



Chiral Phosphines

When Chirality Meets "Buchwald-Type" Phosphines: Synthesis and Evaluation in Frustrated Lewis Pair-, Lewis Base- and Palladium-Promoted Asymmetric Catalysis

Mickaël J. Fer,^[a] Joséphine Cinqualbre,^[a] Julien Bortoluzzi,^[a] Matthieu Chessé,^[a] Frédéric R. Leroux,^[a] and Armen Panossian^{*[a]}

Abstract: We describe the synthesis of axially chiral "Buchwald ligand"-like biphenylphosphines in highly enantioenriched form. These monodentate phosphines, biphenyl analogues of Hayashi's MOP ligands, were evaluated in phosphine-promoted

Introduction

The importance of axially chiral biaryls, especially in catalysis, has motivated intense work towards enabling their synthetic access.^[1] Among such agents, efforts focussed on binaphthylbased bidentate phosphorus ligands have seen tremendous success in asymmetric catalysis.^[2] Hayashi et al. have also demonstrated the high efficiency of simply monodentate binaphthylphosphines -MOP ligands- in transition metal-catalyzed asymmetric reactions.^[3] On the other hand, much less effort has been applied to the study of enantiopure axially chiral biphenylmonophosphines; only a few examples have been reported, including monodentate ligands - i.e. the biphenyl equivalents of Hayashi's MOP ligands.^[4] Considering the remarkable results achieved by Buchwald et al. and others in catalytic reactions mediated by the corresponding achiral biphenylphosphine ligands,^[5] as well as our own interest in the synthesis of C_1 -symmetric biphenylphosphines and atropisomerically pure biphenyls,^[6] we decided to tackle the synthesis of such atropo-enantiopure biphenylphosphines (Figure 1, a). We were interested in assessing the latter structures in catalysis, and to comparing them with binaphthyl analogues. Indeed, biphenyls are expected to allow for better structural and electronic tuning in closer vicinity to the chiral aryl-aryl bond and the phosphorus function (Figure 1, b). Consequently, a highly modular and perfectly enantioselective route to these biphenylphosphines was required. We thus decided to take advantage of our previously developed sulfoxide-based deracemization/desymmetrization strategy. From atropisomerically pure biarylsulfoxides, we had shown that a chemo- and enantioselective sulfoxide/lithium exchange, followed by trapping with various elec-

 [a] CNRS - Université de Strasbourg (ECPM), UMR 7509, COHA25, Rue Becquerel, 67087 Strasbourg, France E-mail: armen.panossian@unistra.fr http://coha-lab.org

Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under http://dx.doi.org/10.1002/ejoc.201600727.

organocatalysis and in hydrosilylations catalyzed by palladium or by frustrated Lewis pairs. As expected, the title phosphines appeared best suited for transition metal catalysis where they provided higher asymmetric induction.

trophiles, was possible and opened access to various enantiopure biphenyls.^[6c] The remaining question was whether or not a phosphorus electrophile could be used in this strategy with retention of axial stereoenrichment and, in the case of chlorodiarylphosphine electrophiles, without preponderant formation of undesired dibenzophospholes.^[6a,6b]



Figure 1. Binaphthyl- vs. biphenylphosphines.

Results and Discussion

We chose to start from 2,2'-dibromo-6-chlorobiphenyl (1) as the platform from which to access desired atropo-enantiopure biphenylphosphines, as well as their racemic counterparts and corresponding oxides (Scheme 1). The racemic synthesis of biphenylphosphines **3** was carried out by means of regioselective bromine/lithium exchange using BuLi and subsequent trapping with chlorophosphines under standard reaction conditions. This strategy delivered the desired compounds in 26–65 % yields, depending on the chlorophosphines used and the air-stability of corresponding products **3** (Table 1). Chlorodicyclohexylphos-





phine gave the best results, whereas the *p*-tolyl and 1-napththyl analogues afforded complex reaction mixtures from which neither phosphine (\pm) -**3e** or (\pm) -**3g** could be isolated. Diisopropylphosphine (\pm) -**3b** was found to be particularly oxidizable and, consequently, also proved elusive. All the remaining phosphines could be handled without need of a glovebox although they were rather air-sensitive when not in the solid state. In such cases, they could be taken up in pentane and concentrated to yield the desired compounds as solids.

Entry	R	3	Yield [%]	4	Yield [%]	er ^[b]
1	Cy	(±)-3a	65	(±)- 4a	76	-
2	<i>i</i> Pr	(±)- 3b	_[c]	(±)- 4b	-	-
3	Ph	(±)- 3c	54	(±)- 4c	82	-
4	<i>o</i> Tol	(±)- 3d	32	(±)- 4d	85	-
5	<i>p</i> Tol	(±)- 3e	_[d]	(±)- 4e	-	-
6	4-F-C ₆ H ₄	(±)- 3f	26	(±)- 4f	86	-
7	1-Naphth	(±)- 3g	_[d]	(±)- 4g	-	-
8	Су	(aR)- 3a	52	(a <i>R</i>)- 4a	76	> 99:1
9	Ph	(a <i>R</i>)- 3c	55	(a <i>R</i>)- 4c	81	99:1
10	<i>o</i> Tol	(a <i>R</i>)- 3d	26	(a <i>R</i>)- 4d	92	98:2
11	4-F-C ₆ H ₄	(a <i>R</i>)- 3f	37	(a <i>R</i>)- 4f	76	98:2
12	Су	(±)- 3′a	51	(±)- 4'a	76	-
13	Ph	(±)- 3′b	61	(±)- 4′b	89	-
14	Су	(aR)- 3′a	54	(a <i>R</i>)- 4′a	83	> 99:1
15	Ph	(aR)- 3′b	62	(a <i>R</i>)- 4′b	87	> 99:1

Table 1. Synthesis of axially chiral biphenylphosphines.^[a]

[a] See Experimental Section and Supporting Information for details. [b] Enantiomeric ratio (*er*) determined on the phosphine oxide by chiral phase HPLC analysis (CP-HPLC). [c] Phosphine **3b** was very air-sensitive and could not be isolated pure.
 [d] Phosphines **3e** and **3g** could not be isolated from complex mixtures.

The synthesis of the target atropo-enantiopure phosphines proceeded efficiently, with yields comparable to those obtained during the racemic synthesis (Table 1, Entries 8–11). To determine the enantiomeric excess of phosphines (a*R*)-**3a,c,d,f**, we converted them to their corresponding phosphine oxides **4** which enabled easier separation of enantiomers by CP- HPLC. Gratifyingly, no loss of axial stereoenrichment was observed, underscoring the efficiency of the synthetic protocol leading to phosphines **3**. Furthermore, from racemic and enantiopure compounds **3a**,**c** we also prepared phosphines **3'a**,**b** using a Suzuki–Miyaura coupling at the brominated position under microwave conditions (80 °C, 1 h); complete retention of axial chirality was validated by chiral HPLC analyses of the corresponding phosphine oxides (a*R*)-**4'a**,**b** (Table 1, Entries 12–15).

Additionally, we synthesized phosphine **6** and its oxide **7**, in both racemic and enantiopure forms. In this case, the sulfoxide/ lithium exchange–trapping sequence was even more critical, as the key biaryllithium intermediate was substituted at positions 2, 2', 6 and 6' by relatively small substituents^[7] (respectively Li/ Cl/H/Me, structure **C** in Figure 2). We had previously shown that intermediate **A**, leading to **3** and **5**, was configurationally stable at –78 °C for at least 10 min, whereas **B**, bearing very small substituents, partially racemized even when trapped after only 5 min at –100 °C (Figure 2).^[6c] We were pleased to see that **C** did not undergo racemization since (a*R*)-**6** was produced with an *er* of 98:2 [measured on (a*R*)-**7**], starting from (a*R*)-**5** with a 96:4 *er*.



Figure 2. Configurational stability of atropisomerically enriched biphenyllithiums.

We then evaluated the newly synthesized biphenylphosphines in different catalytic processes, to estimate their potential for asymmetric induction in reactions where they should behave as simple monodentate Lewis bases or act as hemilabile ligands. We first examined their ability to activate hydrosilanes

(a) BuLi (1 equiv.), THF, -78 °C. (b) CIPR₂ (3 equiv.), -78 °C to r.t. (c) PhLi (2 equiv.), THF, -78 °C. (d) Mel (1 equiv.), -78 °C to r.t. (e) CIPPh₂ (3 equiv.), -78 °C to r.t. (f) PhB(OH)₂ (2 equiv.), CsF (4 equiv.), Pd(PPh₃)₄ (10 mol-%), THF, 80 °C, MW, 1 h. (g) acetone/aq. H₂O₂ (10/1 v/v).



