31.6 (CH_3, *t*-Bu), 31.7 (CH_3, *t*-Bu), 31.8 (CH_3, *t*-Bu), 31.9 (CH_3, *t*-Bu), 34.8 (C, *t*-Bu), 34.9 (C, *t*-Bu), 35.3 (C, *t*-Bu), 35.4 (C, *t*-Bu), 35.6 (C, *t*-Bu), 35.7 (C, *t*-Bu), 35.9 (C, *t*-Bu), 55.3 (OMe), 55.4 (OMe), 55.5 (OMe), 64.8 (C-6), 73.2 (b, C-5), 76.3 (C-3), 77.8 (C-4), 85.6 (C-2), 104.9 (C-1), 112.8 (CMe_2), 124.3 (CH=), 124.4 (CH=), 124.5 (CH=), 124.7 (d, CH=, $J_{C\text{-}P}$ = 6.1 Hz), 125.1 (CH=), 126.1 (d, CH=, $J_{C\text{-}P}$ = 3.2 Hz), 126.7 (d, CH=, $J_{C\text{-}P}$ = 4.2 Hz), 127.6 (CH=), 127.9 (CH=), 129.2 (d, CH=, $J_{C\text{-}P}$ = 8.0 Hz), 134.5 (C), 134.8 (C), 134.9 (C), 136.0 (C), 136.2 (CH=), 136.3 (CH=), 136.5 (C), 138.1 (C), 142.0 (C), 142.4 (C), 142.7 (C), 142.9 (C), 145.1 (C), 145.6 (C), 145.8 (C),

156.0 (C), 156.7 (C), 156.8 (C), 156.9 (C); anal. calcd. (%) for $C_{69}H_{88}O_{14}P_2Si$: C 67.30, H 7.20; found: C 67.56, H 7.11.

3,5-Bis[(3,3′,5,5′-tetra-*tert*-butyl-1,1′-biphenyl-2,2′-diyl)phosphite]-1,2-*O*-isopropylidene-6-*tert*-butyldiphenylsilyl-glucofuranose (7c).

Treatment of phosphrochloridite[13] (2.2 mmol) produced *in situ* and 1,2-*O*-isopropylidene-6-*tert*-butyldiphenylsilyl-glucofuranose (0.46 g, 1 mmol), as described for compound **7b**, afforded diphosphite **7c**, which was purified by flash chromatography (toluene) to produce a white powder. Yield: 0.64 g (48%); ^{31}P NMR: δ = 147.2 (d, $J_{P\text{-}P}$ = 62 Hz), 148.1 (bd, $J_{P\text{-}P}$ = 62 Hz); ^{1}H NMR: δ = 0.83 (s, 9H, CH_3, *t*-Bu-Si), 1.12 (s, 3H, CH_3), 1.30 (s, 9H, CH_3, *t*-Bu), 1.31 (s, 9H, CH_3, *t*-Bu), 1.32 (s, 18H, CH_3, *t*-Bu), 1.35 (s, 9H, CH_3, *t*-Bu), 1.36 (s, 9H, CH_3, *t*-Bu), 1.39 (s, 3H, CH_3), 1.49 (s, 9H, CH_3, *t*-Bu), 1.54 (s, 9H, CH_3, *t*-Bu), 4.05 (dd, 1H, H-6′, $^2J_{H\text{-}H}$ = 9.3 Hz, $^3J_{H\text{-}H}$ = 1.5 Hz),), 4.14 (dd, 1H, H-6, $^2J_{H\text{-}H}$ = 9.3 Hz, $^3J_{H\text{-}H}$ = 1.2 Hz), 4.27 (d, 1H, H-2, $^3J_{H\text{-}H}$ = 3.3 Hz), 4.65 (m, 1H, H-5), 4.85 (dd, 1H, H-4, $^2J_{H\text{-}H}$ = 9.3 Hz, $^3J_{H\text{-}H}$ = 2.7 Hz), 4.96 (m, 1H, H-3), 5.49 (d, 1H, H-1, $^3J_{H\text{-}H}$ = 3.3 Hz), 6.97 (t, 2H, CH=, $^3J_{H\text{-}H}$ = 5.4 Hz), 7.1–7.4 (m, 12H, CH=), 7.51 (d, 2H, CH=, $^3J_{H\text{-}H}$ = 5.4 Hz), =), 7.65 (dd, 2H, CH=, $^3J_{H\text{-}H}$ = 5.1 Hz, $^3J_{H\text{-}H}$ = 1.2 Hz); ^{13}C NMR: δ = 26.7 (CH_3, *t*-Bu-Si) 26.9 (CH_3), 27.0 (CH_3), 31.4 (CH_3, *t*-Bu), 31.5 (CH_3, *t*-Bu), 31.6 (CH_3, *t*-Bu), 31.7 (CH_3, *t*-Bu), 31.8 (CH_3, *t*-Bu), 31.9 (CH_3, *t*-Bu), 34.7 (C, *t*-Bu), 34.8 (C, *t*-Bu), 34.9 (C, *t*-Bu), 35.3 (C, *t*-Bu), 35.4 (C, *t*-Bu), 35.6 (C, *t*-Bu), 35.7 (C, *t*-Bu), 35.8 (C, *t*-Bu), 63.8 (C-6), 71.6 (d, C-5, $J_{C\text{-}P}$ = 16.2 Hz), 76.5 (C-3), 77.4 (C-4), 84.7 (C-2), 105.1 (C-1), 112.2 (CMe_2), 124.1 (CH=), 124.3 (CH=), 124.4 (CH=), 124.5 (d, CH=, $J_{C\text{-}P}$ = 6.1 Hz), 125.5 (CH=), 126.5 (d, CH=, $J_{C\text{-}P}$ = 3.8 Hz), 126.8 (d, CH=, $J_{C\text{-}P}$ = 4.5 Hz), 127.6 (CH=), 127.8 (CH=), 129.4 (d, CH=, $J_{C\text{-}P}$ = 8.3 Hz), 132.5 (C), 132.8 (C), 133.9 (C), 134.0 (C), 135.8 (CH=), 135.9 (CH=), 136.4 (C), 138.1 (C), 140.0 (C), 140.4 (C), 140.7 (C), 140.8 (C), 145.1 (C), 145.6 (C), 145.8 (C), 146.0 (C), 146.7 (C), 146.8 (C), 146.9 (C), 150.0 (C); anal. calcd. (%) for $C_{81}H_{112}O_{10}P_2Si$: C 72.83, H 8.45; found: C 73.01, H 8.31.

