Palladium-Based Supramolecularly Regulated Catalysts for Asymmetric Allylic Substitutions

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Supporting Information

ABSTRACT: Herein is reported the effect of different polyether binders (alkali metal, alkaline earth metal and lanthanide salts) as regulation agents to enhance the catalytic properties of palladium complexes derived from enantiopure bisphosphite ligands in allylic substitutions. The addition of RbOAc or $M(OTf)_x$ ($M = Mg^{2+}$, La^{3+} or Ho^{3+}) led to positive effects in enantioselectivity (by up to 16% ee) for the allylic substitution reactions. These ligands coordinated in the usual *cis*-fashion or in an unprecedented *trans*-fashion to the palladium center, depending on the phosphite group, and presented different reactivity in the allylic substitutions.

INTRODUCTION

The search for efficient chiral catalysts for the broadest possible substrate scope in a given transformation is still a cutting-edge research goal, as structural changes to the substrate(s) and or reagent(s) often translate into a loss of enantioselectivity. Within the supramolecular enantioselective catalysis arena,[1] progress has been made in regulating the size and shape of the chiral catalyst,[2] or in modifying the first-sphere coordination geometry of the active metal.[3] However, there are few examples of fine-modification of the geometry of the active-site that do not imply major alteration of the principal structural features of the enantioselective catalyst.[4,5]

Fan *et al.* pioneered the use of supramolecularly regulated polyether-based ligands for rhodium-mediated hydrogenations.[5b] These authors reported the first example on the use of rhodium complexes derived from bisphosphite-polyether ligands in asymmetric hydrogenation, whose catalytic performance in terms of enantioselectivity was enhanced by the addition of a regulation agent (RA, Figure 1).[5b] Later, we also demonstrated that conformationally transformable bisphosphite ligands[4a-c] incorporating polyether groups behaved as supramolecularly regulated ligands in asymmetric hydroformylations[4a-c] and hydrogenations[4b] (Figure 1). We showed that enantioselectivities in the transformation of interest can be maximized by the choice of whether or not to use an RA (and if so, which one).[4a-c] Computational studies revealed that the significant increase in enantiomeric excess provided by the RAs in hydroformylation reactions resulted from adaptation of the P-Rh-P bond angle (β).[4b]

Pd-mediated allylic substitutions represent an efficient transformation to stereoselectively form C–C and C–X bonds.[6] Palladium complexes derived from *P* ligands are efficient catalysts for the reaction between allylic alcohol derivatives and nucleophiles,[7] which have often been generated *in situ* from the protonated nucleophile (i.e. a malonic ester) in the presence of *N*,*O*-bis(trimethylsilyl)-acetamide (BSA) and catalytic amounts of an alkali metal salt.[8]

Herein we report our efforts in expanding our supramolecular regulation strategy to allylic substitutions. We envisaged that the combination of ligands **1a**–**c** with Pd(II) precursors suitable for this chemistry and an array of metal salts (for both generating the required nucleophile and triggering the regulation mechanism in our ligands) could function as supramolecularly regulated catalysts in allylic substitutions.

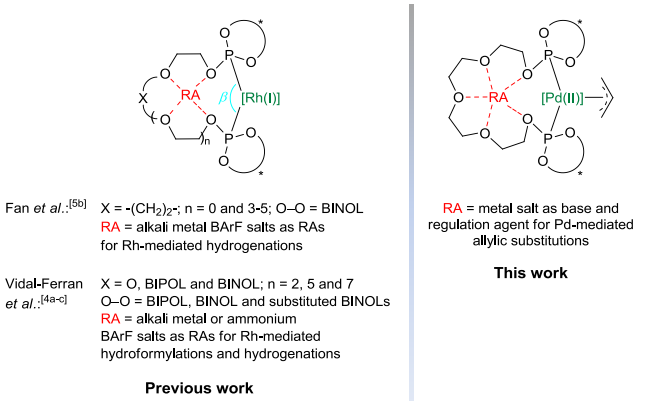


Figure 1. Supramolecularly regulated bisphosphite ligands in enantioselective catalysis (BIPOL = [1,1'-biphenyl]-2,2'-diol, BINOL = [1,1'-binaphthalene]-2,2'-diol).

RESULTS AND DISCUSSION

Ligand Synthesis. We initially designed ligands **1a**–**c** by combining the linker group that showed the highest regulation ability in our hydroformylation studies[4b] (see blue fragment in Figure 2) and an array of stereogenic phosphite groups (see green fragment in Figure 2). Bisphosphites **1a** and **1b** had already been described[9,4b,c] and compound **1c** was prepared in an analogous manner to **1a** and **1b**: reaction of tetraethylene glycol with two equivalents of the corresponding chlorophosphite in the presence of a base (NEt_3).

