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Fine-Tuning Ligands for Catalysis Using Supramolecular Strategies

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Coordinative bonds have been used to prepare *supramolecular ligands* leading to well-defined catalysts formed by assembly. The construction of these ligands is based on selective metal–ligand interactions between nitrogen donor atoms of phosphorus-nitrogen building blocks and various zinc(II) porphyrins. The major advantage of this supramolecular approach of catalyst preparation is the simplification of ligand variation enabling straightforward modification of steric, electronic and chiral properties of the supramolecular ligand. A large number of new ligands becomes accessible by this modular variation of the building blocks. The ligand assembly based on pyridyl phosphites and zinc(II) porphyrin with electron-withdrawing substituents led to a twelve-fold increase in activity and an increase in enantioselectivity from 17 to 50 % in the rhodium-catalyzed hydrogenation of dimethyl itaconate. The first examples of assemblies based on non-chiral ligands and chiral zinc(II) porphyrin template molecules show, as proof of principle, an enantiomeric excess up to 18 % in the asymmetric palladium-catalyzed allylic alkylation.

Introduction

In the past three decades, the exploration of ligand effects in transition-metal catalysis has proven to be a very powerful tool in homogeneous catalysis. Variation of steric[1] and electronic properties,[2] as well as the "natural bite angle"[3] for bidentate ligands, has been used to optimize many catalytic reactions. These ligand parameters have proven to control key features of catalysts, like activity, selectivity and stability, and systematic variation has resulted in better understanding of ligand effects in catalysis.[1–14] For example, electron-withdrawing substituents on the aryl ring of the phosphorus donor atom of mono- and bidentate phosphane ligands increases the activity and selectivity of the catalyst in the rhodium-catalyzed hydroformylation of 1-octene.[15] In the palladium-catalyzed arylation of alkenes, bulky phosphorus amidite ligands yielded very fast catalysts.[16] Both electronic and steric parameters of these ligands were found to be extremely important. The ligand has to be sufficiently bulky to impose formation of monoligated palladium complexes as active catalysts, but ligands that are too large retard the reaction rate.

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Recently, we[17,18] and others[19] have introduced a new class of bidentate ligands that are formed by a self-assembly process of two monodentate ligands. We demonstrated that the SUPRAphos[18b,18e,18f] concept – bringing two monodentate ligands together via zinc(II)–porphyrin–pyridyl interactions to form bidentate ligands – provides easy access to large bidentate ligand libraries, and that these ligands can successfully be applied to various reactions including the rhodium-catalyzed asymmetric hydrogenation. High-throughput screening of a part of the library revealed a catalyst that hydrogenates a trisubstituted cyclic enamide, a notoriously difficult substrate, with the highest enantioselectivity known to date.[18f] This unambiguously shows that the supramolecular approach to create bidentate ligands is a very powerful tool that brings about new catalysts with properties that surpass those already known. In addition, from the library of 64 SUPRAphos ligands that was investigated, only one provided a catalyst that induced high *ee* values, stressing the point that for challenging asymmetric conversion such as the hydrogenation of the trisubstituted cyclic enamide, large ligand libraries are required. One of the advantages typical of supramolecular ligands is the easy access to these large libraries. After the successful exploration of our SUPRAphos[18b,18e,18f] library based on porphyrin-appended ligands we have extended our approach to urea-based homo-bidentate ligands[20] and chiral analogues thereof for the use in asymmetric conversions.[21] This class of supramolecular bidentate ligands are easily accessible, in large variety and at an industrially interesting scale.

Although the preparation of monodentate ligands[22] is much easier than bidentate ligands,[23] a novel supramolecular strategy could also facilitate the preparation of large libraries of monodentate ligands. Here we report such a supramolecular strategy to change the electronic and steric properties of ligands that are equipped with pyridine and amine functional groups for the assembly of phosphorus ligands on zinc(II) porphyrin template molecules (Figure 1). The typical binding motif was previously used in the SUPRAphos concept and for the encapsulation of transition metal catalysts[24] by assembly of zinc(II) porphyrin building blocks.[25] By using the same binding motif we now show that we can vary the steric and electronic properties of phosphorus ligands by the association of the zinc(II) porphyrin templates. In this way, a series of new supramolecular ligands is prepared by just mixing the components. NMR, IR, and UV/Vis spectroscopy have been used to study the selective metal–ligand interactions and to quantify the steric and electronic properties of these supramolecular ligands. The supramolecular ligands control the activity and (enantio)selectivity of the transition metal catalysts as observed in rhodium-catalyzed hydroformylation, asymmetric hydrogenation, and asymmetric palladium-catalyzed allylic alkylation. The approach is extended to the assembly of a chiral environment around a non-chiral catalyst.

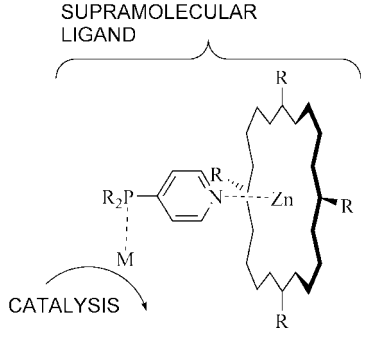


Figure 1. Schematic representation of the assembly of a phosphorus ligand on a zinc(II) porphyrin template molecule.