Scheme 1. Synthesis of racemic and enantiopure axially chiral biphenylphosphines 3, 3' and 6, and phosphine oxides 4, 4' and 7.



in the presence of tris(pentafluorophenyl)borane (BCF, 8), a typical feature of FLPs.^[8] The mixtures of phosphines 3a, 3c or 3d with 8 were converted in all cases, at least partially, into the standard Lewis adducts having ¹¹B NMR signals at approximately -3.5 ppm, and a sensible upfield shift in the ¹⁹F NMR spectra.^[9] However formation of these complexes was reversible since, upon addition of dimethylphenylsilane, we observed the disappearance of their signals and the appearance of characteristic ¹¹B NMR signals representing the corresponding hydridoborate salts at approximately -25 ppm, shaped as doublets with ${}^{1}J_{B-H}$ = about 92 Hz, and a ${}^{29}Si$ NMR signal at δ = 16.4 ppm for the salt derived from (aR)-3c.^[9] With this information in hand, we evaluated the series of compounds **3a,c,d** in FLP-catalyzed hydrosilylation. Indeed, Klankermeyer and coworkers had shown that the phosphine component plays a non-innocent role in the hydrosilvlation of imines and ketones.^[10] Moreover, Du et al. have recently reported that the phosphine is essential for both activity and stereoselectivity in the hydrosilylation of related 1,2-dicarbonyl compounds.^[11] Borane 8, associated with 3a, 3c or 3d, showed catalytic activity in the hydrosilylation of acetophenone and of the corresponding N-phenylimine. Yet, as expected from the mechanism of such hydrosilylations,^[12] the presence of chiral information solely on the Lewis base (or competitive pathways where the phosphine does not participate), led to formation of the products in racemic form (Scheme 2, a).

We also assessed (aR)-3a,c,d in chiral phosphine-catalyzed reactions.^[13] These species showed no activity at room temp. in Lu's [3 + 2] annulation^[14] between ethyl buta-2,3-dienoate and diethyl fumarate. However, unlike the case with (aR)-3a, triarylphosphines (aR)-3c and (aR)-3d proved to be active at 60 °C affording the desired cyclopentene in 57-60 % yield and with very modest 10-11 % ee values (Scheme 2, b). Interestingly, the activity pattern was reversed in the aza-Morita-Baylis-Hillman reaction^[15] of methyl vinyl ketone with N-tosyl-benzaldimine (Scheme 2, c), as only (aR)-3a was active at room temp. even though only the racemic product was generated in this case. At 60 °C, the use of diphenyl-substituted phosphine (aR)-3c ultimately afforded the aza-MBH adduct with 12 % ee; the more congested di-o-tolyl analogue (aR)-3d remained inactive. On the other hand, the three phosphines of interest were found to be efficient at effecting the conjugate borylation^[16] of methyl crotonate; although, in all cases, only racemic products were generated (Scheme 2, d).

Last but not least, we evaluated (aR)-**3a**,c,d, (aR)-**3'a**,b and (aR)-**6** in the palladium-catalyzed hydrosilylation of styrene, an emblematic application of Hayashi's analogous MOP ligands.^[3,17] All phosphines enabled successful conversion of styrene cleanly in 63–92 % yields (Scheme 2, e). Gratifyingly, encouraging asymmetric inductions were also obtained. Phosphines (aR)-**3a** and (aR)-**3c**, bearing cyclohexyl and phenyl groups, respectively, at phosphorus, gave the same 54 % *ee* of the product, with identical (*R*) configuration, whereas the use of *o*-tolyl derivative (aR)-**3d** afforded a poor 8 % *ee*, with the reversed absolute configuration. When the 2'-Br substituent on the biphenyl backbone was replaced by a phenyl group, [phosphines (aR)-**3'a**,b], the alcohol was obtained in racemic form.





(a) Phosphine/borane-catalyzed hydrosilylation

	$(aR)_{-3}$ (10 mol-%)		Х	(a <i>R</i>)- 3	Yield (%)	er
	$B(C_{0}E_{c})_{0}$ (10 mol-%)	1	0	(aR)- 3a	69	rac
х	$HSiMe_Ph(12equiv)$	′ хн		(aR)- 3c	92	rac
Ĩ	1011021 11 (1.2 equiv.)	1		(a <i>R</i>)- 3d	96	rac
Ph Me	C ₆ D ₆ , r.t., 18 h	Ph Me	NPh	(aR)- 3a	51	rac
	then work-up			(aR)- 3c	55	rac
				(aR)-3d	52	rac

(b) Phosphine-catalyzed Lu's annulation

:	_•_/ ^E	+ E (2 ed	Equiv.)	_F tol	PR ₃ (10 r uene, <i>T</i> (E = CC	nol-%) ℃, 18 h 0 ₂ Et)	E	
T (°C)	PR ₃	Yield (%)	er		T (°C)	PR_3	Yield (%)	er
25	(aR)- 3a	n.r.	_		60	(aR)- 3a	n.r.	_
	(a <i>R</i>)- 3c	n.r.	_			(aR)- 3c	57	55:45
	(aR)- 3d	n.r.	-			(aR)-3d	60	56:44
	(aR)- 6	n.r.	-			(aR)- 6	62	rac

(c) Phosphine-catalyzed aza-Morita-Baylis-Hillman reaction

NTs Ph H	Methyl vi (1.2 ((a <i>R</i>)- 3a (THF, <i>T</i>	nyl ke equiv.) 10 mo	tone Ts /-%) ★ Ph	NH O
(a <i>R</i>)- 3	T (°C)	<i>t</i> (h)	Yield (%)	er
(aR)- 3a	25	48	85	rac
(a <i>R</i>)́- 3c	25	24	n.r.	-
(a <i>R</i>)- 3d	25	24	n.r.	-
(a <i>R</i>)- 3c	60	72	77	56:44
(a <i>R</i>)- 3d	60	72	n.r.	-

(d) Phosphine-catalyzed conjugate borylation

$$\overset{O}{\longrightarrow} \overset{(i)}{\longrightarrow} \left[\overset{\text{Bpin O}}{\swarrow} \overset{(ii)}{\longrightarrow} \overset{OBz O}{\longrightarrow} \overset{OBz O}{\longrightarrow} \overset{OBz O}{\longrightarrow} \overset{O}{\longrightarrow} \overset{O}{\longrightarrow}$$

(*i*) B₂pin₂ (1.1 equiv.), (*aR*)-**3** (10 mol-%), Cs₂CO₃ (0.15 equiv.), MeOH (5 equiv.), THF, 70 °C, *t* h. (*ii*) 1) sodium perborate (5 equiv.), THF/water (1/1 v/v), r.t., 18 h; 2) BzCl (5 equiv.), pyridine (2 equiv.), DCM, 0 °C to r.t., 1 h.

(aR)- 3	<i>t</i> (h)	Conv. to boronate (%) (¹ H NMR)	Yield of benzoate (%)	er
(aR)- 3a	6	> 95	42	rac
(a <i>R</i>)- 3c	18	> 95	36	rac
(a <i>R</i>)- 3d	6	> 95	47	rac

(e) Palladium-catalyzed hydrosilylation

 $Ph \xrightarrow{(i)} Ph \xrightarrow{SiCl_3} (ii) \xrightarrow{OH} Ph \xrightarrow{Ph} Ph$

(*i*) HSiCl₃ (2 equiv.), ligand (5 mol-%), [Pd(η^3 -C₃H₅)Cl]₂ (2.5 mol-%), neat, 25 °C, *t* h. (*ii*) KF (6 equiv.), K₂CO₃ (6 equiv.), H₂O₂ (30 wt.-% in H₂O, 6 equiv.), MeOH/THF (1:1 v/v), 25 °C, 18 h.

Ligand	<i>t</i> (h)	Yield of silane (%)	Yield of alcohol (%)	er (abs. config. of major enantiomer)
(aR)- 3a	3	63	73	77:23 (R)
(aR)-3c	3	90	91	77:23 (R)
(a <i>R</i>)- 3d	5	92	86	46:54 (S)
(a <i>R</i>)- 3f	3	85	82	71:29 (R)
(a <i>R</i>)- 3'a	3	86	n.d.	rac
(a <i>R</i>)- 3'b	3	82	n.d.	rac
(a <i>R</i>)-6	3	89	87	29:71 (S)

Scheme 2. Evaluation of axially chiral enantiopure biphenylphosphines in catalysis.

Phosphine (a*R*)-**6**, bearing the PPh₂ group on the non-chlorinated aromatic ring, led to the opposite enantiomer (42 % *ee*) with regard to (a*R*)-**3c**. This could be rationalized by the fact that the larger *o*-substituent of the non-phosphorus ring, respectively Br and Cl in (a*R*)-**3c** and (a*R*)-**6**, point in opposite



directions in each analogue; yet, less obvious parameters influencing asymmetric induction cannot be ruled out.

Conclusions

We successfully accessed a series of atropo-enantiopure monodentate biphenylphosphines, with complete control of axial chirality, and via a synthetic route whose potential for modularity was demonstrated in our previous work and confirmed in this paper. These phosphines exhibited activity in FLP- or Lewis base-catalysis, but afforded low asymmetric inductions. This outcome was suspected due to the remoteness of the chiral environment provided by the phosphines with respect to the substrate in FLP-catalyzed hydrosilylations. Similarly, the conformational flexibility around the biphenyl-phosphorus bond of the phosphines was anticipated to give modest enantioselectivity in phosphine-catalyzed reactions, which was confirmed by our results and is coherent with the need for a second binding site as in Shi's catalysts.^[18] On the other hand, we expected better asymmetric inductions in Pd-catalyzed reactions, where monodentate biarylphosphines are known to behave as hemilabile bidentate ligands due to Pd-arene interactions, thus rigidifying chiral transition states. The encouraging enantioselectivities (up to 77:23 er) obtained in the hydrosilylation of styrene corroborate this hypothesis. With these preliminary results in hand, we are currently tuning biphenyl backbone substituents and those of the phosphorus group so as to achieve optimal stereo-induction in catalysis, where axially chiral biphenylphosphines may complement or even outcompete their established binaphthyl congeners.

