DOI: 10.1002/ejoc.200800499

Synthesis of Building Blocks for the Development of the SUPRAPhos Ligand Library and Examples of Their Application in Catalysis

P. Elsbeth Goudriaan,[a] Xiao-Bin Jang,[a] Mark Kuil,[a] Renske Lemmens,[a] Piet W. N. M. Van Leeuwen,[a] and Joost N. H. Reek*[a]

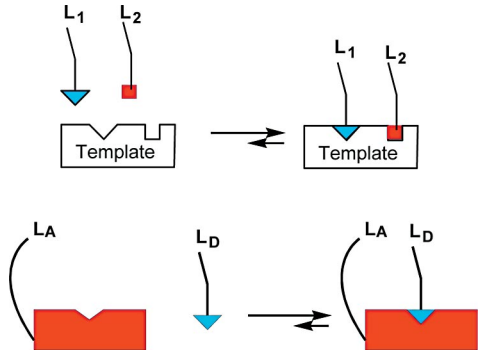
Keywords: Bidentate ligands / Supramolecular chemistry / Ligand libraries / Phosphorus / Asymmetric catalysis

We have previously introduced the SUPRAPhos ligand library, which is based on components that are self-assembled through nitrogen–zinc interactions, and report here an extension of this library, which widens the scope for application in asymmetric homogeneous catalysis. For example, we report the synthesis of phosphorus amidite appended porphyrins and building blocks with stereogenic centers at the phosphorus. With the new building blocks described in this paper we can form a 450-membered SUPRAPhos library, which is based on 45 building blocks (30 pyridyl phosphorus ligands and 15 complementary porphyrin-appended phosphorus ligands). Examples of the use of members of the library in the rhodium-catalyzed asymmetric hydroformylation of styrene are included.

Introduction

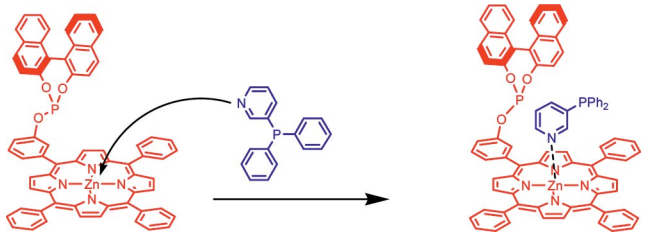
Asymmetric catalysis is an indispensable tool in modern synthetic chemistry as it offers new routes to the efficient preparation of single enantiomers of compounds, which is clearly far more atom-efficient than racemic synthesis combined with resolution. Although asymmetric catalysis is applied to industrial processes,[1] its use in the synthesis of enantiopure products is still limited compared with, for instance, the resolution of enantiomers.[2] One reason for this is the high substrate- and reaction-specificity of the available chiral catalysts. As the selectivity of a catalyst for a certain conversion can hardly be predicted by theoretical models, current strategies for finding selective catalysts rely on the screening of catalyst libraries.[3] Generally this involves the in situ preparation of transition-metal complexes using libraries of ligands. As the time-to-market is a decisive parameter, not much time is available for the screening and identification of catalysts. Hence the rapid search for a suitable catalyst for a certain conversion depends largely on the availability of ligand libraries. Phosphorus-based ligands comprise an important class of ligands that are used in many different transition-metal-catalyzed reactions, and the availability of diverse libraries is highly desirable. Chiral monodentate ligands are intrinsically easier to prepare than bidentate ligands, and several strategies for the preparation of libraries of monodentate ligands have been reported.[4] For example, Lefort and co-workers reported the robotic synthesis of 96 monodentate phosphoramidites (instant ligand libraries) and the robotic screening for asymmetric hydrogenation, which was accomplished in just 2 days, demonstrating the value of simple ligand structures.[5] The preparation of ligand libraries based on bidentate phosphorus ligands is far more difficult and as such these are scarce.[6,7] A new approach, introduced both by us[8,9] and others,[10] is the preparation of bidentate ligands using noncovalent interactions. The supramolecular approach is ideally suited to the development of ligand libraries because 1) the number of bidentate ligands grows exponentially with the number of building blocks prepared, 2) the synthesis of ligand building blocks is generally (not always) easier than that of (hetero)bidentate ligands, 3) a diverse ligand library becomes accessible if building blocks with different phosphorus donor moieties are included, and 4) creation of a sub-library related to a promising ligand structure is much easier. Various supramolecular interactions, such as hydrogen bonds, metal–ligand interactions, and ionic interactions, have been used to bring two ligand building blocks together to provide a supramolecular bidentate ligand. This can be achieved by the assembly of two monodentate ligand building blocks on a template that is functionalized with two complementary binding sites (Scheme 1, left) or by using two monodentate ligand building blocks equipped with complementary binding sites (Scheme 1, right). As these supramolecular bidentate ligands are formed from smaller building blocks, the synthesis is intrinsically less complex than the synthesis of covalent (hetero)bidentate ligands. More importantly, only a small number of building blocks are required for the construction of a large library.

[a] Homogeneous and Supramolecular Catalysis, Van't Hoff Institute for Molecular Sciences,
Nieuwe Achtergracht 166, 1018 WV Amsterdam, The Netherlands
E-mail: reek@science.uva.nl
Supporting information for this article is available on the WWW under http://www.eurjoc.org or from the author.



Scheme 1. Schematic representation of the formation of a supramolecular bidentate ligand by using a template (left) or directly from complementary monodentate ligands (right).

We previously reported SUPRAPhos, a class of bidentate ligands that is formed from porphyrinatozinc(II)···pyridyl interactions. Initially we prepared a 48-membered bidentate ligand library based on 14 building blocks. Six different phosphite-porphyrinatozinc(II) compounds were used in combination with eight nitrogen-donor-functionalized phosphane or phosphite ligands (for an archetypical example, see Scheme 2).[9c,9e]

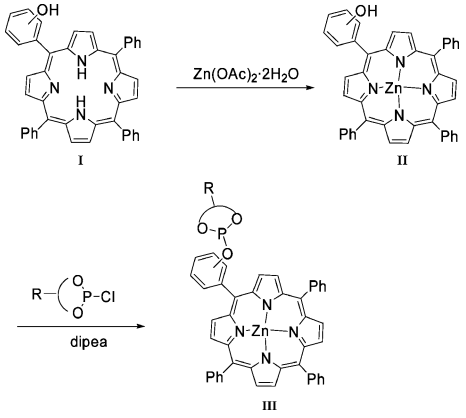


Scheme 2. Formation of a supramolecular bidentate ligand.

The supramolecular ligand library was applied to palladium-catalyzed allylic alkylation reactions, and the large variation in the obtained enantiomeric excesses demonstrated the proof of principle. After these initial results the SUPRAPhos library was extended to a 60-membered library, which was studied in the asymmetric rhodium-catalyzed hydrogenation of trisubstituted cyclic *N*-(3,4-dihydro-2-naphthalenyl)acetamide.[9g] This substrate is known to be a difficult substrate for hydrogenation, and inherently no selective rhodium-based catalysts were known (70% *ee*). Parallel high-throughput screening of the library showed that between 0 and 100% of the substrate was converted and that the *ee* of the product obtained varied between 12% *ee* of one enantiomer and 94% *ee* of the other enantiomer. Importantly, the library produced only one hit, which highlights the challenge involved. Part of the library was also successfully used in the kinetic resolution of cyclohexenyl acetate.[9j] Stimulated by these successes we decided to further expand the ligand library. Herein we report on the synthesis of ligand building blocks for the SUPRAPhos library, including (new) porphyrin phosphites and phosphoramidites, pyridyl phosphoramidites, new pyridyl phosphites, and chiral pyridyl phosphanes. With these new building blocks and those previously reported,[9c–9e,9g,9h] we can form a large (450) and diverse library of bidentate ligands. Some of the ligands in the library were used to form catalysts for the rhodium-catalyzed asymmetric hydroformylation of styrene.

Results and Discussion

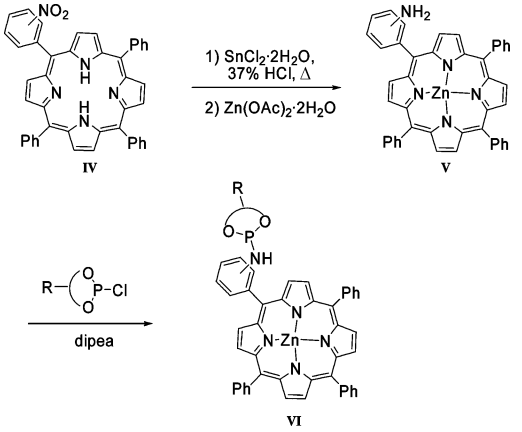
The synthesized SUPRAPhos library can be divided into two parts: The metalloporphyrin acceptor ligands and the nitrogen donor ligands. The phosphite-porphyrinatozinc(II) complexes (Scheme 3, **III**) were synthesized by reaction of hydroxy-functionalized porphyrinatozinc(II) (Scheme 3, **II**) with chlorophosphites according to the procedure previously developed in our laboratory.[9c] The required hydroxyporphyrins (Scheme 3, **I**) were prepared by condensation of benzaldehyde, hydroxybenzaldehyde, and pyrrole in refluxing propionic acid.[11] After isolation the hydroxyporphyrins were metalated using zinc acetate in refluxing chloroform/methanol and were purified by column chromatography over basic alumina.



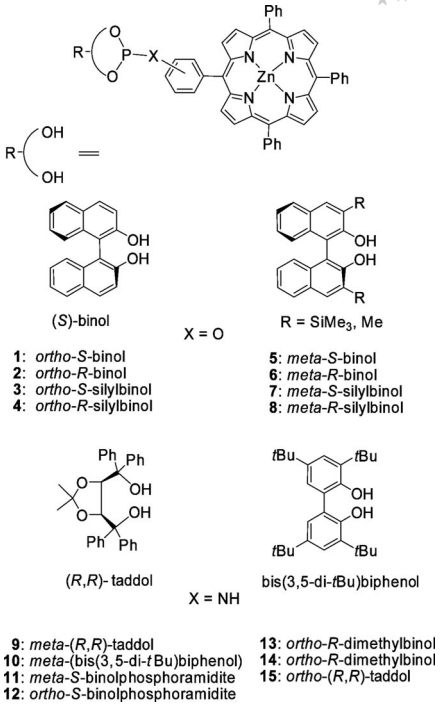
Scheme 3. Synthesis of phosphite-porphyrinatozinc(II) complexes (for R see Scheme 5).

The phosphoramidite-appended porphyrins **11** and **12** (Scheme 5) were prepared by using a similar strategy. The free base aminoporphyrin was synthesized from the free base nitroporphyrin (Scheme 4, **IV**), which was synthesized by condensation of benzaldehyde, nitrobenzaldehyde, and pyrrole under acidic conditions according to a literature procedure (Adler method).[12] After purification by column chromatography, the nitro group was reduced with tin(II) chloride under acidic conditions to provide the aminoporphyrin. To insert zinc(II) into these amino-appended porphyrins we initially used the same procedure as used for the hydroxyporphyrins, that is, refluxing in a chloroform/methanol mixture and subsequent washing with water to remove the excess zinc acetate followed by extraction, concentration, and column chromatography. This method failed, however, as coordination of the amino group to the zinc atom of another porphyrin gives rise to the formation of higher order aggregates that hamper isolation and purification. We therefore used a procedure that had previously been used for the metalation of the 4-analogue. This involved stirring a solution (dichloromethane/methanol) of

the free base porphyrin with 5 equiv. zinc acetate for 12 h followed by precipitation of the product through evaporation of the dichloromethane and the gradual addition of methanol.[13] By using this procedure, compound **V** (Scheme 4) was isolated in almost quantitative yield in high purity. The amidite ligand **VI** was formed after a straightforward reaction of the aminoporphyrin with a chlorophosphite (Scheme 4).



Scheme 4. Synthesis of Zn^{II} porphyrin phosphoramidite ligands [the functional group is either at the *ortho* or at the *meta* position (**11** and **12**); for R, see Scheme 5].



Scheme 5. Acceptor-type building blocks that were prepared in order to construct the Supraphos library.

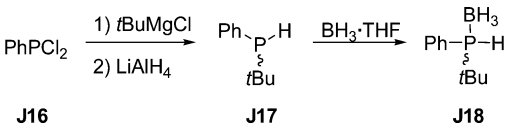
Following these procedures, 15 phosphite-porphyrinatozinc(II) compounds and similar phosphoramidites (Scheme 5) were synthesized from the corresponding hydroxy- and aminoporphyrins in yields varying from 40 to 50%.[14] All new porphyrin-appended ligands were characterized by ^1H, ^{31}P, and ^{13}C NMR spectroscopy and by elemental analysis or HRMS.

Three different types of nitrogen-donor-functionalized ligands were synthesized: Phosphanes [achiral (**A**) and chiral (**B**)], phosphoramidites (**C**), and phosphites (**D**). These will be described below.

The achiral pyridylphosphanes **A1**–**A4** (see Scheme 12) were prepared by lithiation of bromopyridine by using *n*BuLi and TMEDA[15] in a 1:1:1 tetrahydrofuran/ethyl ether/pentane solution at –115 °C followed by the addition of diarylchlorophosphane at –70 °C.[16] The work up of these compounds generally involved aqueous washing and subsequent purification by column chromatography under an inert atmosphere. Yields between 20 and 70% were obtained.