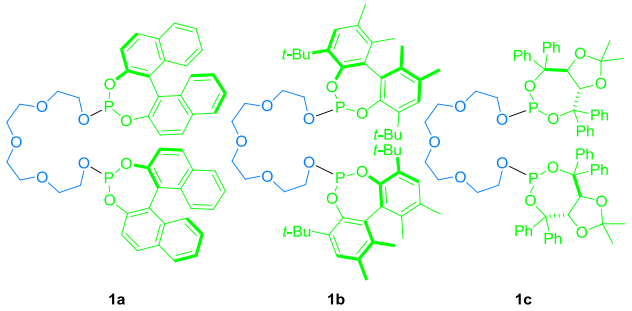
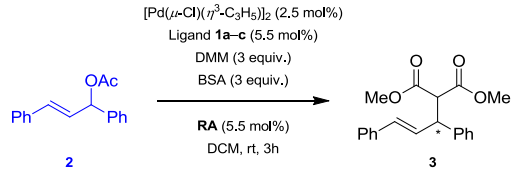


Figure 2. Set of supramolecular bisphosphite ligands **1a**–**c**.

Table 1. Pd-mediated Asymmetric Allylic Alkylation of 2 with Ligands 1a–c and Different Regulation Agents (RAs)[a]



entry	ligand	RA	conv. (%)[b]	ee **3** (%, config.)[c]
1	**1a**		>99	44 (*R*)
2	**1a**	LiOAc	>99	21 (*R*)
3	**1a**	CsOAc	>99	54 (*R*)
4	**1b**		>99	20 (*R*)
5	**1b**	LiOAc	>99	26 (*R*)
6	**1b**	CsOAc	>99	26 (*R*)
7[d]	**1c**		60	43 (*S*)
8	**1c**	LiOAc	>99	24 (*S*)
9[d]	**1c**	CsOAc	90	39 (*S*)

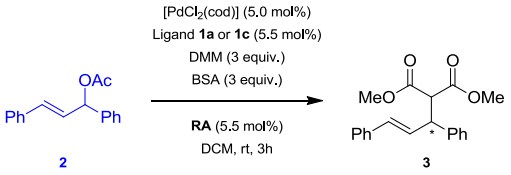
[a] Reaction conditions are indicated in the above scheme unless otherwise stated. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by HPLC on chiral stationary phases. [d] Reaction performed at rt for 24h.

Pd-mediated Asymmetric Allylic Substitutions. With ligands **1a**–**c** in hand, we then assessed their catalytic activity in combination with an array of RAs in allylic substitutions. Initially, we chose 1,3-diphenylallyl acetate **2** as the substrate and dimethyl malonate (DMM) as the nucleophile. The precatalysts were generated *in situ* from [Pd(μ-Cl)(η^3-C_3H_5)]$_2$, the ligands **1a**–**c** and the RA. The reactions were conducted in dichloromethane (CH_2Cl_2) as we considered that this solvent would provide a compromise between the solubility of the RA and its binding strength with the polyether fragment.[4b,10] As illustrated in Table 1, the palladium complexes derived from bisphosphites **1a**–**c** provided active catalysts displaying full conversion in almost all cases (see Table 1). Selectivity in the absence of regulation agents was moderate and highly dependent on the nature of the phosphite fragment.

The palladium complex of ligand **1a** incorporating an (S_a)-BINOL-derived phosphite fragment provided the best enantioselectivity (up to 44% ee, entry 1 in Table 1). A similar ee was observed for ligand **1c**, although reactivity was lower (see entry 7 in Table 1). Finally, the sterically more demanding phosphite groups in ligand **1b** led to a decrease in ee (see entry 4 in Table 1). As our regulation design allows new catalytic systems to be generated by employing a set of RAs, subsequent attempts to improve enantioselectivity following this strategy (addition of LiOAc or CsOAc) resulted in some cases in higher ee's for ligands **1a** and **1b** (increase of up to 10% ee, compare entry 1 with 3 in Table 1).

We then studied the influence of the Pd precursor on the outcome of the allylic substitutions by incorporating [$PdCl_2$(cod)] to our studies (Table 2). Interestingly, [$PdCl_2$(cod)] performed better than [Pd(μ-Cl)(η^3-C_3H_5)]$_2$ in terms of enantioselectivity (for instance, compare entries 1–3 in Table 1 with entries 1, 2 and 9 in Table 2). Of all the RA/ligand combinations tested, RbOAc•**1a** gave the best results: full conversion and 65% ee (increase of 6% ee with respect to when no RA was used, compare entry 1 with 6 in Table 2). Higher amounts of RbOAc did not bring any advantage in the result of the reaction and lower temperatures (0 ºC) resulted in no conversion (see entries 7 and 8 in Table 2, respectively). Two different potassium

Table 2. Allylic Alkylations of 2 with Bisphosphite Ligand 1a or 1c and Different RAs[a]



entry	ligand	RA	conv. (%)[b]	ee **3** (%, config.)[c]
1	**1a**		>99	59 (*R*)
2	**1a**	LiOAc	>99	46 (*R*)
3	**1a**	NaOAc	>99	62 (*R*)
4	**1a**	KOAc	>99	63 (*R*)
5	**1a**	KF	>99	62 (*R*)
6	**1a**	RbOAc	>99	65 (*R*)
7[d]	**1a**	RbOAc	>99	65 (*R*)
8[e]	**1a**	RbOAc	0	n.d.
9	**1a**	CsOAc	>99	56 (*R*)
10[f]	**1a**	$Mg(OTf)_2$	15	56 (*R*)
11[f]	**1a**	$Ba(OTf)_2$	>99	4 (*R*)
12	**1a**	$La(OTf)_3$	>99	3 (*R*)
13	**1a**	$Ho(OTf)_3$	>99	*rac*

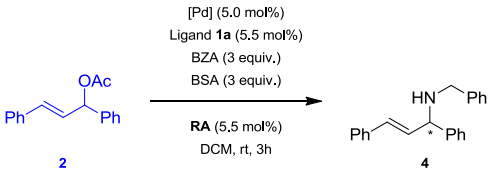
14[f]	**1c**		0	n.d.
15[f]	**1c**	LiOAc	0	n.d.
16[f]	**1c**	CsOAc	0	n.d.