Experimental Section

General: NMR spectra were recorded in CDCl₃, at the following frequencies for each nucleus: ¹H NMR (400 MHz), ¹³C NMR (100 MHz), ³¹P NMR (172 MHz), ¹¹B NMR (128 MHz) and ¹⁹F NMR (377 MHz); except for compound **4c**, whose ¹H NMR sepctrum was recorded in C₆D₆ (400 MHz).

GP1: General Procedure for the Introduction of Dialkyl- and Diarylphosphinyl Groups on Racemic Biphenyls: At -78 °C, butyllithium (1.55–1.60 M in hexane, 1 equiv.) was added dropwise to a solution of 2,2'-dibromo-6-chlorobiphenyl (±)-1 (1 equiv.) in freshly distilled THF (0.5 M). After 15 min at -78 °C, the desired chlorodialkyl- or chlorodiarylphosphine (3 equiv.) was added dropwise if liquid, or as a THF solution if solid. The reaction mixture was allowed to reach 25 °C overnight and was then quenched by addition of sodium thiosulfate. The aqueous layer was extracted with DCM (3 × 15 mL) and the combined organic layers were dried with Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel. When the air-sensitive compound was obtained as an oil, it could be taken up in pentane and concentrated repeatedly to turn into a more stable solid.

GP2. General Procedure for the Sulfoxide/Lithium Exchange. Synthesis of Enantioenriched Phosphines: A pre-cooled solution of (*S*,*aR*)-2-bromo-2'-chloro-6'-(*p*-tolylsulfinyl)biphenyl (*S*,*aR*)-2 (1 equiv.) in dry THF (c = 0.1 M) was added to a solution of phenyl-lithium (2 equiv.) in Et₂O at –78 °C. [*Note:* preparation of the phenyl-lithium solution: At –78 °C, *tert*-butyllithium (1.7 M in pentane, 2 equiv.) was added dropwise to a solution of iodobenzene (1 equiv.) in dry Et₂O (4 mL/mmol iodobenzene)]. The solution was stirred at -78 °C for 10 min then the desired chlorodialkyl- or chlorodiarylphosphine (3 equiv.) was added dropwise if liquid, or as a THF solution if solid. The reaction mixture was allowed to reach 25 °C overnight and was then quenched by addition of sodium thiosulfate. The aqueous layer was extracted with DCM (3 × 15 mL) and the combined organic layers were dried with Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel. When the air-sensitive compound was obtained as an oil, it could be taken up in pentane and concentrated repeatedly to turn into a more stable solid. The enantiomeric ratio of the phosphine was determined by chiral phase HPLC analysis of the corresponding phosphine oxide.

(±)-(2'-Bromo-6-chlorobiphenyl-2-yl)dicyclohexylphosphine (±)-3a: Compound (±)-3a was synthesized according to general procedure **GP1** starting from biphenyl (±)-1 (560 mg, 1.62 mmol, 1 equiv.) and chlorodicyclohexylphosphine (1.1 mL, 4.85 mmol, 3 equiv.). After work up, the residue was purified by flash chromatography on silica gel (pentane/DCM, 10:0 to 7:3) to yield (±)-3a as a white powder (490 mg, 65 % yield): $R_{\rm f} = 0.11$ (cyclohexane/DCM, 8:2); m.p. 71 °C. IR (film): $\tilde{v} = 2922$ (s), 2849 (s), 1719 (m), 1414 (m), 750 (s) cm⁻¹. ¹H NMR: δ = 7.60 (dd, J = 7.9, 1.2 Hz, 1 H), 7.44 (d, J = 7.6 Hz, 1 H), 7.40 (dd, J = 7.9, 1.0 Hz, 1 H), 7.32–7.23 (m, 2 H), 7.19 (t, J = 7.7 Hz, 1 H), 7.07 (dd, J = 7.5, 1.8 Hz, 1 H), 1.95–1.78 (m, 1 H), 1.76–1.49 (m, 10 H), 1.49–1.38 (m, 1 H), 1.28–0.85 (m, 10 H) ppm. 13 C NMR: δ = 147.0 (d, J = 31.3 Hz), 140.6 (d, J = 6.5 Hz), 138.4 (br. s), 134.5 (d, J = 7.6 Hz), 132.6 (d, J = 2.6 Hz), 132.4, 131.3 (d, J = 1.8 Hz), 129.8, 129.4, 128.4, 126.6, 124.5 (d, J = 1.8 Hz), 35.7 (d, J = 14.9 Hz), 34.1 (d, J = 12.7 Hz), 30.9 (d, J = 15.0 Hz), 30.3 (d, J = 12.4 Hz), 30.0 (d, J = 17.2 Hz), 29.4 (d, J = 6.2 Hz), 27.6 (d, J = 4.7 Hz), 27.5, 27.3 (d, J = 5.1 Hz), 27.2 (d, J = 6.6 Hz), 26.5 ppm. $^{31}\text{P}\{^1\text{H}\}$ NMR: δ = –8.0 (s) ppm. HRMS ESI⁺ calcd. for $C_{24}H_{30}BrCIP^+$ [M + H]⁺ 463.0952, found 463.0964.

(a*R*)-(2'-Bromo-6-chlorobiphenyl-2-yl)dicyclohexylphosphine (a*R*)-3a: Compound (a*R*)-3a was synthesized according to general procedure **GP2** starting from sulfoxide (*S*,*aR*)-2 (400 mg, 0.98 mmol, 1 equiv.) and chlorodicyclohexylphosphine (653 µL, 2.98 mmol, 3 equiv.). The crude material was purified in a fashion analogous to that applied to the racemic compound to afford the a*R* derivative as a white powder (238 mg, 52 % yield); Additional data for (a*R*)-3a: $[\alpha]_D = -80$ (c = 1.0, DCM).

(±)-(2'-Bromo-6-chlorobiphenyl-2-yl)diphenylphosphine (±)-3c: Compound (±)-3c was synthesized according to general procedure GP1 starting from biphenyl (±)-1 (500 mg, 1.44 mmol, 1 equiv.) and chlorodiphenylphosphine (777 µL, 4.33 mmol, 3 equiv.). After work up, the residue was purified by flash chromatography on silica gel (pentane/DCM, 10:0 to 7:3) to yield (±)-3c as a white powder (351 mg, 54 % yield): R_f = 0.36 (cyclohexane/DCM, 85:15); m.p. 152 °C. IR (film): $\tilde{v} = 3056$ (m), 1587 (m), 1463 (m), 1428 (w) cm⁻¹. ¹H NMR: δ = 7.59 (dd, J = 8.0, 0.8 Hz, 1 H), 7.41 (dd, J = 8.0, 1.2 Hz, 1 H), 7.26–7.07 (m, 12 H), 7.04 (td, J = 7.2, 0.8 Hz, 1 H), 6.93 (ddd, J = 7.6, 2.8, 0.8 Hz, 1 H), 6.68 (dd, J = 7.6, 1.6 Hz, 1 H) ppm. ¹³C NMR: δ = 144.9 (d, J = 31.7 Hz), 140.5 (d, J = 14.6 Hz), 139.4 (d, J = 6.9 Hz), 136.8 (d, J = 12.4 Hz), 136.1 (d, J = 11.7 Hz), 134.5 (d, J = 7.0 Hz), 134.1 (d, J = 20.4 Hz, 2 C), 133.8 (d, J = 19.7 Hz, 2 C), 132.5, 132.2, 132.1, 132.0, 129.7 (d, J = 30.6 Hz, 2 C), 129.1 (d, J = 28.1 Hz, 2 C), 128.7, 128.6, 128.5, 128.4, 126.8, 124.4 ppm. ${}^{31}P{}^{1}H$ NMR: $\delta =$ -8.6 (s) ppm. HRMS ESI⁺ calcd. for C₂₄H₁₈BrClP⁺ [M + H]⁺ 451.0013, found 451.0013.

(a*R*)-(2'-Bromo-6-chlorobiphenyl-2-yl)diphenylphosphine (a*R*)-3c: Compound (a*R*)-3c was synthesized according to general proce-





dure **GP2** starting from sulfoxide (*S*,*aR*)-**2** (450 mg, 1.10 mmol, 1 equiv.) and chlorodiphenylphosphine (597 μ L, 3.33 mmol, 3 equiv.). The crude compound was purified in a fashion analogous to that applied to the racemic compound to afford the *aR* derivative as a white powder (276 mg, 55 % yield); Additional data for (*aR*)-**3c**: $[\alpha]_{\rm D} = -75$ (*c* = 1.0, DCM).