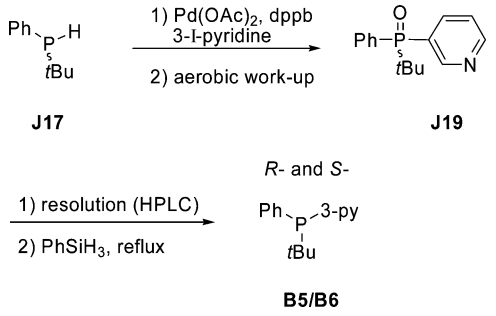
The synthesis of chiral pyridyl-functionalized phosphanes (**B**) proved more challenging than anticipated. In particular, the development of synthetic routes towards P-stereogenic phosphanes was time-consuming. Chiral phosphanes can be prepared in an enantiopure form by either enantioselective synthesis or optical resolution after the preparation of the racemate.[17] For the enantioselective synthesis there are several possibilities, such as the use of heterobifunctional auxiliaries like, for instance, the ephedrine-based method developed by Jugé and coworkers,[18] the lithium–sparteine-mediated synthesis of phosphane boranes,[19] and the palladium-catalyzed cross-coupling of organophosphorus compounds containing a P–H bond with aryl of vinyl halides or triflates.[20]

Two routes for the preparation of P-stereogenic phosphanes equipped with nitrogen donor atoms were found to be successful. We prepared the racemic synthon *tert*-butyl(phenyl)phosphane (**J17**; Scheme 6) by reaction of dichloro(phenyl)phosphane with 1 equiv. of *tert*-butylmagnesium chloride at –78 °C followed (after stirring for 1 h at room temperature) by the addition of 1 equiv. of lithium aluminium hydride. Subsequent addition of the borane–tetrahydrofuran complex resulted in immediate protection of the phosphane, which was, after aqueous work up, purified by vacuum distillation, which provided in the first fraction the unprotected phosphane **J17** (25% yield) and in the second fraction the protected phosphane **J18** (59% yield).[21] The secondary phosphane was further functionalized both by enantioselective lithium–sparteine-mediated synthesis and by palladium-catalyzed cross-coupling of the organophosphorus compound with iodopyridine followed by resolution (Scheme 7 and Scheme 8).

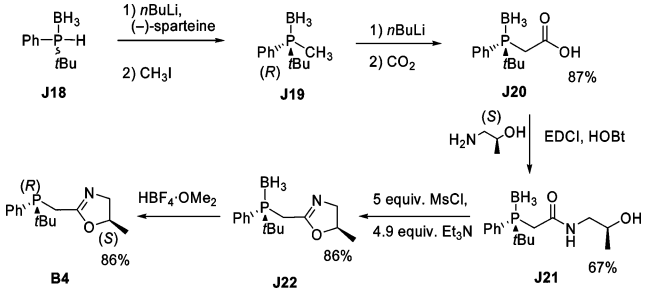


Scheme 6. Synthesis of a racemic secondary phosphane suitable for the preparation of different P-stereogenic phosphane ligands.

3-[*tert*-Butyl(phenyl)phosphanyl]pyridine was prepared by palladium-catalyzed P–C cross-coupling (Scheme 7). The secondary phosphane **J17** was coupled with 3-iodopyr-



Scheme 7. Synthesis of (*R*)- and (*S*)-3-[*tert*-butyl(phenyl)phosphanyl]pyridine.

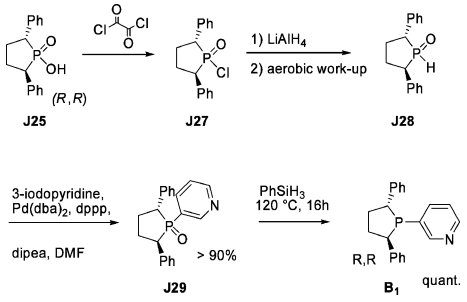


Scheme 8. Synthesis of oxazoline-functionalized phosphane ligands.

idine in DMF at 105 °C by using $Pd(OAc)_2$/dppb as the catalyst. Work up under aerobic conditions provided a racemic mixture of (*R*)- and (*S*)-3-[*tert*-butyl(phenyl)phosphinoyl]pyridine in 62% yield after purification by column chromatography. The enantiomers were resolved by separation on a chiral preparative HPLC column on a 300 mg scale. Subsequent reduction with phenylsilane yielded the pure ligands **B5** and **B6** almost quantitatively.

The *tert*-butyl(phenyl)phosphane–borane building block **J18** was used to prepare phosphane-oxazoline ligands (Scheme 8).[22] The secondary phosphane was transformed into (*R*)-*tert*-butyl(phenyl)methylphosphane–borane **J19** by sparteine-mediated enantioselective lithiation. The product was obtained in 93% enantiomeric excess and isolated in enantiopure form after crystallization from ethyl acetate.[23] Subsequent lithiation of the methyl group followed by the addition of carbon dioxide yielded the corresponding phosphinic acid (**J20**) in 87% yield after crystallization from toluene. To this acid many different amino alcohols can be coupled by using standard peptide coupling procedures, which yield protected phosphane-oxazoline ligands (**J22**) after a cyclization reaction. We used this methodology with an amino alcohol substituted at the carbon atom next to the oxygen functional group. A functional group next to the nitrogen might create too much steric hindrance for proper coordination to the porphyrinatozinc(II) and make the oxazoline, with a substituent on the carbon atom next to the nitrogen, less suitable for the SUPRAPhos ligand library. Under standard conditions the cyclization reaction of non-substituted amino alcohols failed. Apparently, substrate preorganization is important for cyclization in these cases. Most synthesized oxazolines known in the literature have a substituent at the carbon next to the nitrogen.[24] When amino alcohols with a substituent on the carbon next to the oxygen were used, the reaction did proceed under standard conditions, but not smoothly (2 equiv. of methanesulfonyl chloride and 2 equiv. of base). In the presence of 5 equiv. of methanesulfonyl chloride and 4.9 equiv. of base, the cyclized product was obtained in 86% yield. Subsequent deprotection using the tetrafluoroboric acid–dimethyl ether complex yielded pure **B4** in almost quantitative yield after column chromatography.

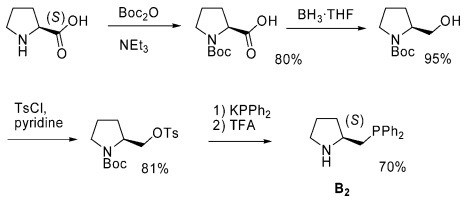
Pyridyl-functionalized phospholane **B1** was prepared following an eight-step process (Scheme 9) that was inspired by a procedure developed by Guillen and Fiaud and coworkers.[25] The phosphole ring was formed by the McCormack cycloaddition of 1,4-diphenylbutadiene and an aminophosphenium cation.[26] The *cis*-phospholene was hydrogenated and isomerized to the *trans*-phospholane. After hydrolysis, the racemic mixture of this acid could easily be resolved by crystallization with quinine from refluxing methanol. The *S*,*S* isomer (**J26**) selectively crystallizes and could be liberated from the quinine by treatment with a basic solution. Reaction of the acid with oxalyl chloride offered the reactive chlorophosphane oxide **J27** in quantitative yield. Reduction with lithium aluminium hydride followed by aerobic work up provided the secondary phosphane oxide **J28** in 90% yield. By palladium-catalyzed P–C coupling, iodopyridine was coupled to the secondary phosphane, which resulted in the formation of the pyridyl-phosphane oxide **J29**. This phosphane oxide could subsequently be reduced by phenylsilane to yield the desired pyridyl-functionalized phospholane **B1** in almost quantitative yield.



Scheme 9. Synthesis of pyridyl-functionalized phospholane ligand **B1**.

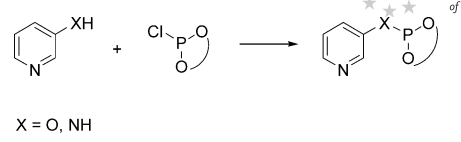
The pyrrolidine-based phosphane **B2** could be prepared starting from L-proline according to a published procedure (Scheme 10).[27] Boc-protected proline was reduced to prolinol by the boron–THF complex to provide *N*-Boc-prolinol. The corresponding tosylate was formed by reaction of the alcohol with tosyl chloride, after which the phosphane could be formed by reaction with potassium diphenylphosphide. Deprotection of the amine rendered phosphane **B2**.

The phosphite and phosphoramidite ligands were easily prepared by reacting hydroxy- and aminopyridines, respectively, with the corresponding chlorophosphite



Scheme 10. Synthesis of pyrrolidine-based phosphane **B2**.

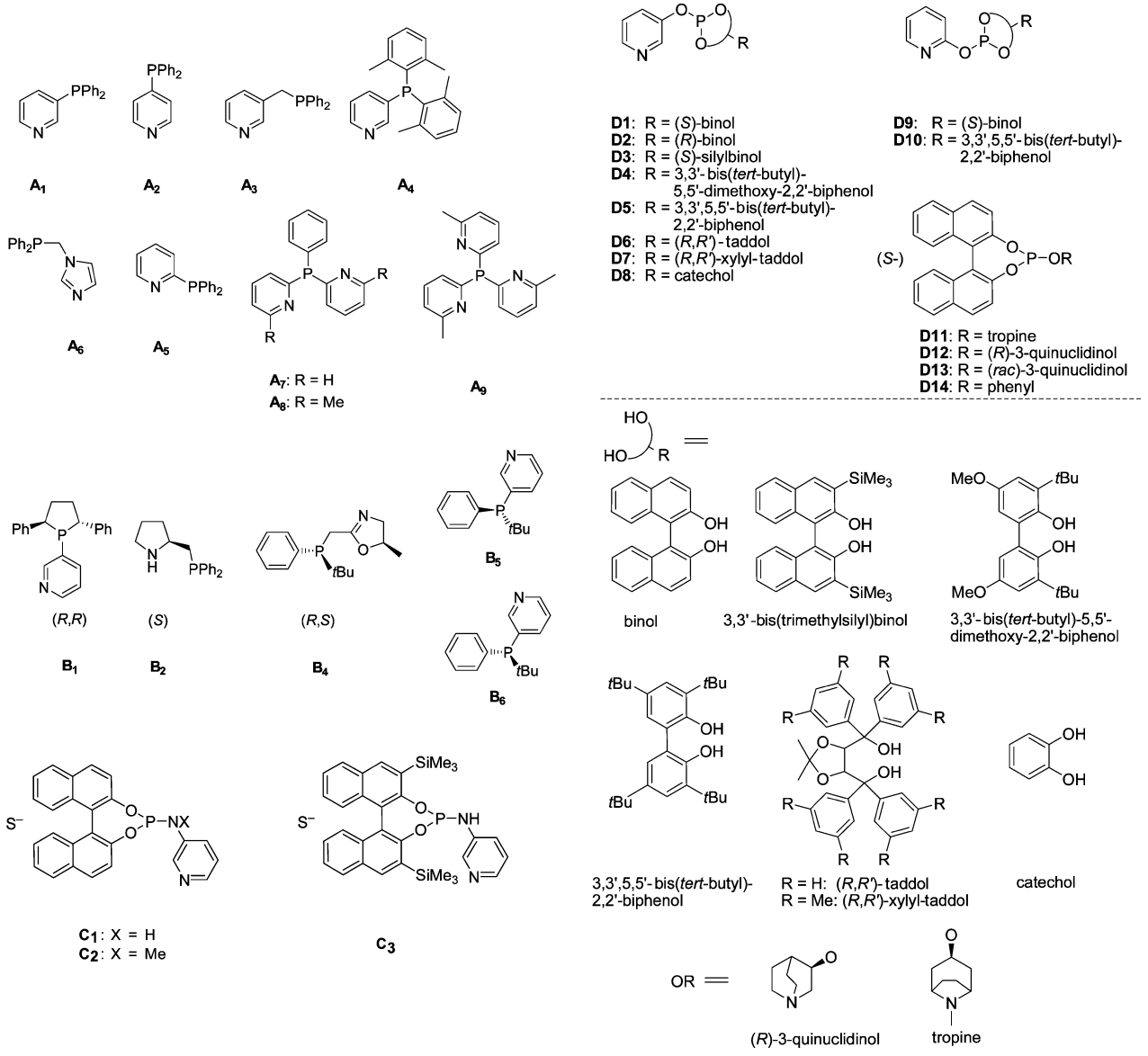
(Scheme 11).[9a,9h] Purification of these type of compound was accomplished by precipitation of impurities in a toluene/hexane mixture (usually 1:2 or 1:3) followed by filtration. The yields were typically between 70 and 90%.



Scheme 11. General route for the synthesis of pyridyl phosphites and phosphoramidites.

By using the above-mentioned methods, 27 different nitrogen-donor phosphorus ligands were prepared. The final library of pyridyl-functionalized phosphorus ligands is depicted in Scheme 12.

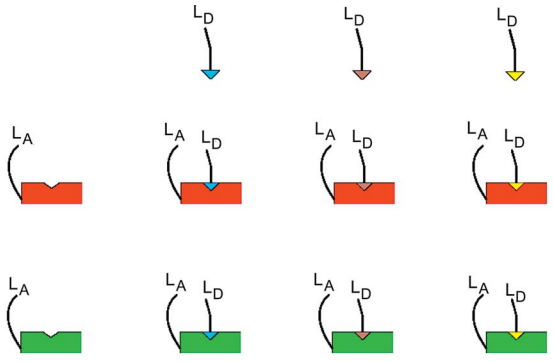
Based on these 30 nitrogen-donor phosphorus ligand building blocks and 15 complementary porphyrin-appended ligand building blocks we constructed a library of $15 \times 30 = 450$ bidentate phosphorus ligands. Of these 450



Scheme 12. Nitrogen-donor phosphorus ligands.

bidentate ligands, 437 are chiral and hence applicable in asymmetric catalysis. Table 1 presents an overview of the types and numbers of (hetero)bidentate ligands that can be formed with these building blocks. With these building blocks we currently have the largest library of supramolecular ligands in hand and we will further explore the properties of these ligands in various transition-metal-catalyzed reactions.