[a] See footnotes a in Table 1. [b] See footnotes b in Table 1. [c] See footnotes c in Table 1. [d] 1.7 equiv of RA relative to Pd precursor was used. [e] Reaction performed at 0 ºC for 24h. [f] Reaction performed at rt for 24h.

salts with different counterions (*i.e.* KOAc and KF) were used as RAs, and no differences in reactivity were observed (compare entry 4 with 5 in Table 2). It should be noted that the use of alkaline earth metal or lanthanide triflates as RAs led to detrimental effects for both reactivity and selectivity (see entries 10–13 in Table 2). The palladium complex derived from bisphosphite **1c** led to inactive catalysts in this chemistry since no reactivity for the allylic alkylation of **2** was observed even in the presence of different RAs (see entries 14–16 in Table 2).

We then assessed the supramolecularly regulated catalysts derived from the lead bisphosphite **1a** in allylic substitutions using benzylamine (BZA) as a nitrogen nucleophile. Standard screening conditions were used and the results of this study are shown in Table 3. Complexes derived from **1a** performed as efficient catalysts in the allylic amination of **2** in terms of conversion (see Table 3). When no RAs were used, a low ee was achieved (30% ee, see entry 1 in Table 3). Interestingly, and in sharp contrast with the results using a *C*-nucleophile, an improvement in ee was obtained by using group II or lanthanides triflates as RAs (increase of up to 16% ee with $Mg(OTf)_2$, $La(OTf)_3$ or $Ho(OTf)_3$; see entries 4, 7, and 8 in Table 3) and [Pd(μ-Cl)(η^3-C_3H_5)]$_2$ as palladium precursor (compare entry 4 with 5 in Table 3).

Table 3. Allylic Amination of 2 with Bisphosphite Ligand 1a and Different RAs[a]

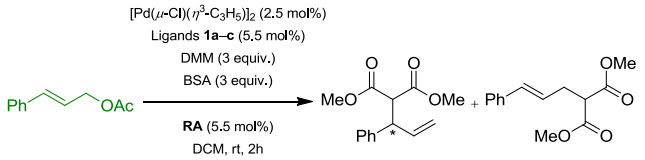


entry	ligand, Pd-precursor	RA	conv. (%)[b]	ee **4** (%, config.)[c]
1	**1a**, [Pd(μ-Cl)(η^3-C_3H_5)]$_2$		>99	30 (*S*)
2[d]	**1a**, [Pd(μ-Cl)(η^3-C_3H_5)]$_2$	LiOAc	>99	33 (*S*)
3	**1a**, [Pd(μ-Cl)(η^3-C_3H_5)]$_2$	CsOAc	0	n.d.
4	**1a**, [Pd(μ-Cl)(η^3-C_3H_5)]$_2$	$Mg(OTf)_2$	>99	46 (*S*)
5	**1a**, [$PdCl_2$(cod)]	$Mg(OTf)_2$	35	29 (*S*)
6	**1a**, [Pd(μ-Cl)(η^3-C_3H_5)]$_2$	$Ba(OTf)_2$	>99	45 (*S*)
7	**1a**, [Pd(μ-Cl)(η^3-C_3H_5)]$_2$	$La(OTf)_3$	>99	46 (*S*)
8	**1a**, [Pd(μ-Cl)(η^3-C_3H_5)]$_2$	$Ho(OTf)_3$	>99	46 (*S*)

[a] See footnotes a in Table 1. [b] See footnotes b in Table 1. [c] See footnotes c in Table 1. [d] Reaction performed at rt for 72h.

Finally, we tested our set of supramolecular bisphosphite ligands in the Pd-mediated allylic substitution of cinnamyl acetate **5** using DMM as nucleophile under standard screening conditions (Table 4). In general terms, palladium complexes derived from bisphosphites **1** were efficient catalysts in the alkylation of substrate **5** in terms of conversion (see Table 4). As expected for palladium-based catalysts,[7d,e] and in the absence of regulation agents, either low branched-to-linear ratios (b/l ratio, see entries 1 and 4 in Table 4) or exclusively the linear product **7** (see entries 5 and 12 in Table 4) were achieved depending on both the bisphosphite and the palladium precursor (see results for ligand **1b**, compare entry 4 with 5 in Table 4). In terms of enantioselectivity, a respectable value of 60% ee at a b/l ratio of 12/88 was achieved by using the palladium complex derived from **1b** and [Pd(μ-Cl)(η^3-C_3H_5)]$_2$ (see entry 4 in Table 4). Interestingly, the use of LiOAc or CsOAc as RAs led to an increase in the regioselectivity of the reaction for the palladium complex derived of **1a** (b/l ratio up to 17/83; entries 2 and 3 in Table 4).[7] Unfortunately, the enantioselectivity could not be further improved for those catalytic systems leading to the highest ratio of branched product.