(±)-(2'-Bromo-6-chlorobiphenyl-2-yl)-di-o-tolylphosphine (±)-3d: Compound (±)-3d was synthesized according to general procedure GP1 starting from biphenyl (±)-1 (418 mg, 1.21 mmol, 1 equiv.) and chlorodi-o-tolylphosphine (900 mg, 4.85 mmol, 3 equiv.) in THF (2 mL). After work up, the residue was purified by flash chromatography on silica gel (pentane/DCM, 10:0 to 7:3) to yield (±)-3d as a white powder (185 mg, 32 % yield): $R_f = 0.56$ (cyclohexane/DCM, 85:15); m.p. 139 °C. IR (film): v = 3055 (w), 1587 (m), 1428 (m), 754 (s), 748 (s) cm⁻¹. ¹H NMR: δ = 7.67 (d, J = 8.0 Hz, 1 H), 7.50 (d, J = 8.0 Hz, 1 H), 7.30–7.10 (m, 7 H), 7.07 (t, J = 7.6 Hz, 1 H), 7.01 (t, J = 7.6 Hz, 1 H), 6.90 (dd, J = 7.6, 2.0 Hz, 1 H), 6.86 (dd, J = 7.2, 3.6 Hz, 1 H), 6.72 (dd, J = 7.2, 4.0 Hz, 1 H), 6.50 (d, J = 7.2 Hz, 1 H), 2.37 (s, 3 H), 2.06 (s, 3 H) ppm. ¹³C NMR: δ = 144.8 (d, J = 32.0 Hz), 143.4 (d, J = 28.4 Hz), 143.0 (d, J = 25.9 Hz), 139.7 (d, J = 14.6 Hz), 139.2 (d, J = 6.9 Hz), 135.0, 134.9 (d, J = 11.7 Hz), 134.7 (d, J = 6.5 Hz),134.5 (d, J = 13.8 Hz), 133.5, 132.4, 131.9 (2 C), 131.6, 130.2 (d, J = 4.0 Hz), 130.0 (d, J = 5.1 Hz), 129.8, 129.3 (d, J = 6.5 Hz, 2 C), 129.0, 128.8, 126.5, 126.1 (d, J = 6.5 Hz), 124.6, 21.7 (d, J = 20.7 Hz), 21.4 (d, J = 24.1 Hz) ppm. ³¹P NMR{¹H}: $\delta = -27.7$ (s) ppm. HRMS ESI+ calcd. for C₂₆H₂₂BrCIP⁺ [M + H]⁺ 479.0326, found 479.0368.

(a*R*)-(2'-Bromo-6-chlorobiphenyl-2-yl)-di-o-tolylphosphine (a*R*)-3d: Compound (a*R*)-3d was synthesized according to general procedure **GP2** starting from sulfoxide (*S*,*aR*)-2 (450 mg, 1.10 mmol, 1 equiv.) and a solution of chlorodi-o-tolylphosphine (827 mg, 3.33 mmol, 3 equiv.) in THF (2 mL). The crude material was purified in a fashion analogous to that applied to the racemic compound to afford the *aR* derivative as a white powder (276 mg, 26 % yield); Additional data for (*aR*)-3d: [α]_D = -52 (*c* = 0.8, DCM).

(±)-(2'-Bromo-6-chlorobiphenyl-2-yl)bis(p-fluorophenyl)phosphine (±)-3f: Compound (±)-3f was synthesized according to general procedure GP1 starting from biphenyl (±)-1 (544 mg, 1.57 mmol, 1 equiv.) and a solution of chlorobis(p-fluorophenyl)phosphine (1.2 g, 4.71 mmol, 3 equiv.) in THF (2 mL). After work up, the residue was purified by flash chromatography on silica gel (pentane/DCM, 10:0 to 7:3) to yield (\pm) -**3f** as a white powder (199 mg, 26 % yield): $R_f = 0.46$ (cyclohexane/DCM, 85:15); m.p. 142 °C. IR (film): $\tilde{v} = 3056$ (w), 1586 (s), 1492 (s), 1221 (s) cm⁻¹. ¹H NMR: δ = 7.80 (dd, J = 8.0, 1.2 Hz, 1 H), 7.63 (dd, J = 8.0, 0.8 Hz, 1 H), 7.43 (t, J = 8.0 Hz, 1 H), 7.40-7.33 (m, 2 H), 7.32-7.23 (m, 5 H), 7.15 (t, J = 8.8 Hz, 4 H), 7.07 (ddd, J = 7.6, 3.2, 1.2 Hz), 6.87 (ddd, J = 7.6, 3.2, 1.2 Hz) ppm. ¹³C NMR: $\delta = 164.8$ (d, J = 8.4 Hz), 162.3 (d, J = 8.4 Hz), 144.7 (d, J = 31.7 Hz), 140.1 (d, J = 14.2 Hz), 139.6 (d, J = 6.9 Hz), 136.2 (d, J = 8.0 Hz), 135.9 (d, J = 8.1 Hz), 135.8 (d, J = 7.6 Hz), 135.6 (d, J = 8.0 Hz), 134.7 (d, J = 7.0 Hz), 132.6, 131.9, 131.9, 131.8, 131.7, 131.6, 131.5, 130.2, 129.8, 129.4, 126.8, 124.3, 116.1 (d, J = 7.7 Hz), 115.8 (d, J = 7.7 Hz) ppm. ³¹P{¹H} NMR: $\delta =$ -13.8 (t, $J_{P-F} = 4.8$ Hz) ppm. ¹⁹F{¹H} NMR: $\delta = -111.6$ (d, $J_{F-P} = 4.8$ Hz), -112.2 (d, $J_{F-P} = 4.8$ Hz) ppm. HRMS ESI⁺ calcd. for $C_{24}H_{16}BrClF_2P^+$ [M + H]⁺ 486.9824, found 486.9792.

(aR)-(2'-Bromo-6-chlorobiphenyl-2-yl)bis(p-fluorophenyl)phosphine (aR)-3f: Compound (aR)-3f was synthesized according to general procedure GP2 starting from sulfoxide (*S*,*a*R)-2 (398 mg, 0.98 mmol, 1 equiv.) and chlorobis(p-fluorophenyl)phosphine (755 mg, 2.94 mmol, 3 equiv.). The crude material was purified in a fashion analogous to that applied to the racemic compound to afford the a*R* derivative as a white powder (177 mg, 37 % yield); Additional data for (a*R*)-**3f**: $[\alpha]_D = -26$ (c = 1.0, DCM).

(±)-(2'-Chloro-6-methylbiphenyl-2-yl)diphenylphosphine (±)-6: Compound (±)-6 was synthesized according to general procedure GP1 starting from (±)-2-bromo-2'-chloro-6'-methylbiphenyl (±)-5^[6c] (206 mg, 0.73 mmol, 1 equiv.) and chlorodiphenylphosphine (422 µL, 2.19 mmol, 3 equiv.). After work up, the residue was purified by flash chromatography on silica gel (pentane/DCM, 10:0 to 7:3) to yield (±)-6 as a white powder (120 mg, 42 % yield): $R_{\rm f} = 0.38$ (cyclohexane/DCM, 8:2); m.p. 134 °C. IR (film): $\tilde{v} = 3051$ (w), 1430 (s), 744 (s), 691 (s) cm⁻¹. ¹H NMR: δ = 7.44 (t, J = 7.3 Hz, 1 H), 7.34 (t, J = 7.5 Hz, 1 H), 7.24 (m, 13 H), 7.14 (dd, J = 4.5, 7.5 Hz, 1 H), 7.07 (d, J = 7.5 Hz, 1 H), 1.76 (s, 3 H) ppm. ¹³C NMR: $\delta = 145.2$, 145.1, 140.0 (d, J = 6.8 Hz), 139.1, 137.6, 137.5 (d, J = 4.0 Hz), 137.3, 137.2, 136.8 (d, J = 12.3 Hz), 134.5, 134.3, 134.3, 134.2 (d, J = 20.8 Hz), 133.9, 133.6 (d, J = 20.1 Hz), 129.7 (d, J = 5.8 Hz), 129.5, 128.7 (d, J = 10.7 Hz), 128.5 (d, J = 7.3 Hz), 128.4, 128.3, 128.1 (d, J = 14.1 Hz), 128.0, 126.7, 29.9 ppm. ³¹P{¹H} NMR: $\delta = -14.3$ (s) ppm. HRMS ESI⁺ calcd. for $C_{25}H_{21}CIP^+$ [M + H]⁺ 387.1064, found 387.1091.

(a*R*)-(2'-Chloro-6-methylbiphenyl-2-yl)diphenylphosphine (a*R*)-6: At -78 °C, butyllithium (461 µL, 1.59 м in hexane, 0.73 mmol, 1 equiv.) was added dropwise to a solution of (a*R*)-2-bromo-2'chloro-6'-methylbiphenyl (a*R*)-5^[6c] (206 mg, 0.73 mmol, 1 equiv.) in freshly distilled THF (4 mL). After 10 min at -78 °C chlorodiphenylphosphine (422 µL, 2.19 mmol, 3 equiv.) was added. The reaction mixture was allowed to reach 25 °C overnight and then quenched by addition of water (10 mL). The aqueous layer was extracted with DCM (3 × 15 mL) and the combined organic layers were dried with Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel (pentane/DCM, 10:0 to 7:3) and the derivative (a*R*)-6 was obtained as a slightly yellow solid. Additional data for (a*R*)-6: [α]_D = -18 (c = 1.0, DCM).

GP3. General Procedure for Suzuki–Miyaura Coupling: An ovendried 10 mL microwave reaction vial was charged with the 2'bromobiphenyl-2-ylphosphine (1 equiv.), phenylboronic acid (2 equiv.), cesium fluoride (4 equiv.) and Pd(PPh₃)₄ (10 mol-%). The vial was purged with argon. Dry and degassed THF (15 mL) was added, and argon was bubbled for 5 min into the resulting yellow reaction medium, which was stirred at 80 °C under microwave irradiation during 1 h. After cooling, the mixture was poured into 5 % aq. HCl and extracted three times with DCM (3 × 5 mL). The combined organic layers were washed twice with water and brine, dried with Na₂SO₄, filtered and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (elution precised below) to afford the desired coupling product.