Table 1. Overview of the library of supramolecular ligands.

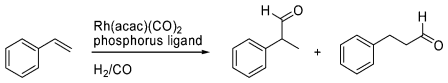


	Chiral porphyrin phosphites: 12	Achiral porphyrin phosphites: 1	Chiral porphyrin phosphor-amidites: 2	Total
Achiral phosphanes: 9	108	9	18	135 (A)
Chiral phosphanes: 5	60	5	10	75 (B)
Achiral phosphites: 4	48	4	8	60 (D)
Chiral phosphites: 9	108	9	18	135 (D)
Chiral phosphor-amidites: 3	36	3	6	45 (C)
Total 360		30	60	450

Some of the ligands in this library have previously been used in palladium-catalyzed allylic alkylation and rhodium-catalyzed hydrogenation reactions. The results of the asymmetric rhodium-catalyzed hydroformylation of styrene performed by using some of these ligands is described below.

Asymmetric Hydroformylation of Styrene

Styrene hydroformylation gives access to valuable propionic aldehydes, which are valuable intermediates in, for instance, the synthesis of pharmaceuticals like ibuprofen, ketoprofen, and naproxen.[28] The hydroformylation of styrene can produce two products: The achiral linear 3-phenylpropionaldehyde and the chiral 2-phenylpropionaldehyde (Scheme 13).



Scheme 13. Rhodium-catalyzed hydroformylation of styrene.

Owing to the stability of the benzylic rhodium species that is formed upon coordination of the alkene in a η^3 fashion, the branched 2-phenylpropionaldehyde is generally the favored product.[29] Part of our SUPRAPhos library was used in the asymmetric hydroformylation of styrene. We chose representatives of all ligand classes in the first screening. This allowed the identification of suitable structures for a second, more focused library. The screening experiments were performed in autoclaves equipped with 8 or 14 mini inner reactors (with magnetic stirrer bars) for parallel screening and the temperature was controlled by using an oil bath. [Rh(acac)(CO)$_2$] was used as a metal precursor and 5 equiv. of each monodentate ligand building block was added. Syngas (20 bar, CO/H$_2$, 1:1) was applied at various temperatures. Some of the results of the first screening are displayed in Table 2. The complete data set are given in the Supporting Information.

Table 2. Selected results of the hydroformylation of styrene using Rh(SUPRAPhos) complexes.[a]

Entry	Ligand	*T* [°C]	*t* [h]	Conv.[b] [%]	b/l[c]	*ee* [%]
1	**1·A1**	60	14	89	2.1	<2
2	**5·A1**	60	14	77	6.1	2.4 (*R*)
3	**1·B1**	50	64	4.8	4.3	17 (*R*)
4	**1·B1**	60	14	16	3.7	9.0 (*R*)
5	**5·B1**	60	14	87	4.5	8.4 (*R*)
6	**8·B1**	50	64	3.3	16	12 (*R*)
7	**9·B1**	60	14	>99	5.6	3.8 (*S*)
8	**1·C1**	40	88	11	7.0	27 (*R*)
9	**5·C1**	40	88	1	1.0	76 (*R*)
10	**5·C2**	40	87	4.1	4.5	5.6 (*R*)
11	**6·C1**	40	88	1.8	3.8	46 (*R*)
12	**11·D1**	40	48	1	3.8	57 (*R*)
13	**11·D3**	40	48	36	7.5	<2
14	**8·D1**	40	16	3.7	4.3	11 (*S*)
15	**8·D3**	40	16	>99	14	<2
16	**1**	50	16	20	3.8	5.6 (*R*)
17	**8**	40	16	>99	15	5.1 (*R*)
18	**9**	60	14	>99	6.7	<2
19	**11**	40	48	5		23 (*R*)
20	**B1**	60	14	>99	5.1	4.6 (*S*)
21	**C1**[d]	60	12	5.3	5.3	16 (*R*)
22	**C1**[e]	60	12	58	6.9	7.8 (*R*)
23	**C2**	40	87	92	8.9	<2
24	**D3**	40	16	>99	14	–

[a] Conditions: [Rh(acac)(CO)$_2$] = 1.00 mM, [porphyrin phosphite] = 5.00 mM, [pyridyl phosphorus donor] = 5.00 mM, [diisopropylethylamine] = 50.5 mM, substrate/Rh = 1000, p(CO/H$_2$) = 20 bar. [b] Percentage conversion of styrene to aldehydes. [c] b/l = branched/linear ratio. [d] Rh/ligand ratio = 1:10. [e] Rh/ligand ratio = 1:5.

The most active rhodium complexes were formed from heterobidentate ligands containing either a phosphane or a bulky phosphite ligand (entries 1, 2, and 7). Unfortunately, these ligands barely induced any enantioselectivity in the reaction. Moderate-to-high enantioselectivities were obtained with rhodium complexes derived from a heterobiden-

ate ligand containing a phosphoramidite ligand. Unfortunately, the complexes of these ligands led, without exception, to very low conversions of styrene. The screening revealed the effects of small changes in the ligand system on the outcome of the catalysis. For instance, **1·B1** gave 16% conversion after 14 hours at 60 °C (entry 4), **5·B1** (entry 5) showed 87% conversion under the same conditions. The only difference between these ligands is the position of the phosphite on the *meso*-phenyl ring of the porphyrin.

Steric bulk played an important role in the branched-to-linear selectivity. Generally, bulky ligands gave rise to higher branched-to-linear ratios. For instance, the catalyst formed upon coordination of ligand **1·B1** resulted, at 50 °C, in a b/l ratio of 4.3 (entry 3). The catalyst formed from the more bulky **8·B1** provided, under the same conditions, a b/l ratio of 16 (entry 6). Both ligands are derived from BINOL phosphites; ligand **8**, however, is considerably more bulky because of the trimethylsilyl group at the *ortho* position of the BINOL backbone. The difference in (enantio)selectivity observed for the catalysts formed by coordination with **1·C1** and **5·C1** is also interesting. Both phosphites **1** and **5** are (*S*)-BINOL phosphites, but are positioned, respectively, at the *ortho* and *meta* positions of the *meso*-phenyl ring of the porphyrin. The catalyst based on **1·C1** converted, with low activity, the styrene into phenylpropionaldehyde with a branched-to-linear selectivity of 7.0 and 27% *ee* of the branched product (entry 8). The catalyst based on **5·C1** formed equimolar amounts of the branched and linear products, but the enantioselectivity was higher: 76% *ee* was obtained although with a rather low conversion (entry 9).[30] The difference between **5·C1** and **5·C2** is also striking; whereas the former catalyzed the conversion of styrene with high enantioselectivity, only 5.6% *ee* was obtained with the latter ligand (entry 10). The only difference between these two ligands is the presence of a secondary or tertiary amine in the phosphoramidite ligand. These minor changes, which result in large differences in catalytic outcome, emphasize the necessity of ligand library screening for identifying suitable catalysts for a process.

Further experiments comprised parameter changes to improve the activity of the catalyst based on **5·C1**. We investigated the influence of steric bulk at the *ortho* position of the BINOL (ligands **7** and **8**), the influence of temperature, the metal-to-ligand ratio, and the (partial) CO/H_2 pressure (Table 3).

The catalysts based on bulky ligand assemblies showed much higher activity than **5·C1**, but the enantioselectivity dropped dramatically. The highest *ee* obtained with the bulky ligands (5.7%; Table 3, entry 4) was reached when 5 equiv. of the bulky porphyrin phosphite and 1 equiv. of the pyridyl phosphoramidite were used. This avoids the formation of homo-phosphoramidite complexes, but the result suggests that the catalysis is dominated by the mono-porphyrin phosphite rhodium complex (cf. Table 2, entry 17; high conversion, low *ee*, b/l close to 15).

When the rhodium catalyst based on **5·C1** was used at 60 instead of 40 °C, the *ee* of the product dropped to 41% (compared with 76% at 40 °C). Thus the increase in temperature resulted in lower enantioselectivity, whereas the conversion increased to only 1.5%.[31] The same trend was observed for the catalyst based on **6·C1** (entry 7). In both experiments there was also an increase in selectivity for the branched product. Lowering the ligand-to-metal ratio resulted in a much higher conversion, but almost complete loss of enantioselectivity was observed (cf. entry 5 with 6 and entry 7 with 8). For the catalysts based on **5·C1** the selectivity for the branched product was significantly enhanced. These results indicate that different rhodium species, such as mono-phosphite and ligand-free rhodium complexes, are formed under these conditions.

Table 3. Hydroformylation of styrene with SUPRAPhos phosphoramidite ligands under different conditions.[a]

Entry	Ligand	*T* [°C]	$p(CO/H_2)$ [bar]	$Rh/L_A/L_D$	Conv.[b] [%]	b/l[c]	*ee*[d] [%]
1	**7·C1**	40	10:10	1:5:5	9.7	6.6	<2
2	**7·C2**	40	10:10	1:5:5	47	10	<2
3	**8·C1**	40	10:10	1:5:5	1.0	5.9	2.1
4	**8·C1**	40	10:10	1:5:1[e]	>99	12	5.7
5	**5·C1**	60	10:10	1:5:5	1.5	1.9	41
6	**5·C1**	60	10:10	1:2.5:2.5	72	4.5	7.0
7	**6·C1**	60	10:10	1:5:5	6.5	4.3	19
8	**6·C1**	60	10:10	1:2.5:2.5	80	5.4	7.4
9[f]	**5·C1**	40	10:10	1:5:5	<1	1.2	76
10	**5·C1**	40	10:20	1:5:5	<1	1.1	71
11[g]	**5·C1**	40	10:20	1:5:5	<1	1.4	N.d.
12	**5·C1**	40	10:20	1:4:4	<1	1.4	N.d.
13	**5·C1**	40	20:10	1:5:5	1.0	1.9	47

[a] Conditions: $[Rh(acac)(CO)_2]$ = 1.00 mM, [porphyrin phosphite] = 5.00 mM, [pyridyl phosphorus donor] = 5.00 mM, [diisopropylethylamine] = 50.5 mM, substrate/Rh = 1000, $p(CO/H_2)$ = 20 bar. [b] Percentage conversion of styrene to aldehydes. [c] b/l = branched/linear ratio. [d] In all cases the *R* enantiomer was obtained in excess. [e] [porphyrin phosphite] = 5.00 mM, [pyridyl phoshoramidite] = 1.0 mM. [f] The styrene was added after 30 min incubation at 40 °C and 20 bar syngas. [g] $[Rh(acac)(CO)_2]$ = 5.00 mM.

Based on the results obtained so far, we developed a second, more focused library. Because high activity was obtained with phosphane-containing SUPRAPhos ligands and high enantioselectivity with (secondary) phosphoramidite SUPRAPhos ligands, we used in situ formed rhodium complexes of phosphoramidite porphyrins **11** and **12** with the phosphane donor ligands **A1**–**A3** and **B5** and **B6** (Table 4).

Interestingly, the activities of the catalysts based on the phosphane-phosphoramidite ligands were much higher than those based on phosphite-phosphoramidite, with conversions up to 39% in 20 hours (entry 6). Unfortunately, the enantioselectivity was not so high, although in general it was higher than for the phosphane-phosphite bidentate ligand systems shown in Table 2. The highest enantioselectivities were obtained for catalysts based on the SUPRAPhos ligands **11·A3** and **12·A3**, 25 and 27%, respectively (entries 3 and 8). The catalysts based on assemblies with the P-stereogenic phosphanes **B5** and **B6** gave (very) low enantioselectivity (varying between 2.2 and 10; entries 4, 5, 9 and 10). A large variation in regioselectivity was obtained with these catalysts, from a b/l ratio of 8.3 for the catalyst

Table 4. Hydroformylation of styrene using a small phosphane phosphoramidite library.[a]

Entry	Ligand	Conv.[b] [%]	b/l[c]	*ee* [%] (config.)
1	**11·A1**	16	8.3	16 (*R*)
2	**11·A2**	8.8	2.5	22 (*R*)
3	**11·A3**	13	0.8	25 (*R*)
4	**11·B5**	8.8	7.9	2.2 (*R*)
5	**11·B6**	5.9	7.5	4.0 (*R*)
6	**12·A1**	39	5.3	7.3 (*S*)
7	**12·A2**	16	6.6	<2
8	**12·A3**	1.9	0.5	27 (*R*)
9	**12·B5**	11	2.9	10 (*R*)
10	**12·B6**	13	3.4	5.2 (*R*)

[a] Conditions: [Rh(acac)(CO)$_2$] = 1.00 mM, [porphyrin phosphoramidite] = 5.00 mM, [pyridylphosphane] = 5.00 mM, [diisopropylethylamine] = 50.5 mM, substrate/Rh = 1000, p(CO/H$_2$) = 20 bar, T = 40 °C, 20 h. [b] Percentage conversion of styrene to aldehydes. [c] b/l = branched/linear ratio.

based on **11·A1** (entry 1) to 0.5 for the catalyst based on **12·A3** (entry 8), the latter implying the formation of mainly the linear aldehyde.[32] In particular, in the case of the chiral phosphanes **B5** and **B6**, a clear influence of the position of the amidite on the porphyrin on the regioselectivity of the reaction was observed. For example, the catalyst based on **11·B5** (2-amidite porphyrin) gave a b/l ratio of 7.9 (entry 4), whereas the catalyst based on the 3-analogue, **12·B5**, gave the aldehydes with a b/l ratio of 2.9 (entry 9).