Table 4. Allylic Alkylation of 5 with Bisphosphite Ligands 1a–c and Different RAs[a]



entry	ligand	RA	conv. (%)[b]	**6**/**7** ratio[b]	ee **6** (%, config.)[c]
1	**1a**		>99	14/86	28 (*R*)
2	**1a**	LiOAc	>99	17/83	19 (*R*)
3	**1a**	CsOAc	>99	17/83	32 (*R*)
4	**1b**		>99	12/88	60 (*R*)
5[d]	**1b**		75	>1/99	n.d.
6	**1b**	LiOAc	>99	14/86	57 (*R*)
7	**1b**	CsOAc	>99	11/89	55 (*R*)
8	**1b**	$Mg(OTf)_2$	>99	15/85	50 (*R*)
9	**1b**	$Ba(OTf)_2$	0	n.d.	n.d.
10	**1b**	$La(OTf)_3$	>99	12/88	42 (*R*)
11	**1b**	$Ho(OTf)_3$	0	n.d.	n.d.
12	**1c**		>99	>1/99	n.d.
13	**1c**	LiOAc	>99	>1/99	n.d.
14	**1c**	CsOAc	>99	>1/99	n.d.

[a] See footnotes a in Table 1. [b] See footnotes b in Table 1. [c] See footnotes c in Table 1.. [d] [$PdCl_2$(cod)] (5.0 mol%) was used as metal precursor and the reaction was performed at rt for 6h.

Coordination studies. After having studied bisphosphite ligands **1a**–**c** in Pd-mediated allylic substitutions, we carried out coordination studies in order to gain insight into the reactivity of the palladium precatalysts derived from **1a** and **1c** (see Table 2) as well as into the regulation mechanism. The reaction of bisphosphites **1a** and **1c** with [$PdCl_2$(cod)] proceeded smoothly to provide the corresponding palladium complexes [$PdCl_2$(**1a**)] (**8a**) and [$PdCl_2$(**1c**)] (**8c**), which were isolated and characterized. The $^{31}P\{^1H\}$ NMR spectra for

compounds **8a** and **8c** showed single resonances at 109.8 and 90.2 ppm, respectively.[11] It is interesting to note that the signal of TADDOL-based bisphosphite **8c** was shielded upfield with respect to the signal of **8a** ($\Delta\delta \approx 20$ ppm), which might hint at important structural differences between palladium complexes **8a** and **8c**. Interestingly, compounds **8a** and **8c** could be crystallized, and X-ray analysis unambiguously established their structures.[12] For **8a**, the palladium center had a distorted square-planar geometry in which the two phosphorus groups of ligand **1a** were coordinated in a *cis*-fashion (see Figure 3 and Table 5). Meanwhile in complex **8c**, the palladium center also displayed a square-planar geometry but with the phosphorus groups of ligand **1c** occupying *trans*-binding sites (see Figure 3 and Table 5). To the best of our knowledge, this is the first reported example of a *trans*-chelating bisphosphite in Pd complexes, which appears to be bound to a lack of reactivity in this chemistry (see entries 14–16 in Table 2). Finally, to support our hypothesis on the regulation mechanism, we studied the interaction of RbOAc with the regulation site of the highest-performing palladium complex **8a**. NMR analysis qualitatively demonstrated the binding of RbOAc within the polyethyleneoxy moieties: the addition of incremental amounts of RbOAc to a solution of **8a** (up to 1.7 equiv.) caused significant changes to the chemical shift, multiplicity, and signal width of the polyethyleneoxy fragments.[12] These results suggest that binding of RbOAc within the polyethyleneoxy moieties is involved in the regulation effects mediated by the RA in the described allylic substitutions.

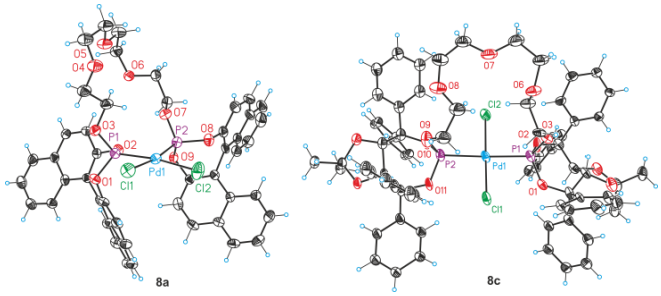


Figure 3. Crystal structures of **8a** and **8c** (ORTEP drawings showing in both cases thermal ellipsoids at 30% probability).

Table 5. Selected Bond Lengths (Å) and Angles (°) for Palladium Complexes 8a and 8c.