(±)-(6-Chloro-[1,1':2',1"-terphenyl]-2-yl)dicyclohexylphosphine (±)-3'a: Compound (±)-3'a was synthesized according to general procedure GP3 starting from phosphine (±)-3a (51 mg, 0.11 mmol, 1 equiv.). After work up, the residue was purified by flash chromatography on silica gel (cyclohexane/DCM, 9:1) to furnish (±)-3'a as a white film (25 mg, 51 % yield): $R_f = 0.15$ (cyclohexane/DCM, 8:2). IR (film): $\tilde{v} = 3069$ (w), 1548 (w), 1143 (m), 746 (s), 695 (s) cm⁻¹. ¹H NMR: δ = 7.50–7.39 (m, 3 H), 7.41–7.36 (m, 2 H), 7.34–7.29 (m, 1 H), 7.24-7.20 (m, 3 H) 7.17-7.09 (m, 3 H), 1.69-1.52 (m, 6 H), 1.48-1.22 (m, 6 H), 1.17–0.88 (m, 10 H) ppm. 13 C NMR: δ = ; 147.6 (d, J = 31.3 Hz), 141.5, 141.0 (d, J = 2.2 Hz), 137.7 (d, J = 6.6 Hz), 135.5 (d, J = 8.1 Hz), 132.3, 131.5, 131.4, 130.0, 129.8 (2 C), 129.5, 128.3, 127.9 (2 C), 127.8, 126.5, 126.3, 36.8 (d, J = 16.7 Hz), 33.2 (d, J = 13.5 Hz), 30.7 (d, J = 13.5 Hz), 29.8, 29.0 (d, J = 6.2 Hz), 28.2 (d, J = 13.2 Hz), 27.7 (d, J = 10.1 Hz), 27.6, 27.0 (2 C), 26.5, 26.4 ppm. ³¹P{¹H} NMR: δ = -8.6 ppm. HRMS ESI⁺ calcd. for C₃₀H₃₅CIP [M + H]⁺ 461.2159, found 461.2146.





(aR)-(6-Chloro-[1,1':2',1''-terphenyl]-2-yl)dicyclohexylphosphine (aR)-3'a: Compound (aR)-3'a was synthesized according to general procedure **GP3** starting from phosphine (aR)-3a (35 mg, 0.08 mmol, 1 equiv.). After work up, the residue was purified by flash chromatography on silica gel (cyclohexane/DCM, 9:1) to furnish (aR)-3'a as a white film (19 mg, 54 % yield).

Additional data for (a*R*)-**3'a**: $[\alpha]_D = -7$ (c = 0.2, DCM).

(±)-(6-Chloro-[1,1':2',1"-terphenyl]-2-yl)diphenylphosphine (±)-3'b: Compound (±)-3'b was synthesized according to general procedure **GP3** starting from phosphine (±)-3c (70 mg, 0.16 mmol, 1 equiv.). After work up, the residue was purified by flash chromatography on silica gel (cyclohexane/DCM, 95:5) to furnish (±)-3'b as a white film (42 mg, 61 % yield): $R_{\rm f} = 0.31$ (cyclohexane/DCM, 9:1). IR (film): $\tilde{v} = 3290$ (m), 1421 (s), 1148 (s), 730 (m) cm⁻¹. ¹H NMR: $\delta =$ 7.47 (m, 2 H), 7.38–7.27 (m, 7 H), 7.25–7.15 (m, 7 H), 7.14–7.07 (m, 3 H), 6.82–6.74 (m, 3 H) ppm. ¹³C NMR: $\delta = 145.7$ (d, J = 14.2 Hz), 141.4 (d, J = 15.0 Hz), 140.5 (d, J = 15.0 Hz), 138.0 (d, J = 14.3 Hz), 136.9 (d, J = 6.6 Hz), 136.6, 136.4, 135.1 (d, J = 7.3 Hz), 134.3, 134.1, 133.9, 133.8, 133.2, 132.9, 132.5, 131.3, 129.9, 129.8, 129.7, 129.6, 128.9, 128.7, 128.6, 128.5 (2 C), 128.4 (2 C), 128.2, 127.8, 126.7 (d, J = 7.6 Hz) ppm. ³¹P{¹H} NMR: $\delta = -11.8$ ppm. HRMS ESI⁺ calcd. for C₃₀H₂₃CIP [M + H]⁺ 449.1220, found 449.1188.

(a*R*)-(6-Chloro-[1,1':2',1''-terphenyl]-2-yl)diphenylphosphine (a*R*)-3'b: Compound (a*R*)-3'b was synthesized according to general procedure **GP3** starting from phosphine (a*R*)-3c (30 mg, 0.07 mmol, 1 equiv.). After work up, the residue was purified by flash chromatography on silica gel (cyclohexane/DCM, 95:5) to furnish (a*R*)-3'b as a white film (18.5 mg, 62 % yield).

Additional data for (a*R*)-**3'b**: $[\alpha]_D = -15$ (c 0.5, DCM).

GP4. General Procedure for the Oxidation of Phosphines: The title phosphine (1 equiv.) was stirred in a mixture of acetone/30 % aqueous hydrogen peroxide solution (10:1 v/v, final concentration 0.25 m) at room temperature overnight. After addition of water (5 mL), the aqueous layer was extracted with DCM (3×15 mL) and the combined organic layers were dried with Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel.

(±)-(2'-Bromo-6-chlorobiphenyl-2-yl)dicyclohexylphosphine Oxide (±)-4a: Compound (±)-4a was synthesized according to general procedure GP4 starting from phosphine (±)-3a (57 mg, 0.12 mmol, 1 equiv.). After work up, the residue was purified by flash chromatography on silica gel (cyclohexane/EtOAc, 5:5 to 3:7) to furnish (±)-4a as a white powder (45 mg, 76 % yield): $R_f = 0.17$ (cyclohexane/ EtOAc, 4:6); m.p. 128 °C. IR (film): $\tilde{v} = 2923$ (s), 2849 (m), 1412 (m), 1168 (s), 754 (s) cm⁻¹. ¹H NMR: δ = 7.84 (ddd, J = 11.6, 7.6, 0.8 Hz, 1 H), 7.68–7.63 (m, 1 H), 7.48 (td, J = 7.6, 7.6, 2.0 Hz, 1 H), 7.42 (td, J = 7.6, 7.6, 1.2 Hz, 1 H), 7.32 (td, J = 7.6, 7.6, 1.6 Hz, 1 H), 7.15 (dd, J = 7.2, 1.6 Hz, 1 H), 1.81–1.50 (m, 11 H), 1.49–0.90 (m, 11 H) ppm. ¹³C NMR: δ = 142.2 (d, J = 7.3 Hz), 140.5 (d, J = 14.6 Hz), 139.1 (d, J = 2.2 Hz), 136.3 (d, J = 11.7 Hz), 133.5, 132.7, 132.6, 132.3 (d, J = 1.5 Hz), 131.2 (d, J = 8.1 Hz), 130.7, 129.8, 128.9 (d, J = 10.9 Hz), 126.9, 125.1, 38.4 (d, J = 46.0 Hz), 37.2 (d, J = 46.3 Hz), 26.8–26.1 (6 C), 25.8, 25.7 ppm. ${}^{31}P{}^{1}H$ NMR: δ = 50.6 (s) ppm. CP-HPLC Chiralpak IA column (hexane/2-propanol 95:5, flow rate: 0.5 mL/min, λ_{max} = 207 nm) $t_{\rm R1}$ = 26.0 min and $t_{\rm R2}$ = 29.1 min. HRMS ESI⁺ calcd. for C₂₄H₃₀BrClOP⁺ [M + H]⁺ 479.0901, found 479.0913.

(aR)-(2'-Bromo-6-chlorobiphenyl-2-yl)dicyclohexylphosphine Oxide (aR)-4a: Compound (aR)-4a was synthesized according to general procedure GP4 starting from phosphine (aR)-3a (57 mg, 0.12 mmol, 1 equiv.). The crude material was purified in a fashion analogous to that applied previously to afford the *aR* derivative as a white powder (45 mg, 76 % yield); Additional data for (a*R*)-**4a**: [α]_D = -62 (c = 1.0, DCM); CP-HPLC Chiralpak IA column (hexane/2propanol 95:5, flow rate: 0.5 mL/min, λ_{max} = 207 nm) t_{R} = 26.1 min, er > 99:1.