Conclusions

Supramolecular chemistry provides efficient tools for making new ligands that are particularly suited to the construction of large ligand libraries. Previously we introduced SUPRAPhos as an example of such a new class of ligands. In this article we have elaborated the synthesis of building blocks that can be used for the formation of supramolecular bidentate ligands (SUPRAPhos), and with the building blocks currently available a 450-membered library of bidentate phosphorus ligands is accessible of which 437 members are chiral. The library contains a large number of diverse ligands: Phosphane-phosphite, phosphane-phosphoramidite, phosphite-phosphite, and phosphite-phosphoramidite heterobidentate ligands. In this library building blocks are available to form 70 heterobidentate phosphorus ligands containing a P-stereogenic phosphorus center, ligands that are difficult to prepare by classical synthesis.

Application of part of the library in the asymmetric hydroformylation of styrene reveals a catalytic performance that is strongly dependent on the ligand class used. Catalysts formed from phosphane-containing or bulky phosphite ligands generally show high activity in the hydroformylation reactions. However, the product enantioselectivities obtained with these catalysts were often very low. In contrast, reactions performed with catalysts formed from a SUPRAPhos ligand containing a phosphoramidite ligand result in relatively high enantioselectivities and low activities. Besides the differences between ligand classes, sometimes large variations were also observed in activity and selectivity within one ligand class between closely related ligands. This stresses the importance of library screening in homogeneous catalysis.

Experimental Section

General Remarks: All experiments were performed under a dry, inert atmosphere of nitrogen using standard Schlenk techniques unless stated otherwise. Solvents were dried and distilled under nitrogen prior to use. Toluene was distilled from sodium, ethyl ether and tetrahydrofuran from sodium/benzophenone, and hexanes from sodium/benzophenone/triethylene glycol dimethyl ether ('triglyme'). Dichloromethane, ethyl acetate, and acetonitrile were distilled from CaH_2. Dimethylformamide was distilled from $CaSO_4$. NMR spectra were recorded with a Varian Mercury 300 or a Varian Inova 500 spectrometer. ^{31}P and ^{13}C NMR spectra were measured with ^{1}H decoupled. $CDCl_3$ was used as the solvent; shifts are given relative to TMS (^{1}H, ^{13}C) and 85% H_3PO_4 (^{31}P). Optical rotations were measured with a Perkin-Elmer 241 polarimeter using a sodium lamp (289 nm) unless stated otherwise. Elemental analyses were performed at the H. Kolbe Mikroanalytisches Laboratorium in Mülheim (Germany). HRMS were recorded at the Department of Mass Spectrometry at the University of Amsterdam with a JEOL JMS SX/SX102A four-sector mass spectrometer using FAB$^+$ ionization with 3-nitrobenzyl alcohol as the matrix. UV/Vis titration experiments were performed with a HP 8453 UV/Vis System. Gas chromatographic analyses for Conversions and regioselectivities were determined by GC with a Shimadzu GC-17A apparatus [split/splitless, equipped with a FID detector and a BPX35 column (internal diameter 0.22 mm, film thickness 0.25 μm, carrier gas 70 kPa He)]. Chiral gas chromatographic analyses were performed with an Interscience Trace GC Ultra instrument (FID detector) equipped with a ph Megadex column (internal diameter 0.1 mm, 5 m column, film thickness 0.1 μm).

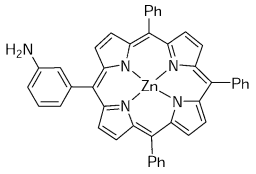
Materials: Chemicals were purchased from commercial suppliers and, unless stated otherwise, used without further purification. Triethylamine and diisopropylethylamine were distilled from CaH_2 prior to use. The following compounds were prepared according to literature procedures: The chlorophosphite of (*S*)-2,2′-binaphthol,[33] the phosphorochloridite of (*S*)-(–)-3,3′-bis(trimethylsilyl)-2,2′-binaphthol,[34] (1*S*,7*S*)-4-chloro-9,9-dimethyl-2,2,6,6-tetrakis-(3,5-dimethylphenyl)-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane,[35] ligands **1**–**10**,[9c,9g] **B2**,[27] **C1**–**3**[9h] and **D1**–**6**, and **9**–**14**.[9c,9g,9h,9o]

Synthesis of (*R*)-[3,3′-Bis(trimethylsilyl)-1,1′-binaphthyl-2,2′-diyl][5-(Phenyl-3-yl)-10,15,20-triphenylporphyrinyl-κ^4*N*^{21},*N*^{22},*N*-zinc(II)] Phosphite (8): A solution of (*R*)-3,3′-bis(trimethylsilyl)-2,2′-binaphthol phosphorus chloridite (1.30 g, 2.62 mmol) in CH_2Cl_2 (10 mL) was added to a mixture of 5-(3-hydroxyphenyl)-10,15,20-triphenylporphyrinatozinc(II) (1.86 g, 2.68 mmol), azeotropically dried with toluene (3 × 10 mL) and DIPEA (4.80 mL, 27.6 mmol) in CH_2Cl_2 (100 mL) was added dropwise at –78 °C. After addition of the PCl compound, the mixture was stirred for 15 min at –78 °C and 3 h at room temperature. The solvent was evaporated and the crude product dissolved in a minimum amount of CH_2Cl_2 and purified over a short column (ca. 3 cm) of basic alumina. After evaporation of the solvent, the product was obtained as a purple solid. Yield 1.66 g (55%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.00–8.97 (m, 4 H), 8.90–8.80 (m, 3 H), 8.32–8.22 (m, 5 H), 8.08 (br. s, 1 H), 7.97 (d, J = 7.80 Hz, 1 H), 7.87 (d, J = 8.10 Hz, 1 H), 7.80–7.71 (m, 9 H), 7.65–7.63 (m, 4 H), 7.55–7.53 (m, 1 H), 7.32 (t, J = 6.90 Hz, 1 H), 7.24–7.19 (m, 1 H), 7.14–7.06 (m, 1 H), 6.97 (d, J = 8.70 Hz, 1 H), 6.77

(d, J = 8.70 Hz, 1 H), 6.64 (d, J = 7.50 Hz, 1 H), 6.37 (t, J = 7.50 Hz, 1 H), 5.92 (t, J = 7.20 Hz, 1 H), 0.54 (s, 9 H), 0.43 (9 H) ppm. ^{31}P NMR (121.3 MHz, $CDCl_3$): δ = 139.0 ppm.

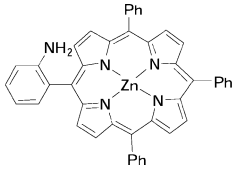
The other enantiomeric form (**7**) was prepared in an identical way and has identical spectroscopic data.

Synthesis of 5-(3-Aminophenyl)-10,15,20-triphenylporphyrinyl-κ^4*N*^{21},*N*^{22},*N*^{23},*N*^{24}-zinc(II)



A solution of *meso*-(3-aminophenyl)triphenylporphyrin (387 mg, 0.61 mmol) and $Zn(OAc)_2{\cdot}2H_2O$ (337 mg, 1.54 mmol) in a CH_2Cl_2/MeOH mixture was stirred for 16 h at room temperature, after which part of the solvent was evaporated. During evaporation of the CH_2Cl_2, methanol was added gradually in order to precipitate the product. After leaving the product to precipitate overnight, it was filtered and washed with methanol. The product was used without further purification. Yield 326 mg (77%). ^{1}H NMR (300 MHz, $CDCl_3$ + 2 drops CD_3CN): δ = 8.78–8.70 (m, 4 H), 8.52 (d, J = 4.20 Hz, 1 H), 8.23–8.15 (m, 4 H), 8.09–8.02 (m, 3 H), 7.94 (d, J = 7.50 Hz, 1 H), 7.65–7.44 (m, 13 H), 7.14 (d, J = 7.20 Hz, 1 H) ppm.

Synthesis of 5-(2-Aminophenyl)-10,15,20-triphenylporphyrinyl-κ^4*N*^{21},*N*^{22},*N*^{23},*N*^{24}-zinc(II)



A solution of *meso*-(2-aminophenyl)triphenylporphyrin (388 mg, 0.62 mmol) and $Zn(OAc)_2{\cdot}2H_2O$ (780 mg, 3.55 mmol) in a CH_2Cl_2/MeOH solvent mixture (2:1, 40 mL) was stirred for 16 h at room temperature, after which part of the solvent was evaporated. During evaporation of the CH_2Cl_2, methanol was added gradually in order to precipitate the product. After precipitation overnight, the product was isolated by filtration and washed with methanol. The product was used without further purification. Yield 278 mg (65%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.03 (d, J = 4.50 Hz, 2 H), 8.90 (d, J = 5.10 Hz, 2 H), 8.57 (d, J = 4.20 Hz, 2 H), 8.49 (br. d, J = 6.00 Hz, 1 H), 8.33 (br. d, J = 6.90 Hz, 1 H), 8.24 (br. s, 2 H), 7.97 (d, J = 7.20 Hz, 2 H), 7.87–7.62 (m, 12 H), 7.37–7.34 (m, 1 H), 6.89–6.87 (m, 2 H), 4.04 (br. s, 2 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 150.6, 150.4, 149.9, 148.7, 143.6, 143.3, 140.7, 134.9, 134.7, 134.6, 134.4, 132.7, 132.2, 130.4, 129.9, 127.8, 127.7 127.5, 126.9, 126.8, 126.7, 126.6, 121.5, 121.2, 121.0, 119.7, 116.6, 112.9 ppm. $C_{44}H_{29}N_5Zn$ (693.14) + 2.5 equiv. H_2O: calcd. C 71.59, H 4.64, N 9.49; found C 71.93, H 4.39, N 8.36.

Synthesis of (*S*)-(1,1′-Binaphthyl-2,2′-diyl) [5-(Phenyl-3-yl)-10,15,20-triphenylporphyrinyl-κ^4*N*^{21},*N*^{22},*N*^{23},*N*^{24}-zinc(II)]phosphoramidite (11): 5-(3-Aminophenyl)-10,15,20-triphenylporphyrin zinc(II) (0.47 mmol, 326 mg) was azeotropically dried with toluene (3 × 2 mL). After dissolving in THF (30 mL), it was cooled to –50 °C, after which DIPEA (4.70 mmol, 0.82 mL) was added. Freshly prepared (*S*)-2,2′-binaphthol phosphorus chloridite (0.47 mmol, 165 mg), dissolved in THF (10 mL), was added dropwise. The mixture was stirred overnight and at the same time allowed to warm up to room temperature. The solvent was evaporated and the product dissolved in CH_2Cl_2 (5 mL) and filtered through a short column of basic alumina (4 cm) using dichloromethane as eluent. Evaporation of the solvent yielded the ligand as a purple solid. Yield 213 mg (45%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.07–9.05 (m, 2 H), 9.01–8.96 (m, 6 H), 8.28–8.21 (m, 6 H), 7.95 (d, J = 5.40 Hz, 1 H), 7.91 (d, J = 8.00 Hz, 1 H), 7.87 (d, J = 7.50 Hz, 1 H) 7.85–7.83 (m, 2 H), 7.79–7.74 (m, 7 H), 7.67 (d, J = 8.00 Hz, 1 H), 7.61 (t, J = 8.00 Hz, 1 H), 7.54 (d, J = 7.50 Hz, 1 H), 7.45–7.40 (m, 4 H), 7.35 (d, J = 9.00 Hz, 1 H), 7.31 (d, J = 8.50 Hz, 1 H), 7.27–7.24 (m, 2 H), 7.13 (t, J = 7.50 Hz, 1 H), 7.07 (t, J = 7.50 Hz, 1 H), 5.44 (s, 1 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 150.5, 150.4, 150.3, 149.0, 147.3, 144.4, 143.2, 139.7 (d, J = 16.2 Hz), 134.7 (d, J = 24.9 Hz), 133.8, 132.9 (J = 16.2 Hz), 132.2, 131.8, 131.3, 130.7 (d, J = 30.0 Hz), 130.1 (d, J = 28.3 Hz), 129.0, 128.7, 128.5, 128.3, 127.8, 127.6, 127.1, 126.9, 126.6, 125.3, 125.1, 124.9, 124.4, 123.9, 122.5, 121.8, 121.7, 121.4, 121.3, 120.7, 117.3 ppm. ^{31}P NMR (300 MHz, $CDCl_3$): δ = 147.8 ppm. MS (FAB): calcd. for $C_{64}H_{40}N_5O_2PZn$ 1007.2368; found 1007.2396.

Synthesis of (*S*)-(1,1′-Binaphthyl-2,2′-diyl) [5-(Phenyl-2-yl)-10,15,20-triphenylporphyrinyl-κ^4*N*^{21},*N*^{22},*N*^{23},*N*^{24}-zinc(II)]phosphoramidite (12): 5-(2-Aminophenyl)-10,15,20-triphenylporphyrinato-zinc(II) (0.40 mmol, 278 mg) was azeotropically dried with toluene (3 × 2 mL). After dissolving in THF (30 mL), it was cooled to –50 °C, after which DIPEA (4.01 mmol, 0.70 mL) was added. Freshly prepared (*S*)-2,2′-binaphthol phosphorus chloridite (0.40 mmol, 141 mg), dissolved in THF (10 mL), was added dropwise. The mixture was stirred overnight and at the same time allowed to warm up to room temperature. The solvent was evaporated and the product dissolved in CH_2Cl_2 (5 mL) and filtered through a very short column of basic alumina (5 cm) using dichloromethane as eluent. Evaporation of the solvent yielded the ligand as a purple solid. Yield 169 mg (42%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.97–8.83 (m, 8 H), 8.25–8.02 (m, 6 H), 7.88–7.66 (m, 14 H), 7.41–7.36 (m, 1 H), 7.19 (d, J = 6.90 Hz, 1 H), 7.14 (d, J = 8.70 Hz, 1 H), 6.97 (d, J = 6.60 Hz, 1 H), 6.87 (d, J = 8.40 Hz, 1 H), 6.58–6.53 (m, 3 H), 6.07 (d, J = 8.10 Hz, 1 H), 5.97 (d, J = 8.70 Hz, 1 H), 4.79 (s, 1 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 150.54, 150.46, 150.3, 150.11, 150.06, 148.3, 146.3, 143.2, 143.0, 142.6 [d, J(C,P) = 17.1 Hz], 135.2, 134.7, 132.9, 132.8, 132.5, 132.2, 131.7, 131.5, 131.4, 130.2, 129.8, 129.6, 128.4, 128.3, 127.8, 127.7, 127.6, 127.3, 126.8, 126.0 [d, J(C,P) = 20.8 Hz], 125.2 [d, J(C,P) = 26.9 Hz], 124.0, 122.6, 121.7, 121.4, 121.2 [d, J(C,P) = 6.12 Hz], 120.4, 116.6 [d, J(C,P) = 22.0 Hz], 114.7 ppm. ^{31}P NMR (300 MHz, $CDCl_3$): δ = 146.4 ppm.