Compound **8a**		Compound **8c**	
Atoms	Lengths (Å) or Angles (°)	Atoms	Lengths (Å) or Angles (°)
Pd1-P1	2.2141(17)	Pd1-P1	2.287(2)
Pd1-P2	2.2191(16)	Pd1-Cl1	2.291(2)
Pd1-Cl2	2.3113(17)	Pd1-Cl2	2.291(2)
Pd1-Cl1	2.3450(16)	Pd1-P2	2.301(2)
P1-Pd1-P2	92.45(6)	P1-Pd1-Cl1	91.30(7)
P1-Pd1-Cl2	172.10(6)	P1-Pd1-Cl2	88.36(8)
P2-Pd1-Cl2	93.27(6)	Cl1-Pd1-Cl2	174.58(10)
P1-Pd1-Cl1	83.41(6)	P1-Pd1-P2	177.39(8)
P2-Pd1-Cl1	171.04(5)	Cl1-Pd1-P2	91.30(7)
Cl2-Pd1-Cl1	91.66(6)	Cl2-Pd1-P2	89.07(8)

CONCLUSIONS

In summary, we designed and prepared supramolecularly regulated ligands for Pd-mediated asymmetric allylic substitutions. The selectivity (both regio- and stereoselectivity) of the allylic substitutions mediated by bisphosphites **1** could be regulated by using several alkali metal, alkaline earth metal or lanthanide salts as regulation agents. Positive increments in the regio- and enantioselectivity were achieved in the allylic substitutions of benchmark substrates using carbon and nitrogen nucleophiles. The distinct reactivity between **8a** and **8c** in allylic substitution reactions may be attributed to the different coordination mode of bisphosphite ligands **1a** and **1c** with [$PdCl_2$(cod)] (in a *cis*- or *trans*-fashion, respectively), as demonstrated by X-ray single crystal analysis.

EXPERIMENTAL SECTION

General considerations. All syntheses were carried out using chemicals as purchased from commercial sources unless otherwise cited. All manipulations and reactions were performed under inert atmosphere. Glassware was dried *in vacuo* before use with a hot air gun. All solvents were dried and deoxygenated by using a Solvent Purification System (SPS). Silica gel 60 (230 – 400 mesh) or C18–SiO_2 (200 – 400 mesh) was used for column chromatography. NMR spectra were recorded in $CDCl_3$ unless otherwise cited. ^{1}H NMR and ^{13}C NMR chemical shifts were quoted in ppm relative to residual solvent peaks, whereas ^{31}P{^{1}H} NMR chemical shifts were quoted in ppm relative to 85% phosphoric acid in water. High-resolution mass spectra (HRMS) were recorded by using an electrospray ionization (ESI) method in positive mode or matrix-assisted laser desorption/ionization (MALDI) method, respectively. Melting points were determined in open capillaries and are uncorrected. Enantiomeric excesses were determined by HPLC equipped with a diode array detector using chiral stationary phases.

General synthetic procedure for bisphosphite ligands (1a–c). Under inert atmosphere, the chlorophosphites (1 equiv) were dissolved in anhydrous toluene (25 mL per mmol of the chlorophosphites) and NEt_3 (3 equiv). A solution of tetraethylene glycol (0.46 equiv., in 50 mL of toluene per mmol of tetraethylene glycol) was slowly added to the previous solution and allowed to react overnight at rt. The reaction mixture was filtered and the solvent evaporated *in vacuo*. The resulting crude mixtures were purified by column chromatography on C18–SiO_2 using acetonitrile/ethyl acetate 1:1 as elution solvent to provide the expected bisphosphites **1** as white solids.

Compound **1c**. Compound **1c** was synthesised from TADDOL-derived chlorophosphite[13] (1.44 g, 2.71 mmol) and a slow addition of tetraethylene glycol (243.0 mg, 1.25 mmol) with NEt_3 (0.52 mL, 3.75 mmol) as base. Purification by C18–SiO_2 column chromatography afforded the expected bisphosphite ligand **1c** as a white solid (1.05 g, 71% yield). mp 90.3–95.3 °C. $[\alpha]_D^{24}$ +162.4 (*c* 0.39 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.57 (6H, s), 0.91 (6H, s), 3.40–3.48 (4H, m), 3.53–3.61 (8H, m), 3.85–4.02 (4H, m), 5.06 (2H, dd, $^3J_{H,H}$ = 8.3 Hz, $^4J_{H,P}$ = 1.8 Hz), 5.19 (2H, d, $^3J_{H,H}$ = 8.3 Hz), 7.19–7.36 (24H, m), 7.42–7.45 (4H, m), 7.50–7.60 (12H, m). ^{13}C{^{1}H,^{31}P} NMR (125 MHz, $CDCl_3$) δ 26.3, 27.0, 61.9, 70.7, 70.8, 81.2, 82.3, 82.9, 85.0, 112.8, 127.2, 127.29, 127.33, 127.4, 127.5, 127.8, 128.0, 128.3, 128.9, 129.2, 141.5, 141.7, 146.2, 146.3. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 134.6 (s). HRMS (ESI$^+$) *m/z* calcd for $C_{70}H_{72}O_{13}P_2Na$ [M + Na]$^+$ 1205.4340, found 1205.4339. Anal. Calcd. for $C_{70}H_{72}O_{13}P_2$: C, 71.05; H, 6.13. Found: C, 71.85; H, 6.25.