Typical Procedure for the Allylic Alkylation of Disubstituted Linear Substrates S1 and S2.

A degassed solution of $[PdCl(\eta^3\text{-}C_3H_5)]_2$ and the diphosphite ligand (1.1 equivs. to Pd) in dichloromethane (0.5 mL) was stirred for 30 min. Subsequently, a solution of substrate (0.5 mmol) in dichloromethane (1.5 mL), dimethyl malonate (171 μL, 1.5 mmol), *N*,*O*-bis(trimethylsilyl)acetamide (370 μL, 1.5 mmol) and a pinch of KOAc were added. The reaction mixture was stirred at room temperature. After the desired reaction time, the reaction mixture was diluted with Et_2O (5 mL) and saturated aqueous NH_4Cl solution (25 mL) was added. The mixture was extracted with Et_2O (3 × 10 mL) and the extract dried over $MgSO_4$. For substrate **S1**, conversion was measured by ^{1}H NMR and enantiomeric excess was determined by HPLC (Chiralcel-OD, 0.5% 2-propanol/hexane, flow 0.5 mL/min). For substrate **S2**, conversion and enantiomeric excess were determined by GC.

Typical Procedure for the Allylic Amination of *rac*-1,3-Diphenyl-3-acetoxyprop-1-ene (S1)

A degassed solution of $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (1.8 mg, 0.005 mmol) and the diphosphite ligand (0.011 mmol) in dichloromethane (0.5 mL) was stirred for 30 min. Subsequently, a solution of *rac*-**8** (126 mg, 0.5 mmol) in dichloromethane (1.5 mL) and benzylamine (131 μL, 1.5 mmol) were added. The reaction mixture was stirred at room temperature. After 1 hour the reaction mixture was diluted with Et_2O (5 mL) and saturated aqueous NH_4Cl solution (25 mL) was added. The mixture was extracted with Et_2O (3 × 10 mL) and the extract dried over $MgSO_4$. The solvent was removed and conversion was measured by ^{1}H-NMR. To determine the ee by HPLC (Chiralcel-OJ, 13% 2-propanol/hexane, flow 0.5 mL/min), a sample was filtered over silica using 10% Et_2O/hexane mixture as the eluent.

Typical Procedure for the Allylic Alkylation of Cyclic Substrates S3–S5

A degassed solution of $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (0.9 mg, 0.0025 mmol) and the diphosphite ligand (0.0055 mmol) in dichloromethane (0.5 mL) was stirred for 30 min. Subsequently, a solution of substrate (0.5 mmol) in dichloromethane (1.5 mL), dimethyl malonate (171 μL, 1.5 mmol), *N*,*O*-bis(trimethylsilyl)acetamide (370 μL, 1.5 mmol) and a pinch of KOAc were added. The reaction mixture was stirred at room temperature. After 30 min the reaction mixture was diluted with Et_2O (5 mL) and aqueous saturated NH_4Cl solution (25 mL) was added. The mixture was extracted with Et_2O (3 × 10 mL) and the extract dried over $MgSO_4$. For substrate **S3**, conversion and enantiomeric excess were determined by GC using an FS-Cyclodex β-I/P 25 m column, internal diameter 0.2 mm, film thickness 0.33 mm, carrier gas: 100 kPa He, FID detector). For substrates **S4** and **S5**, conversion was determined by GC and enantiomeric excess was determined by ^{1}H NMR using $Eu(hfc)_3$.

Typical Procedure for the Allylic Alkylation of Monosubstituted Linear Substrates S6 and S7

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

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