Synthesis of (*R*)-(+)-3,3′-Dimethyl-2,2′-binaphthol Phosphorus Chloridite: (*R*)-(+)-3,3′-Dimethyl-1,1′-bi-2-naphthol (3.42 g, 10.9 mmol) was azeotropically dried with toluene (3 × 3 mL), dissolved in CH_2Cl_2 (30 mL) and added dropwise to a solution of PCl_3 (9.48 mL, 109 mmol) and Et_3N (3.02 mL, 21.7 mmol) in CH_2Cl_2 (80 mL) at –60 °C. When the addition of (*R*)-3,3′-dimethyl-1,1′-bi-2-naphthol was complete, the cooling bath was removed and the mixture was stirred for 3 h at room temperature. The reaction mixture was concentrated in vacuo, redissolved in toluene (30 mL), after which hexanes (60 mL) were added. The precipitated salts were removed by filtration under nitrogen. After evaporation of the solvent, the product was obtained as a white-yellowish foam in quantitative yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.91 (br. s, 2 H), 7.89 (br. s, 2 H), 7.51–7.43 (m, 2 H), 7.35–7.30 (m, 2 H), 7.27–7.22 (m, 2 H), 2.66 (s, 6 H) ppm. ^{31}P NMR (300 MHz, $CDCl_3$): δ = 175.3 ppm.

Synthesis of (*R*)-(3,3′-Dimethyl-1,1′-binaphthyl-2,2′-diyl) [5-(Phenyl-2-yl)-10,15,20-triphenylporphyrinyl-κ^4*N*^{21},*N*^{22},*N*^{23},*N*^{24}-zinc(II)] Phosphite (13): A solution of (*R*)-3,3′-dimethyl-2,2′-binaphthol phosphorus chloridite in CH_2Cl_2 (3 mL) was added dropwise to a mixture of 5-(2-hydroxyphenyl)-10,15,20-triphenylporphyrin zinc(II) (319 mg, 0.46 mmol), azeotropically dried with toluene (3 × 2 mL), and DIPEA (0.80 mL, 4.60 mmol) in CH_2Cl_2 (20 mL) at –78 °C. After addition of the PCl compound, the mixture was stirred for 15 min at –78 °C and 3 h at room temperature. The solvent was evaporated and the crude product dissolved in a minimum amount of CH_2Cl_2 and purified through a short column (±3 cm) of basic alumina. After evaporation of the solvent, the product was obtained as a purple solid. Yield 224 mg (47%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.00–8.93 (m, 4 H), 8.89 (d, *J* = 9.00 Hz, 1 H), 8.87 (d, *J* = 9.00 Hz, 1 H), 8.75 (d, *J* = 4.80 Hz, 1 H), 8.67 (d, *J* = 4.50 Hz, 1 H), 8.35–8.34 (br. m, 2 H), 8.25–8.17 (m, 3 H), 8.04 (d, *J* = 7.20 Hz, 1 H), 7.86–7.50 (m, 14 H), 7.23–7.11 (m, 2 H), 6.67 (t, *J* = 7.65 Hz, 1 H), 6.45 (d, *J* = 8.40 Hz, 1 H), 5.93–5.83 (m, 3 H), 5.76 (br. s, 2 H), 2.18 (s, 6 H) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 151.5 (d, *J* = 3.52 Hz), 150.7, 150.33, 150.30 (d, *J* = 2.39 Hz), 150.25 (d, *J* = 2.39 Hz), 150.0 (d, *J* = 8.04 Hz), 146.8 (d, *J* = 5.78 Hz), 145.8 (d, *J* = 3.52 Hz), 143.3 (d, *J* = 6.40 Hz), 143.1, 136.3, 135.7, 134.8, 134.7, 134.6, 132.4, 132.1, 132.0, 131.7, 131.4, 131.2, 129.9, 129.54, 129.49, 129.3, 129.2, 128.9, 128.5, 127.7 (d, *J* = 2.89 Hz), 127.5, 127.4, 126.8, 126.7 (d, *J* = 4.02 Hz), 126.6, 125.5, 125.1 (d, *J* = 9.30 Hz), 124.9 (d, *J* = 6.28 Hz), 123.9 (d, *J* = 5.15 Hz), 123.4, 123.1 (d, *J* = 5.15 Hz), 121.5, 121.4 (d, *J* = 2.89 Hz), 121.1, 121.0, 119.8 (d, *J* = 10.4 Hz) ppm. ^{31}P NMR (121.3 MHz, $CDCl_3$): δ = 143.7 ppm. MS (FAB): calcd. for $C_{66}H_{43}N_4O_3PZn$ 1036.2521; found 1036.2526. $C_{66}H_{43}N_4O_3PZn$ (1036.46) + 1 equiv. H_2O: calcd. C 75.18, H 4.30, N 5.31; found C 74.77, H 4.65, N 5.39.

Synthesis of (*R*)-(3,3′-Dimethyl-1,1′-binaphthyl-2,2′-diyl) [5-(Phenyl-3-yl)-10,15,20-triphenylporphyrinyl-κ^4*N*^{21},*N*^{22},*N*^{23},*N*^{24}-zinc(II)] Phosphite (14): A solution of (*R*)-3,3′-dimethyl-2,2′-binaphthol phosphorus chloridite in CH_2Cl_2 (3 mL) was added dropwise to a mixture of 5-(3-hydroxyphenyl)-10,15,20-triphenylporphyrin zinc(II) (319 mg, 0.46 mmol), azeotropically dried with toluene (3 × 2 mL), and DIPEA (0.80 mL, 4.60 mmol) in CH_2Cl_2 (20 mL) at –78 °C. After addition of the PCl compound, the mixture was stirred for 15 min at –78 °C and 3 h at room temperature. The solvent was evaporated and the crude product dissolved in a minimum amount of CH_2Cl_2 and purified through a short column (±3 cm) of basic alumina. After evaporation of the solvent, the product was obtained as a purple solid. Yield 229 mg (48%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.00–8.93 (m, 7 H), 8.28–8.08 (m, 5 H), 8.08–8.03 (m, 2 H), 7.82–7.68 (m, 13 H), 7.64–7.61 (m, 2 H), 7.40–7.35 (m, 2 H), 7.30–7.25 (m, 2 H), 7.22–7.14 (m, 3 H), 7.08–7.03 (m, 1 H), 2.65 [d. *J*(H,P) = 11.1 Hz] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 150.56 (s), 150.49 (s), 150.16 (s), 147.86 (s), 147.79 (s), 146.48 (s), 146.45 (s), 145.00 (s), 143.09 (s), 134.72 (s), 132.43 (s), 132.33 (s), 132.28 (s), 132.01 (s), 131.92 (s), 131.76 (s), 131.59 (s), 131.37 (s), 130.84 (s), 130.29 (s), 130.0 (s), 127.99 (s), 127.77 (s), 127.62 (s), 127.16 [d, *J*(C,P) = 3.70 Hz], 126.81 (s), 126.37 [d, *J*(C,P) = 8.61 Hz], 125.62 (s), 125.44 (s), 125.37 (s), 125.05 (s), 124.94 (s), 124.86 (s), 123.03 (s), 121.60 (s), 121.48 (s), 119.84 (s), 119.22 [d, *J*(C,P) = 8.53 Hz] ppm. ^{31}P NMR (121.3 MHz, $CDCl_3$): δ = 142.5 ppm. MS (FAB): calcd. for $C_{66}H_{43}N_4O_3PZn$ 1036.2521; found 1036.2526. $C_{66}H_{43}N_4O_3PZn$ (1036.46): calcd. C 76.48, H 4.18, N 5.41; found C 76.55, H 4.10, N 5.40.

Synthesis of 3-[Bis(2,6-dimethylphenyl)phosphanyl]pyridine (A4): *n*-Butyllithium (5.28 mL of a 2.5 M solution in hexanes; 13.2 mmol) and TMEDA (1.99 mL, 1.53 g, 13.2 mmol) were stirred for 15 min at room temperature. After cooling to –70 °C, a THF/Et_2O/pentane solution (50 mL, 1:1:1) was added. The mixture was cooled to –120 °C and 3-bromopyridine (1.60 mL, 2.61 g, 16.5 mmol), dissolved in a 1:1:1 mixture of THF/Et_2O/pentane (10 mL), was added slowly. The mixture was stirred for 10 min at –120 °C, after which bis(2,6-dimethylphenyl)chlorophosphane (prepared according to a literature procedure[36]), dissolved in THF, was added dropwise. The resulting reaction mixture was stirred overnight and warmed to room temperature. The orange solution was washed once with brine, dried with $MgSO_4$, and filtered (all under nitrogen). After adding some silica, the mixture was concentrated in vacuo (and simultaneously impregnated on silica). The product was purified by column chromatography using PE 40–65 with 10% Et_3N as eluent. The product was further purified by chromatographic separation with a Chromatotron® using CH_2Cl_2 as eluent. When the impurity was removed, 1% MeOH was added to the eluent (R_f on silica with 1% MeOH/CH_2Cl_2: 0.37). Yield 1.2 g (23%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.60 (br. s, 1 H), 8.50 (dd, *J* = 4.65, *J* = 1.65 Hz, 1 H), 7.59 (br. t, *J* = 6.30 Hz, 1 H), 7.20–7.14 (m, 3 H), 7.03–6.99 (m, 4 H), 2.13 (s, 12 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 154.7 [d, *J*(C,P) = 28.1 Hz], 149.1 (s), 142.9 [d, *J*(C,P) = 15.9 Hz], 141.0 [d, *J*(C,P) = 18.3 Hz], 133.9 [d, *J*(C,P) = 17.0 Hz], 132.6 [d, *J*(C,P) = 19.6 Hz], 129.6 (s) 129.3 (d, *J* = 34.1 Hz), 123.4 [d, *J*(C,P) = 3.70 Hz], 23.6 [d, *J*(C,P) = 15.9 Hz] ppm. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = –26.4 ppm. $C_{21}H_{22}NP$ (319.38): calcd. C 78.97, H 6.94, N 4.39; found C 78.74, H 6.87, N 4.46.

Synthesis of (*R*,*R*)-2,5-Diphenylphospholane 1-Oxide: (*R*,*R*)-1-Oxo-2,5-diphenyl-1λ^5-phospholan-1-ol (1.22 g, 4.51 mmol), prepared according to a literature procedure,[25] was three times azeotropically dried with toluene and suspended in THF. After cooling to 0 °C, Oxalyl chloride (1.55 mL, 2.29 g, 18.1 mmol) was added. After 5 min stirring at 0 °C, the cooling bath was removed and the mixture stirred for 2 h at room temperature. The solvent and excess oxalyl chloride were removed by evaporation and the product was dissolved in Et_2O. After 5 min sonification in the ultrasound bath, $LiAlH_4$ (0.17 g, 4.51 mmol) was added in portions at 0 °C. After stirring overnight, all the phosphinic acid was reduced to the hydride, as judged by ^{31}P NMR (singlet, –19 ppm). The work up was performed under air, thereby oxidizing the product. A 1.0 M aq. HCl solution was added, followed by separation of the layers. The aqueous layer was once extracted with EtOAc. Afterwards, the combined organic layers were twice washed with a sat. aq. K_2CO_3 solution and once with a sat. NaCl solution. The organic layer was dried with $MgSO_4$, filtered, and concentrated in vacuo. The white solid was crystallized from EtOAc and immediately used in the next step. Yield 1.06 g (92%)

Synthesis of 3-(1-Oxo-2,5-diphenylphospholan-1-yl)pyridine (Both Enantiomers): $Pd(OAc)_2$ (43.6 mg, 0.19 mmol) and 1,3-bis(diphenylphosphanyl)propane (dppp) (88.2 mg, 0.21 mmol) were placed in a dry, degassed Schlenk tube and degassed by three vacuum/nitrogen cycles. The catalyst precursor was dissolved in DMF (10 mL) and stirred for 15 min at room temperature. 3-Iodopyridine (478 mg, 2.33 mmol) was added and the mixture was stirred for an additional 15 min. A solution of (*R*,*R*)-2,5-diphenylphospholane 1-oxide (498 mg, 1.94 mmol), three times azeotropically dried with toluene, and DIPEA in DMF (5 mL) was added to the catalyst solution. The resulting dark-red solution was stirred for 16 h at 105 °C. After cooling to room temperature, the DMF was evaporated. The crude product was redissolved in dichloromethane, washed twice with 5% aq. $NaHCO_3$ and once with brine. The organic layer was dried with $MgSO_4$, filtered, and the solvents evaporated. After a very fast purification over a small layer of silica to remove the main impurities, the product was purified by means of

chromatographic separation with a Chromatotron® using EtOAC/PE (3:1) as the eluent.