General synthetic procedure for Pd-complexes based on bisphosphite ligands (8a and 8c). A solution of enantiomerically pure bisphosphite ligand **1a** or **1c** (0.059 mmol) in dry CH_2Cl_2 (1.8 mL) was slowly added to a solution of [$PdCl_2$(cod)] (0.054 mmol) in CH_2Cl_2 (0.2 mL) at room temperature under inert atmosphere. The reaction mixture was stirred for 2 h, after which the CH_2Cl_2 solvent was evaporated off until the mixture had one fourth of its original volume. Hexane (15.0 mL) was added, leading to the formation of a

precipitate, which was filtered off and then washed with a small quantity of hexane (1 x 5.0 mL) to give the desired Pd(II) complexes [$PdCl_2$(**1**)] as yellowish powders.

Compound **8a.** Palladium complex **8a** was prepared following the general procedure, starting from ligand **1a** (117 mg, 0.142 mmol) and [$PdCl_2$(cod)] (37 mg, 0.129 mmol). It was obtained as a yellowish powder (27 mg, 20% yield). mp 187.0–190.0 °C. $[\alpha]_D^{25}$ –40.4 (*c* 0.10 in CH_2Cl_2). ^{1}H NMR (500 MHz, C_4D_8O) δ 3.65–3.85 (12H, m), 4.23–4.26 (2H, m), 4.65–4.70 (2H, m), 6.75 (2H, d, $^3J_{H,H}$ = 8.8 Hz), 7.25–7.35 (8H, m), 7.44–7.47 (2H, m), 7.52–7.55 (2H, m), 7.63 (2H, d, $^3J_{H,H}$ = 8.8 Hz), 7.77 (2H, d, $^3J_{H,H}$ = 8.9 Hz), 7.97 (2H, d, $^3J_{H,H}$ = 8.2 Hz), 8.06–8.08 (4H, m). ^{13}C{^{1}H} NMR (125 MHz, C_4D_8O) δ 70.8, 71.5, 71.7, 72.0, 121.8, 122.0, 122.6, 123.6, 126.6, 126.8, 127.6, 127.7, 127.9, 129.4, 129.6, 131.9, 132.1, 132.8, 133.1, 133.2, 133.4, 147.1. ^{31}P{^{1}H} NMR (202 MHz, C_4D_8O) δ 109.8 (s). HRMS (MALDI$^+$) *m*/*z* calcd for $C_{48}H_{40}O_9P_2ClPd$ [M – Cl]$^+$ 963.0865, found 963.0839. Anal. Calcd. for $C_{48}H_{40}O_9P_2Cl_2Pd$: C, 57.65; H, 4.03. Found: C, 57.33; H, 4.44.

Compound **8c.** Palladium complex **8c** was prepared following the general procedure, starting from ligand **1c** (70 mg, 0.059 mmol) and [$PdCl_2$(cod)] (15 mg, 0.053 mmol). It was obtained as a yellowish powder (47 mg, 65% yield). mp 210.2–214.9 °C. $[\alpha]_D^{27}$ +160.6 (*c* 0.04 in CH_2Cl_2). ^{1}H NMR (500 MHz, C_4D_8O) δ 0.41 (6H, s), 1.25 (6H, s), 2.76–2.80 (2H, m), 2.86–2.91 (2H, m), 3.20–3.25 (2H, m), 3.35–3.39 (6H, m), 3.54–3.60 (2H, m), 3.75–3.81 (2H, m), 5.07 (2H, d, $^3J_{H,H}$ = 8.4 Hz), 5.74 (2H, d, $^3J_{H,H}$ = 8.4 Hz), 7.24–7.40 (24H, m), 7.51–7.52 (4H, m), 7.72–7.74 (4H, m), 7.83–7.85 (8H, m). ^{13}C{^{1}H} NMR (125 MHz, C_4D_8O) δ 23.1, 24.8, 66.7, 68.6, 68.9, 77.6, 80.1, 86.6, 86.67, 86.71, 86.87, 86.92, 87.0, 111.1, 125.1, 125.3, 125.4, 125.6, 125.7, 125.9, 126.5, 127.5, 138.4, 139.2, 142.7, 143.5. ^{31}P{^{1}H} NMR (202 MHz, C_4D_8O) δ 90.2 (s). HRMS (ESI$^+$) *m*/*z* calcd for $C_{70}H_{73}O_{14}P_2ClPd$ [M + OH – Cl]$^+$ 1340.3213, found 1340.3233. Anal. Calcd. for $C_{70}H_{72}O_{13}P_2Cl_2Pd\cdot0.5CH_2Cl_2$: C, 60.35; H, 5.24. Found: C, 60.78; H, 5.68.