Results and Discussion

The Assembly of Phosphorus Ligands and Zinc(II) Porphyrin Building Blocks

For the preparation of supramolecular ligands with different steric and electronic properties, we synthesized several phosphorus ligands functionalized with a nitrogen donor atom and zinc(II) porphyrins (Figure 2). The phosphite ligands **2**–**4** were obtained in high yields by a reaction of the phosphor chloridite[26] with 3-hydroxypyridine. Zinc(II) *meso*,*meso*,*meso*,*meso*-tetraphenylporphyrin (**1a**) was prepared according to standard procedures.[27,28] All new compounds were fully characterized with ^{1}H NMR, ^{31}P-NMR and ^{13}C-NMR spectroscopy, elemental analysis and mass spectrometry.

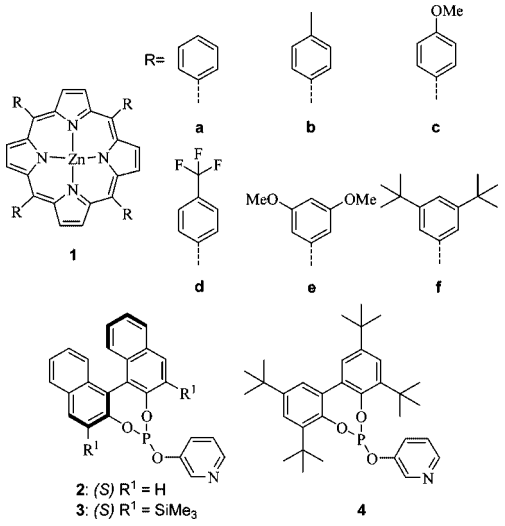
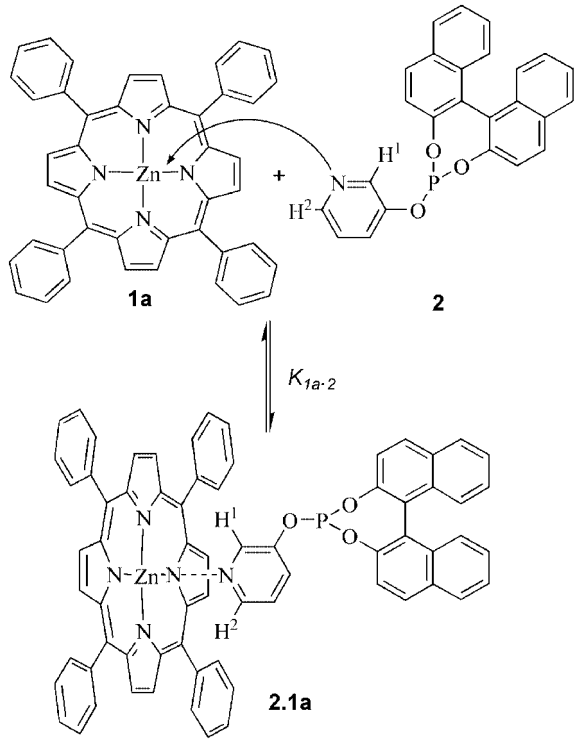


Figure 2. Various building blocks used to construct supramolecular ligands.

The coordination behavior of the pyridine phosphorus ligands **2** to **1a** has been studied using NMR and UV/Vis spectroscopy.[29,30] The addition of **1a** to a solution of **2** resulted in large upfield shifts of the protons on the pyridyl ring in ^{1}H NMR spectroscopy ($\Delta\delta^{H1}$ = 5.7 ppm, $\Delta\delta^{H2}$ = 5.8 ppm), which is typical of axial binding of pyridine ligands to zinc(II) porphyrins (Scheme 1).[24,25] Also in ^{31}P



Scheme 1. Assembly of (*S*)-(1,1′-binaphthyl-2,2′-diyl) (3-pyridyl) phosphite (**2**) on zinc(II) *meso*,*meso*,*meso*,*meso*-tetraphenylporphyrin (**1a**).

NMR spectroscopy, a large shift to higher field ($\Delta\delta^P$ = 4.6 ppm) was observed on binding of **2** to the complex **1a**. In the UV/Vis spectrum of **1a** the typical red-shift of the Q-bands of the porphyrin on the addition of **2** was observed, indicating axial coordination of the pyridine to the zinc, and the associated binding constant determined by UV titrations was found to be high ($K_{1a.2} = 1.3 \times 10^3$ M^{-1}).