Analytical Data for the *S*,*S* Enantiomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (br. s, 1 H), 8.54 (br. s, 1 H), 7.82–7.76 (m, 1 H), 7.31–7.25 (m, 5 H), 7.12–7.02 (m, 6 H), 4.01–3.88 (m, 1 H), 3.57–3.74 (m, 1 H), 2.80–2.52 (m, 3 H), 2.33–2.23 (m, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 151.7 (s), 150.6 (s), 150.5 (s), 140.4 (br. s), 135.5 (s), 135.2 (s), 129.0 (br. s), 127.6 (s), 127.3 [d, *J*(C,P) = 4.76 Hz], 127.1 (s), 123.6 [d, *J*(C,P) = 7.32 Hz], 51.1 [d, *J*(C,P) = 62.5 Hz], 47.3 [d, *J*(C,P) = 62.3 Hz], 31.9 [d, *J*(C,P) = 7.40 Hz], 27.7 [d, *J*(C,P) = 8.53 Hz] ppm. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 52.9 ppm. $C_{21}H_{20}NOP$ (333.36): calcd. C 75.66, H 6.05, N 4.20; found C 75.75, H 6.08, N 4.04.

Analysis Data for the *R*,*R* Enantiomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.61 (d, *J* = 3.30 Hz), 8.51 (dd, *J* = 4.65, *J* = 2.25 Hz, 1 H), 7.80–7.73 (m, 1 H), 7.31–7.17 (m, 5 H), 7.12–7.02 (m, 6 H), 3.96–3.85 (m, 1 H), 3.53–3.46 (m, 1 H), 2.71–2.52 (m, 3 H), 2.32–2.23 (m, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 152.4 (s), 151.3 (s), 151.2 (s), 139.8 (s), 135.4 [d, *J*(C,P) = 3.77 Hz], 135.1 [d, *J*(C,P) = 6.03 Hz], 129.1 [d, *J*(C,P) = 5.28 Hz], 129.0 [d, *J*(C,P) = 1.51 Hz], 128.9 (br. s), 127.6 [d, *J*(C,P) = 2.26 Hz], 127.3 [d, *J*(C,P) = 4.52 Hz], 127.1 [d, *J*(C,P) = 3.02 Hz], 123.3 [d, *J*(C,P) = 7.32 Hz], 51.1 [d, *J*(C,P) = 62.3 Hz], 47.3 [d, *J*(C,P) = 62.3 Hz], 31.9 [d, *J*(C,P) = 7.32 Hz], 27.7 [d, *J*(C,P) = 9.74 Hz] ppm. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 52.6 ppm.

Synthesis of (*R*,*R*)-3-(2,5-Diphenylphospholan-1-yl)pyridine (B1): (*R*,*R*)-3-(1-Oxo-2,5-diphenylphospholan-1-yl)pyridine (300 mg, 0.90 mmol) was azeotropically dried with toluene (3 × 2 mL). $PhSiH_3$ (ca. 4 mL) was added, the mixture was heated at reflux with stirring for 16 h. After evaporation, the product was dissolved in CH_2Cl_2 and purified using a Chromatotron® with CH_2Cl_2 as eluent. Yield 234 mg (84%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.40 (d, *J* = 4.80 Hz, 2 H), 7.43–7.21 (m, 6 H), 7.12–6.91 (m, 6 H), 4.11–4.03 (m, 1 H), 3.97–3.85 (m, 1 H), 2.82–2.75 (m, 1 H), 2.47–2.38 (m, 1 H), 2.36–2.25 (m, 1 H), 2.17–2.05 (m, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 153.4 (d, *J* = 17.1 Hz), 149.6, 144.1 (d, *J* = 18.3 Hz), 141.1 (d, *J* = 19.6 Hz), 138.1, 132.3 (d, *J* = 34.2 Hz), 129.0, 128.4, 128.1 (d, *J* = 9.74 Hz), 127.8 (d, *J* = 3.70 Hz), 126.5 (d, *J* = 2.42 Hz), 126.2 (d, *J* = 2.42 Hz), 122.9 (d, *J* = 6.12 Hz), 48.6 (d, *J* = 17.1 Hz), 46.8 (d, *J* = 15.9 Hz), 37.1, 32.9 (d, *J* = 3.62 Hz) ppm. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 15.9 ppm. $C_{21}H_{20}NP$ (317.36): calcd. C 78.16, H 6.25, N 4.34; found C 78.37, H 6.28, N 3.95 (33% oxide present in sample during elemental analysis).

***tert*-Butyl(phenyl)phosphane–Borane:** The complex was prepared according to a literature procedure.[37]

(*R*)-*tert*-Butyl(methyl)phenylphosphane–Borane: The complex was prepared according to a literature procedure.[23]

Synthesis of (*R*)-{[Boronato(*tert*-butyl)(phenyl)]phosphanyl}acetic Acid: (*R*)-*tert*-Butyl(methyl)phenylphosphane–borane (1.00 g, 5.15 mmol) was dried azeotropically (3 × 4 mL) and dissolved in Et_2O (40 mL). *tert*-Buthyllithium (4.47 mL, a 1.5 M solution in pentane, 6.70 mmol) was added at –78 °C. After 1 h stirring at this temperature, CO_2 gas was bubbled through the solution. For that purpose, a round-bottomed flask was filled with CO_2 (s) and connected to a column with Sicapent® in order to dry the released gas. The gas was transferred to the flask through a polyflow® tube. The CO_2 was bubbled through for 1 h at –78 °C, and for 1 h at room temperature Et_2O (40 mL) was added to keep the solvent level constant. CO_2 bubbling was stopped and the mixture was stirred at room temperature for 16 h. Then the mixture was poured into ice–water with 37% aq. HCl (a few mL). The layers were separated and the aqueous layer was twice extracted with chloroform. A 0.5 M aq. Na_2CO_3 solution (100 mL) was added to the combined organic layers, which resulted in deprotonation of the product. As a consequence, the deprotonated acid moves to the aqueous layer. The layers were separated, after which 4 M aq. HCl (100 mL) and $CHCl_3$ (200 mL) were added to the aqueous layer. The protonated product immediately moved to the organic layer, which was collected. The aqueous layer was three times extracted with $CHCl_3$. The combined organic layers were dried with Na_2SO_4, filtered, and concentrated in vacuo. The product was crystallized from toluene to yield 1.0 g (87%) of the acid as a white solid. $[\alpha]_D$ = +50.1 (*c* = 0.974, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.33 (br. s, 1 H), 7.78–7.71 (m, 2 H), 7.53–7.41 (m, 3 H), 3.23 [t, *J*(P,H) = 13.2 Hz, 1 H], 3.00 [dd, *J*(P,H) = 13.2, *J*(H,H) = 9.3 Hz, 1 H], 1.12 [d, *J*(P,H) = 14.4 Hz, 9 H], 0.8–0.2 (br. s, 3 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 173.3 (s), 133.6 [d, *J*(C,P) = 8.53 Hz], 131.9 [d, *J*(C,P) = 2.49 Hz], 128.6 [d, *J*(C,P) = 9.82 Hz], 125.1 [d, *J*(C,P) = 48.8 Hz], 30.3 [d, *J*(C,P) = 31.8 Hz], 27.6 [d, *J*(C,P) = 25.7 Hz], 25.5 [d, *J*(C,P) = 2.42 Hz] ppm. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 33.4 (d, $J_{P,B}$ = 61.2 Hz) ppm. $C_{12}H_{20}BO_2P$ (238.07): calcd. C 60.54, H 8.47; found C 60.42, H 8.42.

Synthesis of 2-[(*R*)-Boronato(*tert*-butyl)(phenyl)phosphanyl]-*N*-[(*S*)-2-hydroxypropyl]acetamide: *tert*-Butyl(phenyl)(carboxymethyl)-phosphane–borane (250 mg, 1.11 mmol) was azeotropically dried (2×, toluene), dissolved in THF (15 mL), and cooled to 0 °C. 1-Hydroxybenzotriazole (HOBt) (301 mg, 2.23 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (256 mg, 1.34 mmol) were added and the resulting mixture was stirred for 30 min at room temperature. After cooling to 0 °C, (*S*)-(+)-1-amino-2-propanol (100 mg, 1.34 mmol) was added and the mixture was stirred overnight at room temperature. 1 M aq. HCl solution (10 mL) was added to the reaction mixture, followed by $CHCl_3$ (50 mL). The layers were separated and the aqueous layer was twice extracted with chloroform. The combined organic layers were washed once with sat. aq. $NaHCO_3$ and once with brine. After drying with Na_2SO_4, the solution was filtered and concentrated in vacuo. Column chromatography (silica, eluent: pure EtOAc, R_f = 0.32) yielded 219 mg (67%) of the product as a white solid. $[\alpha]_D$ = +70.4 (*c* = 0.100, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.77–7.71 (m, 2 H), 7.53–7.41 (m, 3 H), 6.74 (br. s, 1 H), 3.65–3.59 (m, 1 H), 3.37–3.29 (m, 1 H), 3.15 (t, *J* = 14.3 Hz, 1 H), 3.02–2.97 (m, 1 H), 2.88–2.79 (m, 1 H), 2.65 (br. s, 1 H), 1.10 [d, *J*(P,H) = 14.7 Hz, 9 H], 0.95 (d, *J* = 6.30 Hz, 3 H), 0.90–0.20 (br., 3 H, BH_3) ppm. ^{13}C APT NMR (75.5 MHz, $CDCl_3$): δ = 166.8 (s), 133.7 (d, *J* = 8.61 Hz), 132.0 (s), 128.6 (d, *J* = 9.74 Hz), 124.7 (d, *J* = 51.3 Hz), 66.7 (s), 47.6 (s), 30.1 (d, *J* = 30.6 Hz), 28.9 (d, *J* = 25.7 Hz), 25.3 (s), 20.5 (s) ppm. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 30.2 [br. d, $J_{(P,B)}$ = 66.3 Hz] ppm. $C_{15}H_{27}BNO_2P$ (295.17): calcd. C 61.04, H 9.22, N 4.75; found C 61.18, H 8.78, N 4.71.

Synthesis of 2-{(*R*)-[Boronato(*tert*-butyl)(phenyl)phosphinyl]methyl}-(5*S*)-5-methyl-2-oxazoline: 2-[(*R*)-Boronatophenyl(*tert*-butyl)phosphanyl]-*N*-[(*S*)-2-hydroxypropyl]acetamide (0.82 g, 2.77 mmol) was azeotropically dried with toluene (3 × 3 mL) and dissolved in CH_2Cl_2 (50 mL). The reaction mixture was cooled to 0 °C and Et_3N (1.9 mL, 13.6 mmol, 4.9 equiv.) and methanesulfonyl chloride (1.1 mL, 13.8 mmol, 5 equiv.) were added. After 30 min stirring, the ice bath was removed and the reaction mixture was stirred for 13 h at room temperature. The reaction was quenched by the addition of sat. aq. $NaHCO_3$, diluted with $CHCl_3$, and the layers were separated. The aqueous layer was twice extracted with $CHCl_3$. The combined organic layers were washed with brine and dried with Na_2SO_4. After filtration, the solvent was evaporated under reduced

pressure, after which the product was purified by column chromatography over basic alumina. Eluent: petroleum ether/ethyl acetate (1:1), with gradient to pure ethyl acetate. R_f = 0.34; yield 664 mg (86%). $[\alpha]_D$ = +35.1 (c = 0.480, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.80 (t, J = 8.4 Hz, 2 H), 7.54–7.42 (m, 3 H), 4.63–4.55 (m, 1 H), 3.89–3.80 (m, 1 H), 3.27–3.18 (m, 2 H), 3.05–2.95 (m, 1 H), 1.14 (d, J = 13.8 Hz, 9 H), 1.02 (d, J = 3 H, 6.60 Hz), 0.82–0.20 (br., 3 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 161.8, 133.9 (d, J = 8.67 Hz), 131.7 (d, J = 2.39 Hz), 128.4 (d, J = 9.30 Hz), 125.7 (d, J = 48.4 Hz), 61.4, 30.2 (d, J = 30.7 Hz), 25.6, 21.3 (d, J = 29.4 Hz), 21.0 ppm. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 33.5 (br. d, J = 60.0 Hz) ppm. $C_{15}H_{25}BNOP$ (277.15): calcd. C 65.00, H 9.09, N 5.05; found C 64.77, H 8.98, N 5.02.

Synthesis of 2-[(*R*)-(*tert*-Butyl)(phenyl)phosphanylmethyl]-(5*S*)-5-methyl-2-oxazoline (B4): (5*S*)-2-{(*R*)-[Boronatophenyl(*tert*-butyl)-phosphanyl]methyl}-5-methyl-2-oxazoline (155.2 mg, 0.59 mmol) was azeotropically dried with toluene (3 × 2 mL) and dissolved in CH_2Cl_2 (10 mL). The solution was cooled to –20 °C, after which tetrafluoroboric acid–dimethyl ether complex (0.61 mL, 5.90 mmol) was added. The mixture was stirred for 16 h at room temperature. A degassed sat. aq. $NaHCO_3$ solution was added and the mixture was stirred for an additional hour. The layers were separated and the aqueous layer was three times extracted with Et_2O. The combined organic layers were dried with Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified over a small column of basic alumina (ca. 5 cm), using Et_2O as eluent. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 47.5 ppm.