General procedure for Pd-mediated allylic alkylation of *rac*-1,3-diphenylallyl acetate (2). A solution of [Pd(μ-Cl)(η^3-C_3H_5)]$_2$ (2.50 μmol) or [$PdCl_2$(cod)] (5.00 μmol) and enantiopure bisphosphite **1** (5.50 μmol) in CH_2Cl_2 (0.30 mL) was stirred for 15 min. Subsequently a solution of 1,3-diphenylallyl acetate **2** (0.1 mmol) in CH_2Cl_2 (0.10 mL), dimethyl malonate (0.3 mmol), *N*,*O*-bis(trimethylsilyl)-acetamide (0.3 mmol) and regulation agent (RA, 5.50 μmol; if appropriate) were added. The reaction mixture was stirred at room temperature for the appropriate reaction time. The reaction mixture was then diluted with Et_2O (4.0 mL) and washed with water (2 x 2.0 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The conversion was determined by ^{1}H NMR spectroscopy and the enantiomeric excess was determined by HPLC on chiral stationary phases (Daicel Chiralcel® OD–H, 99:1 *n*-hexane/2-propanol, 0.5 mL/min, 216 nm).[14]

General procedure for Pd-mediated allylic amination of *rac*-1,3-diphenylallyl acetate (2). A solution of [Pd(μ-Cl)(η^3-C_3H_5)]$_2$ (2.50 μmol) and enantiopure bisphosphite **1** (5.50 μmol) in CH_2Cl_2 (0.30 mL) was stirred for 15 min. Subsequently a solution of 1,3-diphenylallyl acetate **2** (0.1 mmol) in CH_2Cl_2 (0.10 mL), benzylamine (0.3 mmol), *N*,*O*-bis(trimethylsilyl)-acetamide (0.3 mmol) and regulation agent (RA, 5.50 μmol; if appropriate) were added. The reaction mixture was stirred at rt for the appropriate reaction time. The reaction mixture was then diluted with Et_2O (4.0 mL) and washed with water (2 x 2.0 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The conversion was determined by ^{1}H NMR spectroscopy and the enantiomeric excess was determined by HPLC on chiral stationary phases (Daicel Chiralcel® OD–H, 99:1 *n*-hexane/2-propanol, 0.6 mL/min, 254 nm).[15]

General procedure for Pd-mediated allylic alkylation of cinnamyl acetate (5). A solution of [Pd(μ-Cl)(η^3-C_3H_5)]$_2$ (2.50 μmol) and enantiopure bisphosphite **1** (5.50 µmol) in CH_2Cl_2 (0.30 mL) was stirred for 15 min. Subsequently a solution of cinnamyl acetate **5** (0.1 mmol) in CH_2Cl_2 (0.10 mL), dimethyl malonate (0.3 mmol), *N*,*O*-bis(trimethylsilyl)-acetamide (0.3 mmol) and regulation agent (RA, 5.50 μmol; if appropriate) were added. The reaction mixture was stirred at rt for the appropriate reaction time. The reaction mixture was then diluted with Et_2O (4.0 mL) and washed with water (2 x 2.0 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The conversion was determined by ^{1}H NMR spectroscopy and the enantiomeric excess was determined by HPLC on chiral stationary phases (Daicel Chiralcel® OJ–H, 97:3 *n*-hexane/2-propanol, 0.7 mL/min, 220 nm).[14]

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.5b00962.

Text and figures giving characterization data, and NMR spectra for new compounds (PDF)

Crystallographic data for **8a** and **8c** (CIF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) For selected reviews see: (a) Raynal, M.; Ballester, P.; Vidal-Ferran, A.; van Leeuwen, P. W. N. M. *Chem. Soc. Rev.* **2014**, *43*, 1660–1733. (b) Raynal, M.; Ballester, P.; Vidal-Ferran, A.; van Leeuwen, P. W. N. M. *Chem. Soc. Rev.* **2014**, *43*, 1734–1787.

(2) (a) Gianneschi, N. C.; Bertin, P. A.; Nguyen, S. T.; Mirkin, C. A.; Zakharov, L. N.; Rheingold, A. L. *J. Am. Chem. Soc.* **2003**, *125*, 10508–10509. (b) Gianneschi, N. C.; Cho, S.-H.; Nguyen, S. B. T.; Mirkin, C. A. *Angew. Chem. Int. Ed. Engl.* **2004**, *43*, 5503–5507. (c) Sud, D.; Norsten, T. B.; Branda, N. R. *Angew. Chem. Int. Ed.* **2005**, *44*, 2019–2021. (d) Wang, J.; Feringa, B. L. *Science* **2011**, *331*, 1429–1432.

(3) (a) Bellini, R.; Chikkali, S. H.; Berthon-Gelloz, G.; Reek, J. N. H. *Angew. Chem., Int. Ed.* **2011**, *50*, 7342–7345. (b) Bellini, R.; Reek, J. N. H. *Chem.-Eur. J.* **2012**, *18*, 7091–7099. (c) Bellini, R.; Reek, J. N. H. *Chem.-Eur. J.* **2012**, *18*, 13510–13519.

(4) (a) Mon, I.; Jose, D. A.; Vidal-Ferran, A. *Chem.-Eur. J.* **2013**, *19*, 2720–2725. (b) Vidal-Ferran, A.; Mon, I.; Bauza, A.; Frontera, A.; Rovira, L. *Chem. - Eur. J.* **2015**, *21*, 11417–11426. (c) Rovira, L.; Vaquero, M.; Vidal-Ferran, A. *J. Org. Chem.* **2015**, *80*, 10397–10403. (d) Fernández-Pérez, H.; Mon, I.; Frontera, A.; Vidal-Ferran, A. *Tetrahedron* **2015**, *71*, 4490–4494.