(±)-(2'-Bromo-6-chlorobiphenyl-2-yl)diphenylphosphine Oxide (±)-4c: Compound (±)-4c was synthesized according to general procedure GP4 starting from phosphine (±)-3c (110 mg, 0.12 mmol, 1 equiv.). After work up, the residue was purified by flash chromatography on silica gel (cyclohexane/EtOAc, 5:5 to 3:7) to furnish (±)-**4c** as a white powder (93 mg, 82 % yield): $R_f = 0.17$ (cyclohexane/ EtOAc, 4:6); m.p. 176 °C. IR (film): v = 2990 (m), 1581 (m), 1431 (w) cm⁻¹. ¹H NMR (C₆D₆): δ = 7.75 (ddd, J = 11.6, 8.0, 1.2 Hz, 2 H), 7.61 (ddd, J = 11.6, 7.6, 1.2 Hz, 2 H), 7.43 (dd, J = 7.6, 1.2 Hz, 1 H), 7.30 (dd, J = 13.2, 7.6 Hz, 1 H), 7.24 (br. d, J = 8.0 Hz, 1 H), 7.09 (br. d, J = 8.0 Hz, 1 H), 7.04–6.84 (m, 8 H), 6.66 (td, J = 7.6, 7.6, 2.4 Hz, 1 H), 6.58 (td, J = 8.0, 8.0, 1.6 Hz, 1 H) ppm. $^{13}{\rm C}$ NMR: δ = 143.4 (d, J = 9.1 Hz), 137.0 (d, J = 4.0 Hz), 136.7 (d, J = 12.8 Hz), 135.1, 134.1, 133.1, 133.1, 132.9, 132.6, 132.3, 132.2, 131.9, 131.8, 131.7, 131.5, 131.4, 131.4, 131.3, 129.6, 128.8 (d, J = 13.5 Hz), 128.5 (d, J = 16.1 Hz), 128.2 (d, J = 12.1 Hz), 126.4, 125.1 ppm. ³¹P{¹H} NMR: $\delta =$ 26.6 (s) ppm. CP-HPLC Chiralpak IA column (hexane/2-propanol 95:5, flow rate: 0.5 mL/min, λ_{max} = 207 nm) t_{R1} = 48.9 and t_{R2} = 53.0 min. C₂₄H₁₇BrClOP: C 61.63, H 3.66; found C 61.56, H 3.77.

(aR)-(2'-Bromo-6-chlorobiphenyl-2-yl)diphenylphosphine Oxide (aR)-4c: Compound (aR)-4c was synthesized according to general procedure **GP4** starting from phosphine (aR)-3c (26 mg, 0.057 mmol, 1 equiv.). The crude material was purified in a fashion analogous to that applied to the racemic compound to afford the *aR* derivative as a white powder (21.8 mg, 81 % yield); Additional data for (aR)-4c: $[\alpha]_D = -48$ (c = 1.0, DCM); CP-HPLC Chiralpak IA column (hexane/2-propanol 95:5, flow rate: 0.5 mL/min, $\lambda_{max} =$ 207 nm) $t_R = 48.9$ min, er = 99:1.

(±)-(2'-Bromo-6-chlorobiphenyl-2-yl)di-o-tolylphosphine Oxide (±)-4d: Compound (±)-4d was synthesized according to general procedure **GP4** starting from phosphine (±)-3d (40 mg, 0.081 mmol, 1 equiv.). After work up, the residue was purified by flash chromatography on silica gel (cyclohexane/EtOAc, 6:4 to 3:7) to furnish (±)-4d as a white powder (35 mg, 85 % yield): $R_f = 0.43$ (cyclohexane/ EtOAc, 4:6); m.p. 168 °C. IR (film): $\tilde{v} = 2921$ (m), 2951 (m), 1591 (m), 1419 (w), 754 (s) cm⁻¹. ¹H NMR: δ = 7.71–7.07 (m, 1 H), 7.45–7.32 (m, 5 H), 7.31–7.23 (m, 2 H), 7.13–6.93 (m, 5 H), 6.85 (dd, J = 14.4, 7.6 Hz, 1 H), 6.80 (dd, J = 7.6, 1.2 Hz, 1 H), 2.48 (s, 3 H), 2.43 (s, 3 H) ppm. ¹³C NMR: δ = 143.9–143.6 (m, 3 C), 137.8 (d, J = 3.3 Hz), 136.6 (d, J = 12.8 Hz), 134.8, 133.8, 132.9-132.8 (m, 3 C), 132.1-131.8 (m, 4 C), 131.6–131.5 (m, 2 C), 131.0 (d, J = 5.1 Hz), 130.9, 130.1 (d, J = 4.8 Hz), 129.2, 128.6 (d, J = 13.5 Hz), 126.1, 125.2–125.0 (m, 2 C), 22.2 (d, J = 3.7 Hz), 22.1 (d, J = 3.3 Hz) ppm. ³¹P{¹H} NMR: δ = 33.8 (s) ppm. CP-HPLC Chiralpak IA column (hexane/2-propanol 95:5, flow rate: 0.5 mL/min, λ_{max} = 207 nm) t_{R1} = 28.0 min and t_{R2} = 30.5 min. HRMS ESI⁺ calcd. for C₂₆H₂₂BrClOP⁺ [M + H]⁺ 495.0275, found 495.0309.

(aR)-(2'-Bromo-6-chlorobiphenyl-2-yl)di-o-tolylphosphine Oxide (aR)-4d: Compound (aR)-4d was synthesized according to general procedure **GP4** starting from phosphine (aR)-3d (20 mg, 0.04 mmol, 1 equiv.). The crude material was purified in a fashion analogous to that applied to the racemic compound to afford the *aR* derivative as a white powder (19.1 mg, 92 % yield); Additional data for (aR)-4d: $[\alpha]_D = -62$ (c = 1.0, DCM); CP-HPLC Chiralpak IA column (hexane/2-propanol 95:5, flow rate: 0.5 mL/min, $\lambda_{max} =$ 207 nm); $t_R = 28.3$ min, er = 98:2.

(±)-(2'-Bromo-6-chlorobiphenyl-2-yl)bis(*p*-fluorophenyl)phosphine Oxide (±)-4f: Compound (±)-4f was synthesized according





to general procedure GP4 starting from phosphine (±)-3f (40 mg, 0.082 mmol, 1 equiv.). After work up, the residue was purified by flash chromatography on silica gel (cyclohexane/EtOAc, 5:5 to 3:7) to furnish (±)-4f as a white powder (35 mg, 86 % yield): $R_f = 0.17$ (cyclohexane/EtOAc, 4:6); m.p. 132 °C. IR (film): $\tilde{v} = 2912$ (m), 2906 (m), 1594 (m), 1390 (w) cm⁻¹. ¹H NMR: δ = 7.70–7.60 (m, 3 H), 7.51– 7.36 (m, 4 H), 7.23-7.18 (m, 3 H), 7.13-7.09 (m, 2 H), 7.07-6.97 (m, 3 H) ppm. ¹³C NMR: δ = 166.1 (dd, J = 24.0, 2.9 Hz), 163.6 (dd, J = 24.0, 3.0 Hz), 143.2 (d, J = 9.1 Hz), 136.8, 136.8 (d, J = 11.3 Hz), 134.6 (t, J = 11.6 Hz), 133.8 (t, J = 9.1 Hz), 133.5, 133.2, 133.1, 132.6, 132.1, 132.0, 132.1, 129.9, 129.1, 128.9, 128.7 (d, J = 2.9 Hz), 128.1 (d, J = 2.9 Hz), 127.6 (d, J = 2.9 Hz), 127.1 (d, J = 2.9 Hz), 126.6, 125.1, 116.2–115.6 (m) ppm. ${}^{31}P{}^{1}H$ NMR: δ = 25.5 (t, J_{P-F} = 2.6 Hz) ppm. CP-HPLC Chiralpak IA column (hexane/2-propanol 95:5, flow rate: 0.5 mL/min, λ_{max} = 207 nm) t_{R1} = 39.0 min and t_{R2} = 44.1 min. HRMS ESI⁺ calcd. for $C_{24}H_{16}BrCIF_2OP^+$ [M + H]⁺ 502.9773, found 502 9811

(a*R*)-(2'-Bromo-6-chlorobiphenyl-2-yl)bis(*p*-fluorophenyl)phosphine Oxide (a*R*)-4f: Compound (a*R*)-4f was synthesized according to general procedure **GP4** starting from phosphine (a*R*)-3f (40 mg, 0.082 mmol, 1 equiv.). The crude reaction was purified in a fashion analogous to that applied previously to afford the *aR* derivative as a white powder (35 mg, 76 % yield); Additional data for (a*R*)-4f: [α]_D = -13 (*c* = 0.7, DCM); CP-HPLC Chiralpak IA column (hexane/ 2-propanol 95:5, flow rate: 0.5 mL/min, $\lambda_{max} = 207$ nm) $t_{R} =$ 38.1 min, *er* = 98:2.

(±)-(2'-Chloro-6-methylbiphenyl-2-yl)diphenylphosphine Oxide (±)-7: Compound (±)-7 was synthesized according to general procedure GP4 starting from phosphine (±)-6 (30 mg, 0.078 mmol, 1 equiv.). After work up, the residue was purified by flash chromatography on silica gel (cyclohexane/EtOAc, 10:0 to 6:4) to furnish (±)-7 as a white film (27 mg, 86 % yield): $R_f = 0.23$ (cyclohexane/ EtOAc, 6:4). IR (film): $\tilde{v} = 3293$ (m), 1439 (s), 1161 (s), 719 (m) cm⁻¹. ¹H NMR: δ = 7.70 (d, J = 11.7 Hz, 1 H), 7.68 (d, J = 11.7 Hz, 1 H), 7.61 (t, J = 7.6 Hz, 1 H), 7.46-7.42 (m, 9 H), 7.27-7.22 (m, 2 H), 7.17 (dd, J = 7.8, 3.5 Hz, 1 H), 6.99 (d, J = 3.8 Hz, 1 H), 6.98 (s, 1 H), 6.88 (dd, J = 6.5, 2.9 Hz, 1 H), 2.00 (s, 3 H) ppm. ¹³C NMR: $\delta = 143.9$ (d, J = 8.0 Hz), 139.2, 137.9 (d, J = 3.3 Hz), 134.5 (d, J = 13.1 Hz), 133.4, 132.9, 132.5, 132.3, 132.2, 132.1, 132.0, 131.9, 131.8, 130.7, 130.3, 129.9, 129.1, 128.8 (d, J = 12.4 Hz), 128.5 (d, J = 12.4 Hz), 128.3, 127.6 (d, J = 12.4 Hz), 126.4, 110.9, 109.7 (d, J = 5.1 Hz), 20.7 ppm. ³¹P{¹H} NMR: δ = 28.2 ppm. CP-HPLC Chiralpak IA column (hexane/ 2-propanol 95:5, flow rate: 0.5 mL/min, $\lambda_{max} = 207$ nm) $t_{R1} =$ 42.0 min and t_{R2} = 54.0 min. HRMS ESI⁺ calcd. for C₂₅H₂₀CIOP (M⁺) 402.0935, found 402.0982.