(*rac*)-3-[(*tert*-Butyl)(phenyl)phosphinoyl]pyridine: In a dry, degassed Schlenk tube, $Pd(OAc)_2$ (135 mg, 0.60 mmol) and dppb (282 mg, 0.66 mmol) were dissolved in freshly distilled DMF (15 mL). After 5 min stirring, 3-iodopyridine (1.48 g, 7.22 mmol) was added, after which the mixture was stirred for 10 min at room temperature. *tert*-Butyl(phenyl)phosphane (1.0 g, 6.02 mmol) and DIPEA (4.2 mL, 3.11 g, 24.1 mmol) dissolved in DMF (5 mL) were added, after which the mixture was stirred at 105 °C for 16 h. The solution was cooled to room temperature and the DMF evaporated. The resulting brown-red oil was dissolved in chloroform, washed twice with 5% aq. $NaHCO_3$ and once with brine (under air; oxidation of phosphane). The organic layer was dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude product (oxide) was purified by means of chromatographic separation with a Chromatotron® equipped with a silica plate using EtOAc/CH_2Cl_2 (1:1) with 1% Et_3N as eluent. Yield 0.97 g (62%) of an off-white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.12 (m, 1 H), 8.73 (m, 1 H), 8.31 (m, 1 H), 7.92 (m, 2 H), 7.49 (m, 4 H), 1.25 [d, J(H,P) = 15.3 Hz, 9 H] ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 152.2 [d, J(C,P) = 1.76 Hz], 152.1 [d, J(C,P) = 9.80 Hz], 140.8 [d, J(C,P) = 5.78 Hz], 132.2 [d, J(C,P) = 8.67 Hz], 132.2 [d, J(C,P) = 2.89 Hz], 130.4 [d, J(C,P) = 92.4 Hz], 128.8 [d, J(C,P) = 10.9 Hz], 128.3 [d, J(C,P) = 85.5 Hz], 123.8 [d, J(C,P) = 7.54 Hz], 34.3 [d, J(C,P) = 71.6 Hz], 25.2 ppm. ^{31}P NMR (300 MHz, $CDCl_3$): δ = 38.2 ppm. $C_{15}H_{18}NOP$ (259.28): calcd. C 69.48, H 7.00, N 5.40; found C 69.58, H 8.44, N 5.20.

The enantiomers were separated at DSM by preparative HPLC equipped with an AD column [l = 25 cm, eluent: *n*-heptane/*tert*-butyl alcohol (72.5:27.5), 1 mL/min]. t_1 = 15.5 min (enantiomeric purity: 98.5 ± 0.5%), t_2 = 20.3 min (enantiomeric purity: 97.6%). Elemental analysis after separation of the enantiomers: Enantiomer 1: $C_{15}H_{18}NOP$ (259.28): calcd. C 69.48, H 7.00, N 5.40; found C 69.33, H 6.93, N 5.32. Enantiomer 2: $C_{15}H_{18}NOP$ (259.28): calcd. C 69.48, H 7.00, N 5.40; found C 69.34, H 6.96, N 5.30.

3-[(*tert*-Butyl)(phenyl)phosphanyl]pyridine (Both Enantiomers B5 and B6): The phosphane oxide (120 mg, 0.46 mmol) was dissolved in $PhSiH_3$ (5 mL) and heated at reflux with stirring for 40 h. Then the solvent was removed in vacuo and the product was purified over a short silica column (±5 cm) using EtOAc/PE (1:1) as eluent.

Analytical Data for Enantiomer 1: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.77 (br. s, 1 H), 8.56 (d, J = 5.10 Hz, 1 H), 7.83–7.81 (m, 1 H), 7.58–7.53 (m, 2 H), 7.38–7.35 (m, 3 H), 7.29–7.25 (m, 1 H), 1.19 (d, J = 12.9 Hz, 9 H) ppm. ^{31}P NMR (300 MHz, $CDCl_3$): δ = 12.8 ppm. $C_{15}H_{18}NO_2P + H_2O$: calcd. C 64.97, H 7.27, N 5.05; found C 65.18, H 6.75, N 4.82.

Analytical Data for Enantiomer 2: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.78 (br. s, 1 H), 8.57 (d, J = 4.80 Hz, 1 H), 7.87–7.82 (m, 1 H), 7.62–7.52 (m, 2 H), 7.44–7.26 (m, 4 H), 1.20 (d, J = 12.9 Hz, 9 H) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 154.1, 153.8 (d, J = 9.81 Hz), 149.8, 148.8, 142.5, 136.2, 134.6 (d, J = 37.9 Hz), 129.5 (d, J = 29.4 Hz), 128.4, 123.5, 31.1, 28.8 (d, J = 14.7 Hz) ppm. ^{31}P NMR (300 MHz, $CDCl_3$): δ = 12.8 ppm.

Synthesis of (*S*,*S*)-3-[4,4,8,8-Tetrakis(3,5-dimethylphenyl)-2,2-dimethyl-3a,4,8,8a-tetrahydro-2*H*-[1,3]dioxolo[4,5-*e*][1,3,2]dioxaphosphepin-6-yloxy]pyridine (D7): 3-Hydroxypyridine (0.58 g, 6.13 mmol), azeotropically dried with toluene (3 × 5 mL), and triethylamine (0.94 mL, 6.74 mmol) were dissolved in dichloromethane (20 mL) and the solution was cooled to –50 °C. Freshly prepared (1*S*,7*S*)-4-chloro-9,9-dimethyl-2,2,6,6-tetrakis(3,5-dimethylphenyl)-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (3.94 g, 6.13 mmol) dissolved in dichloromethane (20 mL) was added dropwise. The cooling bath was removed, the solution was warmed to room temperature, and stirring was continued for 2 h. The solvent was evaporated after which the product was extracted with a mixture of toluene (20 mL) and hexanes (60 mL). After filtration the solvent was removed in vacuo to give **D7** (3.31 g, 4.72 mmol, 77%) as a white foam: ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.26 (dd, J = 4.65, 1.50 Hz, 1 H), 7.90 (br. d, J = 2.70 Hz, 1 H), 7.28–7.26 (m, 1 H), 7.21–7.15 (m, 5 H), 7.10–7.02 (m, 5 H), 6.97–6.91 (m, 3 H), 6.84 (br. d, J = 9.60 Hz, 2 H), 5.45 (d, J = 7.80 Hz, 1 H), 5.06 (dd, J = 8.25, 0.60 Hz, 1 H), 2.32 (d, J = 11.4 Hz, 15 H), 2.24 (s, 9 H), 0.85 (s, 3 H), 0.73 (s, 3 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 149.9, 149.2, 149.1, 145.9, 144.3, 142.5, 142.4, 141.1, 141.0, 137.6, 137.4, 136.7, 136.6, 129.7, 129.3, 129.2, 129.1, 128.5, 127.1, 127.0, 126.9, 126.7, 125.6, 125.2, 125.1, 123.5, 113.2, 86.9, 86.8, 85.9, 85.8, 82.6, 82.5, 80.1, 27.0, 26.7, 21.9, 21.8 ppm. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 126.45 ppm. $C_{44}H_{48}NO_5P$ (701.83): calcd. C 75.30, H 6.89, N 2.00; found C 75.18, H 6.77, N 1.96.

General Procedure for the Hydroformylation of Styrene: The experiments were performed in a stainless steel autoclave (volume 150 mL) charged with an inset suitable for 14 reaction vials (including Teflon® stirring bars) to conduct parallel reactions. The vessels (GC vials) were oven-dried, cooled under vacuum, and filled under nitrogen. The substrate styrene was freshly filtered through neutral alumina before use to remove possible peroxide impurities. In a typical experiment, the vials were filled with [Rh(acac)(CO)$_2$] (0.50 μmol), acceptor-type phosphorus ligand (porphyrin phosphite; 2.50 μmol), donor-type phosphorus ligand (e.g., pyridyl phosphane; 2.50 μmol), *N*,*N*-diisopropylethylamine (4.4 μL), styrene (57.3 μL), and decane (28.7 μL; as internal standard) in toluene (0.50 mL). The vials were closed and a needle was inserted to ensure gas-uptake. The autoclave was closed and four times purged with 15 bar of syngas (H_2/CO, 1:1), pressurized to 20 bar syngas, and subsequently the reactions were stirred (see main text in for details of temperature and reaction time). After the required time, the autoclave was cooled to 0 °C, after which the pressure was reduced to 1 bar. Two drops of tri-*n*-butyl phosphite were added to all the reaction vials to prevent any further reaction. From each

vial two samples were taken and diluted with dichloromethane for GC and chiral GC analysis. The samples for chiral GC analysis were filtered through a plug of silica; the samples for normal GC analysis were not filtered because retention of the aldehydes on silica causes inaccuracies in the determination of the conversion and branched-to-linear selectivity. The enantiomeric purity was determined by chiral GC [ph Megadex column, internal diameter 0.1 mm, 5 m column, film thickness 0.1 μm; initial temperature = 40 °C and ΔT = 25 °C min^{-1}; t_R (*R*) = 5.65 min and t_R (*S*) = 5.73 min]. All reactions were performed in duplicate.

Supporting Information (see also the footnote on the first page of this article): Data of all the ligands that are applied in the initial screening hydroformylation of styrene.

Acknowledgments

Ilse Maes and Dr. André H. M. de Vries from DSM are kindly acknowledged for the preparative HPLC resolution of phosphanes **B5** and **B6**. Dr. A. H. M. de Vries is also gratefully acknowledged for the donation of (*R*)-(+)-3,3′-dimethyl-2,2′-binaphthol and Dr. P. H. M. Budzelaar (Koninklijke/Shell Laboratorium Amsterdam) is gratefully acknowledged for the donation of pyridyl phosphorus ligands **A1**–**3**, **A5**, and **A7**–**9**.

[1] H. U. Blaser, E. Schmidt (Eds.), *Asymmetric Catalysis on Industrial Scale*, Wiley-VCH, Weinheim, **2004**.

[2] J. S. Carey, D. Laffan, C. Thomson, M. T. Williams, *Org. Biomol. Chem.* **2006**, *4*, 2337–2347.

[3] a) A. Hagemeyer, B. Jandeleit, Y. Liu, D. M. Poojary, H. W. Turner, A. F. Volpe Jr., W. H. Weinberg, *Appl. Catal. A: Gen.* **2001**, *221*, 23–43; b) B. Archibald, O. Brümmer, M. Devenney, S. Gorer, B. Jandeleit, T. Uno, W. H. Weinberg, T. Weskamp in *Handbook of Combinatorial Chemistry* (Eds.: K. C. Nicolaou, R. Hanko, W. Hartwig), Wiley-VCH, Weinheim, **2002**, vol. 2, pp. 885–979; c) C. Gennari, U. Piarulli, *Chem. Rev.* **2003**, *103*, 3071–3100; d) B. Jandeleit, D. J. Schaefer, T. S. Powers, H. W. Turner, W. H. Weinberg, *Angew. Chem. Int. Ed.* **1999**, *38*, 2494–2532; e) R. H. Crabtree, *Chem. Commun.* **1999**, 1611–1616; f) A. Hagemeyer, B. Jandeleit, Y. Liu, D. M. Poojary, H. W. Turner, A. F. Volpe Jr., W. H. Weinberg, *Appl. Catal. A* **2001**, *221*, 23–43; g) M. T. Reetz, *Angew. Chem. Int. Ed.* **2002**, *41*, 1335–1338; h) P. Chen, *Angew. Chem. Int. Ed.* **2003**, *42*, 2832–2847; i) M. T. Reetz, *Angew. Chem. Int. Ed.* **2001**, *40*, 284–310; j) M. T. Reetz, *Angew. Chem. Int. Ed.* **2008**, *47*, 2556–2588; k) J. G. De Vries, A. H. M. de Vries, *Eur. J. Org. Chem.* **2003**, 799–811; l) C. Jäkel, R. Paciello, *Chem. Rev.* **2006**, *106*, 2912.

[4] a) J. G. de Vries, L. Lefort, *Chem. Eur. J.* **2006**, *12*, 4722–4734; b) T. Jerphagnon, J.-L. Renaud, C. Bruneau, *Tetrahedron: Asymmetry* **2004**, *15*, 2101, and references cited therein; c) J. G. de Vries in *Handbook of Chiral Chemicals*, 2nd ed. (Eds.: D. Ager, S. Laneman), CRC Press, New York, **2005**; d) M. T. Reetz, G. Mehler, *Angew. Chem. Int. Ed.* **2000**, *39*, 3889; e) M. van den Berg, A. J. Minnaard, E. P. Schudde, J. van Esch, A. H. M. de Vries, J. G. de Vries, B. L. Feringa, *J. Am. Chem. Soc.* **2000**, *122*, 11539; f) C. Claver, E. Fernandez, A. Gillon, K. Heslop, D. J. Hyett, A. Martorell, A. G. Orpen, P. G. Pringle, *Chem. Commun.* **2000**, 961; g) M. T. Reetz, X. Li, *Angew. Chem. Int. Ed.* **2005**, *44*, 2959; h) M. T. Reetz, X. Li, *Tetrahedron* **2004**, *60*, 9709; i) M. T. Reetz, G. Mehler, A. Meiswinkel, *Tetrahedron: Asymmetry* **2004**, *15*, 2165; j) M. T. Reetz, T. Sell, A. Meiswinkel, G. Mehler, *Angew. Chem. Int. Ed.* **2003**, *42*, 790; k) C. Monti, C. Gennari, U. Piarulli, J. G. de Vries, A. H. M. de Vries, L. Lefort, *Chem. Eur. J.* **2005**, *11*, 6701; l) R. Hoen, J. A. F. Boogers, H. Bernsmann, A. J. Minnaard, A. Meetsma, T. D. Tiemersma-Wegman, A. H. M. de Vries, J. G. de Vries, B. L. Feringa, *Angew. Chem. Int. Ed.* **2005**, *44*, 4209; m) D. Peña, A. J. Minnaard, J. A. F. Boogers, A. H. M. de Vries, J. G. de Vries, B. L. Feringa, *Org. Biomol. Chem.* **2003**, *1*, 1087; n) W. Tang, X. Zhang, *Chem. Rev.* **2003**, *103*, 3029.