(5) (a) Clarke, M. L.; Fuentes, J. A. *Angew. Chem. Int. Ed.* **2007**, *46*, 930–933. (b) Li, Y.; Ma, B.; He, Y.; Zhang, F.; Fan, Q.-H. *Chem. Asian J.* **2010**, *5*, 2454–2458. (c) van Leeuwen, P. W. N. M.; Rivillo, D.; Raynal, M.; Freixa, Z. *J. Am. Chem. Soc.* **2011**, *133*, 18562–18565. (d) Dydio, P.; Rubay, C.; Gadzikwa, T.; Lutz, M.; Reek, J. N. H. *J. Am. Chem. Soc.* **2011**, *133*, 17176–17179. (e) Song, F.-T.; Ouyang, G.-H.; Li, Y.; He, Y.-M.; Fan, Q.-H. *Eur. J. Org. Chem.* **2014**, 6713–6719. f) Ouyang, G.-H.; He, Y.-M.; Fan, Q.-H. *Chem. - Eur. J.* **2014**, *20*, 16454–16457.

(6) For selected contributions see: (a) Trost, B. M.; Lee. C. Asymmetric Carbon-Carbon Bond-Forming Reactions: Asymmetric Allylic

Alkylation Reactions. In *Catalytic Asymmetric Synthesis*; Ojiwa, I., Ed.; Wiley-VCH: New York, 2000, Vol. 8e, pp 593–649. (b) Trost, B. M.; Zhang, T.; Sieber, J. D. *Chem. Sci.* **2010**, *1*, 427–440.

(7) For selected contributions see: (a) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921–2944. (b) Gavrilov, K. N.; Bondarev, O. G.; Polosukhin, A. I. *Russ. Chem. Rev.* **2004**, *73*, 671–699. (c) Takacs, J. M.; Reddy, D. S.; Moteki, S. A.; Wu, D.; Palencia, H. *J. Am. Chem. Soc.* **2004**, *126*, 4494–4495. (d) Lu, Z.; Ma, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 258–297. (e) Diéguez, M.; Pàmies, O. *Acc. Chem. Res.* **2010**, *43*, 312–322. (f) Grabulosa, A.; Doran, S.; Brandariz, G.; Muller, G.; Benet-Buchholz, J.; Riera, A.; Verdaguer, X. *Organometallics* **2014**, *33*, 692–701.

(8) (a) El Gihani, M. T.; Heaney, H. *Synthesis* **1998**, 357–375. (b) Trost, B. M.; Murphy, D. J. *Organometallics* **1985**, *4*, 1143–1145.

(9) Reetz, M. T.; Mehler, G.; Bondarev, O. *Chem. Commun.* **2006**, 2292–2294.

(10) Jose, D. A.; Mon, I.; Fernandez-Perez, H.; Escudero-Adan, E. C.; Benet-Buchholz, J.; Vidal-Ferran, A. *Org. Lett.* **2011**, *13*, 3632–3635.

(11) The $^{31}P\{^{1}H\}$ NMR chemical shift for **8a** is similar to that previously reported for a related Pd-complex. See: Sheff, J. T.; Lucius, A. L.; Owens, S. B.; Gray, G. M. *Organometallics* **2011**, *30*, 5695–5709.

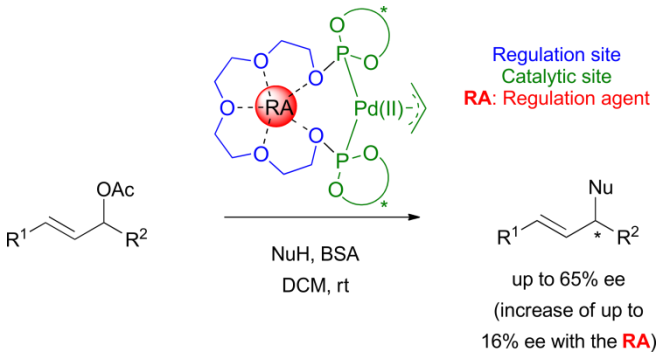
(12) See the Supporting Information for details.

(13) Wassenaar, J.; de Bruin, B.; Reek, J. N. H. *Organometallics* **2010**, *29*, 2767–2776.

(14) Popa, D.; Puigjaner, C.; Gómez, M.; Benet-Buchholz, J.; Vidal-Ferran, A.; Pericàs, M. A. *Adv. Synth. Catal.* **2007**, *349*, 2265–2278.

(15) Popa, D.; Marcos, R.; Sayalero, S.; Vidal-Ferran, A.; Pericàs, M. A. *Adv. Synth. Catal.* **2009**, *351*, 1539–1556.

TOC graphic:


OAc
R1
R2
RA
Pd(II)
Regulation site
Catalytic site
RA: Regulation agent
NuH, BSA
DCM, rt
Nu
R1
R2
up to 65% ee
(increase of up to
16% ee with the RA)