(aR)-(2'-Chloro-6-methylbiphenyl-2-yl)diphenylphosphine Oxide (aR)-7: Compound (aR)-7 was synthesized according to general procedure **GP4** starting from phosphine (aR)-6 (35 mg, 0.090 mmol, 1 equiv.). The crude material was purified in a fashion analogous to that applied before to afford the *aR* derivative as a white film (29 mg, 80 % yield); Additional data for (aR)-6: $[\alpha]_D = +3$ (c = 1.0, DCM); CP-HPLC Chiralpak IA column (hexane/2-propanol 95:5, flow rate: 0.5 mL/min, $\lambda_{max} = 207$ nm) $t_R = 52.5$ min, er = 98:2.

(±)-(6-Chloro-[1,1':2',1''-terphenyl]-2-yl)dicyclohexylphosphine Oxide (±)-4'a: Compound (±)-4'a was synthesized according to general procedure **GP4** starting from phosphine (±)-3'a (10 mg, 0.021 mmol, 1 equiv.). After work up, the residue was precipitated in pentane to furnish (±)-4'a as a white film (7.9 mg, 76 % yield): IR (film): $\tilde{v} = 2925$ (s), 2832 (m), 1403 (m), 1163 (s), 748 (s) cm⁻¹. ¹H NMR: $\delta = 7.65-7.63$ (m, 1 H), 7.52–7.47 (m, 2 H), 7.40–7.33 (m, 3 H), 7.32–7.26 (m, 2 H), 1.77–1.49 (m, 8 H), 1.49–1.31 (m, 2 H), 1.23–0.72 (m, 12 H) ppm. ¹³C NMR: $\delta = 145.1$, 140.9 (d, J = 26.3 Hz), 138.1, 135.6, 132.5, 131.1, 130.4, 130.1, 129.9, 129.8, 129.7 (2 C), 128.9, 128.2 128.1, 128.0 (2 C), 126.6 (d, *J* = 10.5 Hz), 38.2 (d, *J* = 64.6 Hz), 36.5 (d, *J* = 65.1 Hz), 26.6–26.4 (3 C), 25.8–25.7 (3 C), 25.2, 24.8, 20.9, 20.8 ppm. ³¹P{¹H} NMR: δ = 52.8 ppm. CP-HPLC Chiralpak IA column (hexane/2-propanol 95:5, flow rate: 0.5 mL/min, λ_{max} = 207 nm) t_{R1} = 16.5 min and t_{R2} = 18.1 min. HRMS ESI⁺ calcd. for C₃₀H₃₅CIOP [M + H]⁺ 477.2109, found 477.2100.

(a*R*)-(6-Chloro-[1,1':2',1''-terphenyl]-2-yl)dicyclohexylphosphine Oxide (a*R*)-4'a: Compound (a*R*)-4'a was synthesized according to general procedure **GP4** starting from phosphine (a*R*)-3'a (12 mg, 0.026 mmol, 1 equiv.). The crude material was purified in a fashion analogous to that applied to the racemic compound to afford the *aR* derivative as a white film (8.6 mg, 83 % yield); Additional data for (a*R*)-4'a: [α]_D = -12 (*c* = 0.2, DCM); CP-HPLC Chiralpak IA column (hexane/2-propanol 95:5, flow rate: 0.5 mL/min, $\lambda_{max} = 207$ nm) $t_{R} = 16.5$ min, *er* > 99:1.

(±)-(6-Chloro-[1,1':2',1"-terphenyl]-2-yl)diphenylphosphine Oxide (±)-4'b: Compound (±)-4'b was synthesized according to general procedure GP4 starting from phosphine (±)-3'b (9.7 mg, 0.021 mmol, 1 equiv.). After work up, the residue was precipitated in pentane to furnish (±)-4'b as a white film (8.9 mg, 89 % yield): IR (film): $\tilde{v} = 3292$ (m), 1439 (s), 1161 (s), 726 (m) cm⁻¹. ¹H NMR: $\delta =$ 7.70-7.60 (m, 1 H), 7.60-7.47 (m, 4 H), 7.46-7.30 (m, 9 H), 7.26-7.18 (m, 3 H), 7.17–7.11 (m, 3 H), 7.06–7.02 (m, 1 H), 6.58 (d, J = 7.6 Hz, 1 H) ppm. ¹³C NMR: δ = 141.8, 140.9, 134.7 (d, J = 3.6 Hz), 133.5 (d, J = 3.7 Hz), 132.8, 132.8, 132.7, 132.6, 132.5, 132.3, 132.3, 132.2 (d, J = 5.9 Hz), 132.1, 132.0 (d, J = 3.5 Hz), 131.9 (d, J = 3.2 Hz), 131.8, 131.7, 130.3, 129.9, 129.6 (2 C), 129.0, 128.9, 128.9 (d, J = 13.2 Hz), 128.5 (d, J = 12.1 Hz), 128.1, 127.9, 127.5 (2 C), 126.6 (d, J = 5.4 Hz) ppm. ³¹P{¹H} NMR: δ = 34.7 ppm. CP-HPLC Chiralpak IA column (hexane/2-propanol 95:5, flow rate: 0.5 mL/min, λ_{max} = 207 nm) t_{B1} = 71.0 min and t_{B2} = 75.4 min. HRMS ESI⁺ calcd. for C₃₀H₂₃CIOP [M + H]⁺ 465.1170, found 465.1210.

(a*R*)-(6-Chloro-[1,1':2',1''-terphenyl]-2-yl)diphenylphosphine Oxide (a*R*)-4'b: Compound (a*R*)-4'b was synthesized according to general procedure **GP4** starting from phosphine (a*R*)-3'b (11 mg, 0.025 mmol, 1 equiv.). The crude material was purified in a fashion analogous to that applied to the racemic compound to afford the a*R* derivative as a white film (9.9 mg, 87 % yield); additional data for (a*R*)-4'b: [α]_D = -8 (c = 0.1, DCM); CP-HPLC Chiralpak IA column (hexane/2-propanol 95:5, flow rate: 0.5 mL/min, λ_{max} = 207 nm) t_{R} = 75.4 min, er > 99:1.

GP5. General Procedure for the FLP-Catalyzed Hydrosilylation of Acetophenone and Acetophenone *N*-Phenylimine

Hydrosilylation of Acetophenone: A dry Schlenk tube was transferred into a glovebox under vacuum and was charged successively with tris(pentafluorophenyl)borane (22.4 mg, 0.044 mmol, 0.1 equiv.) and the appropriate phosphine (0.044 mmol, 0.1 equiv.). Acetophenone (53 mg, 0.44 mmol, 1 equiv.) was added as a solution in C_6D_6 (1 mL). The resulting solution was stirred for 10 min at room temperature and dimethylphenylsilane (80 µL, 0.53 mmol, 1.2 equiv.) was added dropwise resulting in an instantaneous slightly exothermic reaction. The solution was stirred at room temperature for 18 h. The crude mixture was quenched by addition of TBAF (1 m in THF, 1.32 mL, 1.32 mmol, 3 equiv.) at room temperature and stirring for 1 h. It was then concentrated in vacuo, and purified by flash chromatography on silica gel (cyclohexane/EtOAc, 9:1 to 8:2) to furnish 1-phenylethanol as a colorless oil (yields are reported in Scheme 2, a). Spectral data were in agreement with literature. $R_{\rm f}$ = 0.20 (cyclohexane/EtOAc, 8:2). The enantiomeric ratio was measured by CP-HPLC on a Chiracel OD-H column (hexane/2-prop-





anol 95:5, flow rate: 0.5 mL/min, λ_{max} = 204 nm); t_{R1} = 16.2 min, t_{R2} = 18.2 min. All runs depicted in Scheme 2 (a) afforded the racemic product.

Hydrosilylation of Acetophenone *N*-**Phenylimine:** The hydrosilylation of acetophenone *N*-phenylimine was carried out on a 0.16– 0.47 mmol scale without notable changes on conversions or yields, following the same procedure as for acetophenone except for the TBAF quench which was avoided. After concentration of the crude reaction in vacuo, the residue was purified by flash chromatography on silica gel (cyclohexane/Et₂O, 5:1) to afford *N*-(1-phenylethyl)aniline as a colorless oil (yields are reported in Scheme 2, a). Spectral data were in agreement with literature. The enantiomeric ratio was measured by CP-HPLC on a Chiralpak IB column (hexane/2-propanol 95:5, flow rate: 0.5 mL/min, $\lambda_{max} = 210$ nm); $t_{R1} = 10.1$ min, $t_{R2} =$ 12.5 min. All runs depicted in Scheme 2 (a) afforded the racemic product.