[5] a) L. Lefort, J. A. F. Boogers, A. H. M. de Vries, J. G. de Vries, *Org. Lett.* **2004**, *6*, 1733; b) J. G. de Vries, L. Lefort, *Chem. Eur. J.* **2006**, *12*, 4722; c) R. B. C. Jagt, P. Y. Toullec, E. P. Schudde, J. G. de Vries, B. L. Feringa, A. J. Minnard, *J. Comb. Chem.* **2007**, *9*, 407.

[6] P. E. Goudriaan, P. W. N. M. van Leeuwen, M.-N. Birkholtz, J. N. H. Reek, *Eur. J. Inorg. Chem.* **2008**, 2939.

[7] a) F. Agbossou-Niedercorn, I. Suisse, *Coord. Chem. Rev.* **2003**, *242*, 145–158; b) P. W. N. M. van Leeuwen, P. C. J. Kamer, J. N. H. Reek, P. Dierkes, *Chem. Rev.* **2000**, *100*, 2741; c) O. Lavastre, F. Bonnette, L. Gallard, *Curr. Opin. Chem. Biol.* **2004**, *8*, 311.

[8] For reviews, see: a) M. J. Wilkinson, P. W. N. M. van Leeuwen, J. N. H. Reek, *Org. Biomol. Chem.* **2005**, *3*, 2371–2383; b) B. Breit, *Angew. Chem. Int. Ed.* **2005**, *44*, 6816; c) A. J. Sandee, J. N. H. Reek, *Dalton Trans.* **2006**, 3385.

[9] a) V. F. Slagt, P. W. N. M. van Leeuwen, J. N. H. Reek, *Chem. Commun.* **2003**, *19*, 2474–2475; b) V. F. Slagt, P. W. N. M. van Leeuwen, J. N. H. Reek, *Angew. Chem. Int. Ed.* **2003**, *42*, 5619–5623; c) V. F. Slagt, M. Röder, P. C. J. Kamer, P. W. N. M. van Leeuwen, J. N. H. Reek, *J. Am. Chem. Soc.* **2004**, *126*, 4056–4057; d) J. N. H. Reek, R. Chen, P. C. J. Kamer, V. F. Slagt, P. W. N. M. van Leeuwen, EP 1479439, **2004**; e) J. N. H. Reek, M. Röder, P. E. Goudriaan, P. C. J. Kamer, P. W. N. M. van Leeuwen, V. F. Slagt, *J. Organomet. Chem.* **2005**, *690*, 4505–4516; f) L. K. Knight, Z. Freixa, P. W. N. M. van Leeuwen, J. N. H. Reek, *Organometallics* **2006**, *25*, 954–960; g) X.-B. Jiang, L. Lefort, P. E. Goudriaan, A. H. M. de Vries, P. W. N. M. van Leeuwen, J. G. de Vries, J. N. H. Reek, *Angew. Chem. Int. Ed.* **2006**, *45*, 1223–1227; h) M. Kuil, P. E. Goudriaan, P. W. N. M. van Leeuwen, J. N. H. Reek, *Chem. Commun.* **2006**, *45*, 4679–4681; i) A. J. Sandee, A. M. van der Burg, J. N. H. Reek, *Chem. Commun.* **2007**, 864–866; j) X.-B. Jiang, P. W. N. M. van Leeuwen, J. N. H. Reek, *Chem. Commun.* **2007**, 2287–2289; k) V. F. Slagt, P. W. N. M. van Leeuwen, J. N. H. Reek, *Dalton Trans.* **2007**, 2302–2310; l) M. Kuil, P. E. Goudriaan, A. W. Kleij, D. M. Tooke, A. L. Spek, P. W. N. M. van Leeuwen, J. N. H. Reek, *Dalton Trans.* **2007**, 2311–2320; m) F. W. Patureau, M. Kuil, A. J. Sandee, J. N. H. Reek, *Angew. Chem. Int. Ed.* **2008**, *47*, 3180–3183; n) J. Flapper, J. N. H. Reek, *Angew. Chem. Int. Ed.* **2007**, *46*, 8590; o) V. F. Slagt, P. Kaiser, A. Berkessel, M. Kuil, A. M. Kluwer, P. W. N. M. van Leeuwen, J. N. H. Reek, *Eur. J. Inorg. Chem.* **2007**, 4653.

[10] a) B. Breit, W. Seiche, *J. Am. Chem. Soc.* **2003**, *125*, 6608–6609; b) B. Breit, W. Seiche, *Angew. Chem. Int. Ed.* **2005**, *44*, 1640–1643; c) W. Seiche, A. Schuschkowski, B. Breit, *Adv. Synth. Catal.* **2005**, *347*, 1488–1494; d) C. Jäkel, M. Volland, T. Mackewitz, R. Paciello, B. Breit, W. Seiche, M. Weis, C. Waloch, WO 2005051964, **2005**; e) B. Breit, W. Seiche, *Pure Appl. Chem.* **2006**, *78*, 249–256; f) M. Weis, C. Waloch, W. Seiche, B. Breit, *J. Am. Chem. Soc.* **2006**, *128*, 4188–4189; g) F. Chevallier, B. Breit, *Angew. Chem. Int. Ed.* **2006**, *45*, 1599–1602; h) M.-N. Birkholz, N. V. Dubrovina, H. Jiao, D. Michalik, J. Holz, R. Paciello, B. Breit, A. Börner, *Chem. Eur. J.* **2007**, *13*, 5896–5907; i) C. Waloch, J. Wieland, M. Keller, B. Breit, *Angew. Chem. Int. Ed.* **2007**, *46*, 3037–3039; j) M.-N. Birkholz, N. V. Dubrovina, I. A. Shuklov, J. Holz, R. Paciello, C. Waloch, B. Breit, A. Börner, *Tetrahedron: Asymmetry* **2007**, *18*, 2055–2060; k) A. Ch. Laungani, B. Breit, *Chem. Commun.* **2008**, 844–846; l) T. Šmejkal, B. Breit, *Angew. Chem. Int. Ed.* **2008**, *47*, 311–315; m) I. Usui, S. Schmidt, M. Keller, B. Breit, *Org. Lett.* **2008**, *10*, 1207–1210; n) J. M. Takacs, D. S. Reddy, S. A. Moteki, D. Wiu, H. Palencia, *J. Am. Chem. Soc.* **2004**, *126*, 4494–4495; o) J. M. Takacs, P. M. Hrvatin, J. M. Atkins, D. S. Reddy, J. L. Clark, *New J. Chem.* **2005**, *29*, 263–265; p) J. M. Takacs, K. Chaiseeda, S. A. Moteki, S. G. DiMagno, J. M. Takacs, *Org.*

Lett. **2006**, *8*, 2759–2762; q) S. A. Moteki, J. M. Takacs, *Angew. Chem. Int. Ed.* **2008**, *47*, 894–897; r) P. A. Duckmanton, A. J. Blake, J. B. Love, *Inorg. Chem.* **2005**, *44*, 7708–7710; s) H. Gulyás, J. Benet-Buchholz, E. C. Escudero-Adan, Z. Freixa, P. W. N. M. van Leeuwen, *Chem. Eur. J.* **2007**, *13*, 3424–3430.
[11] A. D. Adler, F. R. Longo, J. D. Finarelli, J. Goldmacher, J. Assour, L. Korsakoff, *J. Org. Chem.* **1967**, *32*, 476.
[12] a) F. A. Walker, M. Benson, *J. Am. Chem. Soc.* **1980**, *102*, 5530–5538; b) J. P. Collman, J. I. Braumann, K. M. Doxsee, T. R. Halbert, E. Brunnenberg, R. E. Linder, G. N. Lamar, J. Del Gaudio, G. Lang, K. Spartalian, *J. Am. Chem. Soc.* **1980**, *102*, 4182–4192.
[13] E. Barragán, B. Gordillo, G. Vargas, L. Velazco, *Appl. Organomet. Chem.* **2004**, *18*, 311–317.
[14] The crude products were obtained in almost quantitative yields, but 50–60% is lost upon purification by column chromatography.
[15] TMEDA: *N*,*N*,*N*′,*N*′-tetramethylethylenediamine.
[16] For comparable syntheses, see: a) A. Buhling, P. C. J. Kamer, P. W. N. M. van Leeuwen, *J. Mol. Catal. A* **1995**, *98*, 69–80; b) R. J. Bowen, A. C. Garner, S. J. Berners-Price, I. D. Jenkins, R. E. Sue, *J. Organomet. Chem.* **1998**, *554*, 181–184.
[17] For a recent review, see: A. Grabulosa, J. Granell, G. Muller, *Coord. Chem. Rev.* **2007**, *251*, 25–90.
[18] a) S. Jugé, M. Stephan, J. A. Laffitte, J. P. Genêt, *Tetrahedron Lett.* **1990**, *31*, 6357–6360; b) S. Jugé, M. Stephan, R. Merdès, J. P. Genêt, S. Halut-Desportes, *J. Chem. Soc., Chem. Commun.* **1993**, 531–533.
[19] A. R. Muci, K. R. Campos, D. A. Evans, *J. Am. Chem. Soc.* **1995**, *117*, 9075.
[20] a) J. R. Moncarz, T. J. Brunker, D. S. Glueck, R. D. Sommer, A. L. Rheingold, *J. Am. Chem. Soc.* **2003**, *125*, 1180; b) S. Pican, A. C. Gaumont, *Chem. Commun.* **2005**, 2393–2395; c) C. Korff, G. Helmchen, *Chem. Commun.* **2004**, 530–531; d) A. L. Schwan, *Chem. Soc. Rev.* **2004**, *33*, 218–224, and references cited in these articles.
[21] T. Imamoto, T. Oshiki, T. Onozawa, T. Kusumoto, K. Sato, *J. Am. Chem. Soc.* **1990**, *112*, 5244–5252.
[22] H. Danjo, M. Higuchi, M. Yada, T. Imamoto, *Tetrahedron Lett.* **2004**, *45*, 603–606.
[23] B. Wolfe, T. Livinghouse, *J. Am. Chem. Soc.* **1998**, *120*, 5116–5117.
[24] See, for instance: a) G. Helmchen, A. Pfaltz, *Acc. Chem. Res.* **2000**, *33*, 336–345; b) H.-U. Blaser, C. Malan, B. Pugin, F. Spindler, H. Steiner, M. Studer, *Adv. Synth. Catal.* **2003**, *345*, 103–151; c) G. Desimoni, G. Faita, K. A. Jørgensen, *Chem. Rev.* **2006**, *106*, 3561–3651, and references cited therein.
[25] F. Guilllen, M. Rivard, M. Toffano, J. Y. Legros, J. C. Daran, J. C. Fiaud, *Tetrahedron* **2002**, *58*, 5895–5904.
[26] a) C. K. SooHoo, S. G. Baxter, *J. Am. Chem. Soc.* **1983**, *105*, 7443–7444; b) A. H. Cowley, R. A. Kemp, J. G. Lasch, N. C. Norman, C. A. Stewart, *J. Am. Chem. Soc.* **1983**, *105*, 7444–7445; c) R. P. Polniaszek, *J. Org. Chem.* **1992**, *57*, 5189–5195.
[27] G. Bartoli, M. Bosco, R. Dalpozzo, A. Giuliani, E. Marcantoni, T. Mecozzi, L. Sambri, E. Torregiani, *J. Org. Chem.* **2002**, *67*, 9111–9114.
[28] a) W. A. Nugent, T. V. Rajanbabu, M. J. Burk, *Science* **1993**, *259*, 479–483; b) J.-P. Rieu, A. Boucherle, H. Cousse, G. Mouzin, *Tetrahedron* **1986**, *42*, 4095–4131; c) I. T. Harrison, B. Lewis, P. Nelson, W. Rooks, A. Roszkowski, A. Tomolonis, J. H. Fried, *J. Med. Chem.* **1970**, *13*, 203–205.
[29] L. A. van der Veen, M. D. K. Boele, F. R. Bregman, P. C. J. Kamer, P. W. N. M. van Leeuwen, K. Goubitz, J. Fraanje, H. Schenk, C. Bo, *J. Am. Chem. Soc.* **1998**, *120*, 11616–11626, and references cited therein.
[30] Although the conversion with [Rh(**5**·**C1**)$(CO)_2$] was very low, the *ee* could be measured accurately. See the Supporting Information for the GC chromatogram.
[31] ^{31}P NMR spectroscopy indicates that ligand **C1** is not stable in the presence of phenylpropionaldehyde (the hydroformylation product). The stability is enhanced in the presence of diisopropylethylamine, but in the presence of large amounts of amine, the conversion is very low (see the Supporting Information).
[32] More detailed investigations into the peculiar branched-to-linear selectivity obtained with ligand **11**·**A3** will be published elsewhere.
[33] K. Nozaki, N. Sakai, T. Nanno, T. Higashijima, S. Mano, T. Horiuchi, H. Takaya, *J. Am. Chem. Soc.* **1997**, *119*, 4413–4423.
[34] G. J. H. Buisman, L. A. van der Veen, A. Klootwijk, W. G. J. de Lange, P. C. J. Kamer, P. W. N. M. van Leeuwen, D. Vogt, *Organometallics* **1997**, *16*, 2929–2939.
[35] M. D. K. Boele, P. C. J. Kamer, M. Lutz, A. L. Spek, J. G. de Vries, P. W. N. M. van Leeuwen, G. P. F. van Strijdonck, *Chem. Eur. J.* **2004**, *10*, 6232–6246.
[36] A. L. Casalnuovo, T. V. Rajanbabu, T. A. Ayers, T. H. Warren, *J. Am. Chem. Soc.* **1994**, *116*, 9869–9882.
[37] T. Imamoto, T. Oshiki, T. Onozawa, T. Kusumoto, K. Sato, *J. Am. Chem. Soc.* **1990**, *112*, 5244–5252.

Received: May 22, 2008
Published Online: November 10, 2008