GP6. General Procedure for Lu's [3 + 2] Annulation of Ethyl Buta-2,3-dienoate with Diethyl Fumarate: In a dried Schlenk tube flushed with argon, to a mixture of diethyl fumarate (74 mg, 0.43 mmol, 2 equiv.) and the appropriate phosphine catalyst (0.02 mmol, 0.1 equiv.) in dried, degassed toluene (700 µL), was added under argon atmosphere ethyl buta-2,3-dienoate (25 µL, 0.22 mmol, 1 equiv.). The solution was stirred at room temperature or at 60 °C for 18 h. The crude mixture was concentrated in vacuo, and purified by flash chromatography on silica gel (cyclohexane/ EtOAc, 9:1 to 8:2) to afford the annulation product as a colorless oil (yields are reported in Scheme 2, b): $R_{\rm f} = 0.22$ (cyclohexane/EtOAc, 8:2). Spectral data were in agreement with literature. The enantiomeric ratio was measured by CP-HPLC on a Chiralpak IB column (hexane/2-propanol 95:5, flow rate: 0.5 mL/min, $\lambda_{\rm max} = 211$ nm); $t_{\rm R1} = 12.5$ min, $t_{\rm R2} = 15.7$ min.

GP7: General Procedure for the Phosphine-Catalyzed Aza-Morita–Baylis–Hillman Reaction of *N*-Tosyl-Benzaldimine with Methyl Vinyl Ketone: To a solution of *N*-tosyl-benzaldimine (30.0 mg, 0.12 mmol) and the appropriate phosphine catalyst (0.01 mmol, 0.1 equiv.) in THF (1.0 mL) was added methyl vinyl ketone (11 µL, 0.14 mmol, 1.2 equiv.). The reaction mixture was stirred at room temperature or 60 °C. When the reaction was completed, as monitored by ¹H NMR, the solvent was removed in vacuo and the residue was purified by flash chromatography on silica gel (cyclohexane/EtOAc, 9:1 to 7:3) to afford *N*-(1-phenylethyl)aniline as a white solid (yields are reported in Scheme 2, c): $R_{\rm f} = 0.35$ (cyclohexane/EtOAc, 7:3). Spectral data were in agreement with literature. The enantiomeric ratio was measured by CP-HPLC on a Chiralpak IA column (hexane/2-propanol 80:20, flow rate: 0.5 mL/min, $\lambda_{\rm max} = 208$ nm); $t_{\rm B1} = 17.1$ min, $t_{\rm B2} = 18.4$ min.

GP8: General Procedure for Phosphine-catalyzed Conjugate Borylation of Methyl Crotonate and Determination of Enantiomeric Excess: A dry Schlenk tube flushed with argon was charged with the appropriate phosphine catalyst (0.05 mmol, 0.1 equiv.), cesium carbonate (25 mg, 0.08 mmol, 0.15 equiv.) and bis(pinacolato)diboron (140 mg, 0.55 mmol, 1.1 equiv.). Freshly distilled THF (2 mL) was then added and the mixture was stirred for 10 min at room temperature to dissolve the phosphine and the borane reagents completely. Methyl crotonate (50 mg, 0.50 mmol, 1 equiv.) and MeOH (100 µL, 2.5 mmol, 5 equiv.) were then successively added and the reaction mixture was stirred at 70 °C until complete conversion (followed by ¹H NMR). The reaction mixture was cooled to room temperature and concentrated in vacuo. After filtration through a silica pad, the crude compound was directly engaged in the oxidation step for determination of enantiomeric excess. Alternately, it could be purified by flash chromatography on silica gel (cyclohexane/EtOAc, 95:5 to 8:2) to furnish methyl 3-(pinacolatoboranyl)butanoate: $R_{\rm f}$ = 0.67 (cyclohexane/EtOAc, 8:2). Spectral data were in agreement with literature.

Enantiomeric Excess Determination. Boronic Ester Conversion to Corresponding Benzoate: To the crude borylation product (0.5 mmol, 1 equiv.) in THF (2 mL) and water (2 mL), sodium perborate (769 mg, 2.5 mmol, 5 equiv.) was added in one portion. The reaction mixture was stirred vigorously for 18 h at room temperature, diluted with water and then extracted with dichloromethane $(3 \times 20 \text{ mL})$. The combined organic layers were dried with Na₂SO₄, filtered and concentrated in vacuo. At 0 °C, to a solution of crude methyl 3-hydroxybutanoate (0.5 mmol, 1 equiv.) in dry DCM (5 mL), pyridine (100 µL, 1.01 mmol, 2 equiv.) and benzoyl chloride (115 µL, 2.5 mmol, 5 equiv.) were successively added dropwise. The mixture was stirred 1 h at room temperature and was then guenched at 0 °C by addition of a saturated aqueous solution of NaHCO₃ (10 mL). The aqueous phase was extracted with DCM (3×15 mL) and the combined organic layers were dried with Na₂SO₄, filtered and concentrated in vacuo. The resulting oily residue was purified by flash chromatography on silica gel (cyclohexane/EtOAc, 9:1 to 8:2) to afford methyl 3-(benzoyloxy)butanoate as a colorless oil (yields over 3 steps are reported in Scheme 2, d). $R_f = 0.45$ (cyclohexane/EtOAc, 8:2). Spectral data were in agreement with literature. The enantiomeric ratio was measured by CP-HPLC on a Chiralpak IB column (hexane/2-propanol 98:2, flow rate: 0.5 mL/min, λ_{max} = 208 nm); t_{B1} = 12.8 min, t_{B2} = 13.3 min. All runs depicted in Scheme 2 (d) afforded the racemic product.

GP9. General Procedure for Palladium-Catalyzed Hydrosilylation of Styrene and Determination of Enantiomeric Excess: A dry Schlenk tube flushed with Ar was charged with styrene (50 mg, 0.48 mmol, 1 equiv.), allylpalladium chloride dimer (4.4 mg, 0.012 mmol, 2.5 mol-%) and the appropriate phosphine ligand (0.024 mmol, 5 mol-%). The mixture was stirred for 20 min and quickly sonicated to furnish a clean yellow solution. Trichlorosilane (100 µL, 0.96 mmol, 2 equiv.) was then slowly added and the mixture took instantaneously a black coloration. It was stirred until complete conversion (followed by ¹H NMR) and concentrated in vacuo. The crude material was redissolved in DCM, transferred into a 10 mL flask and volatiles were removed. The crude compound was purified by bulb-to-bulb distillation (high vacuum) to furnish the corresponding trichloro(1-phenylethyl)silane with 63-92 % yields as a colorless oil. Spectral data were in agreement with literature.

Enantiomeric Excess Determination. Alkyltrichlorosilane Conversion to Corresponding Alcohol by Fleming-Tamao Oxidation: The reaction scale for ee determination is based on yield of the previous step. The freshly distilled alkyltrichlorolsilane (72-105 mg, 0.3-0.44 mmol, 1 equiv.) was dissolved in a mixture of THF (8 mL) and MeOH (8 mL). K₂CO₃ (248–364 mg, 1.8–2.64 mmol, 6 equiv.), KF (104–153 mg, 1.8–2.64 mmol 6 equiv.) and 30 % aqueous solution of hydrogen peroxide (300 µL) were then successively added. The resulting suspension was vigorously stirred overnight. Water (10 mL) was then added and the mixture was extracted with Et_2O (3 × 15 mL), dried with Na_2SO_4 , filtered and concentrated in vacuo. The resulting oily residue was purified by column chromatography on silica gel (cyclohexane/EtOAc, 8:2) to afford 1-phenylethanol as an oil (yields are given in Scheme 2, e). Spectral data were in agreement with literature. The enantiomeric ratio was measured by CP-HPLC on a Chiracel OD-H column (hexane/2-propanol 95:5, flow rate: 0.5 mL/min, λ_{max} = 204 nm); t_{R1} = 16.2 min, t_{R2} = 18.2 min.



Acknowledgments

This work was supported by the Centre National de la Recherche Scientifique (CNRS), as well as the University of Strasbourg Institute for Advanced Study (USIAS) and the International Centre for Frontier Research in Chemistry (ICFRC) (project AxLAB 2014). The authors thank Dr. D. Bourissou and Dr. G. Bouhadir (LHFA, UMR 5069, Toulouse) for the recording of ²⁹Si NMR spectra and for fruitful discussions.

Keywords: Organocatalysis · Asymmetric catalysis · Homogeneous catalysis · Enantioselectivity · Palladium · Axial chirality · Atropoisomerism · Biaryls · Phosphines

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Received: June 14, 2016 Published Online: ■





Chiral Phosphines

 When Chirality Meets "Buchwald-Type" Phosphines: Synthesis and Evaluation in Frustrated Lewis Pair-, Lewis Base- and Palladium-Promoted Asymmetric Catalysis



Axially chiral "Buchwald ligand"-like biphenylphosphines were prepared in highly enantioenriched form and were evaluated in phosphine-promoted organocatalysis and hydrosilylations catalyzed by Pd or by frustrated Lewis pairs (FLPs). The title phosphines are best suited for transition metal catalysis where asymmetric induction proved much higher.

DOI: 10.1002/ejoc.201600727