The binding of zinc(II) porphyrin building blocks through the nitrogen donor atom is very selective and therefore the phosphorus atom is available for coordination to transition metals that potentially can act as catalysts. Mixing two equivalents **1a** (with respect to the complex and one equivalent with respect to the ligand) with in situ formed [Rh(acac)(**2**)$_2$] yielded an assembly in which the transition metal is embedded between the two porphyrin building blocks [Rh(acac)(**2**·**1a**)$_2$], as was evident from the shifts in NMR spectroscopy. In the ^{31}P NMR spectra the addition of the porphyrin **1a** resulted in an interestingly large upfield shift of the phosphite signals, from δ = 151.3 ppm (doublet, J_{P-Rh} = 303 Hz) to δ = 144.5 ppm (doublet, J_{P-Rh} = 304 Hz) (Figure 3). The large shift of $\Delta\delta^P$ = 6.8 ppm is attributed to a combination of effects: changes in the electronic and steric properties of the phosphite and the ring-current effect of the nearby complexed zinc(II) porphyrin **1a**.

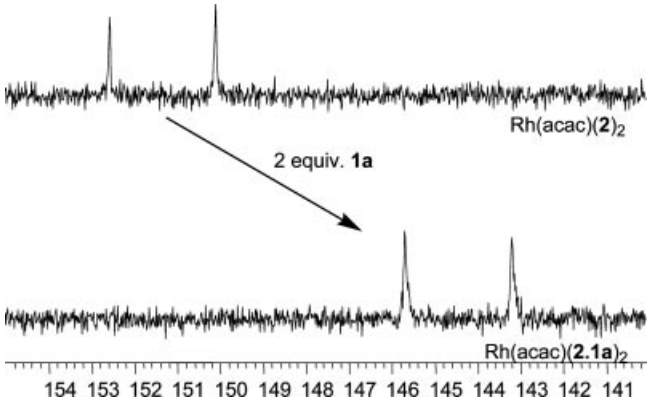
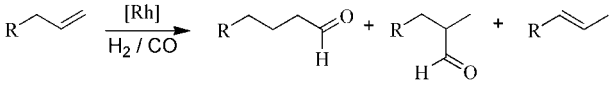


Figure 3. ^{31}P NMR spectra before (above) and after (below) addition of two equivalents of zinc(II) *meso*,*meso*,*meso*,*meso*-tetraphenylporphyrin (**1a**) to the complex [Rh(acac)(**2**)$_2$].

Assemblies of Zinc(II) Porphyrin and Phosphorus Ligands in Transition-Metal Catalysis

The supramolecular complexes based on the zinc(II) porphyrin **1a** and pyridyl phosphite ligands **2** and **4** were studied in the rhodium-catalyzed hydroformylation of 1-octene (Scheme 2).[9,31] The experiments were carried out in toluene under 20 bar of syngas (H_2/CO = 1:1) and the results are summarized in Table 1. The catalyst formed by ligand **2** yielded a moderate activity and reasonable selectivity in the hydroformylation of 1-octene at 120 °C, and the isomerization side reaction resulted in 25% internal alkenes. The assembly based on the zinc(II) porphyrin **1a** and **2** did not influence the catalytic behavior and similar activity, selectivity and isomerization were observed.[32] The more bulky ligand **4** yielded a catalyst with different properties; an increase in activity and decrease in selectivity (linear-branched ratio, l/b = 2.1) was observed for this system compared to ligand **2**. These differences are explained by the formation of monoligated rhodium phosphite complexes, as previously observed for other bulky phosphite ligands.[33] Upon using assembly **4**·**1a** an increase in activity and isomerization was observed, showing that the assembly of zinc(II) porphyrin templates to ligands with nitrogen donor atoms influences the performance of the transition metal catalyst based on these ligands, which stimulated further studies on these assembled ligand systems.



Scheme 2. The rhodium-catalyzed hydroformylation leading to the linear and branched aldehyde.

Table 1. Rhodium-catalyzed hydroformylation of 1-octene using assemblies of pyridyl phosphite and zinc(II) porphyrins template as ligands.[a]

Ligand[b]	Temp. [°C]	T.O.F.[c]	l/b[d]	% 2-Octene[e]
2	120	1.2×10^3	6.0	24.6
2·**1a**	120	1.3×10^3	7.0	19.8
4	80	2.3×10^3	2.1	21.6
4·**1a**	80	3.0×10^3	2.0	26.0

[a] [Rh(acac)(CO)$_2$] = 0.084 mmol/L in toluene, pressure: 20 bar (CO/H_2 = 1:1), 1-octene/rhodium = 5160. [b] [Phosphorus ligand **2** or **4**] = 2.1 mmol/L, [porphyrin] = 2.1 mmol/L. [c] T.O.F. = average turn over frequency: (mol aldehyde)(mol Rh)$^{-1}$ h^{-1}, the reaction was stopped after 1 h. [d] l/b = linear/branched. [e] Percent isomerization to 2-octene (and some 3- and 4-octene).

Changing the Electronic Properties of Phosphorus Ligands

To study these new self-assembled ligands based on selective nitrogen–zinc interactions in more detail, several zinc(II) porphyrins **1a**–**d** were synthesized with different electron-withdrawing and -donating substituents.[27,28] The binding constants of zinc(II) porphyrins **1a**–**d** to diphenyl(4-pyridyl)-phosphane (**7**) (Figure 4) in toluene were determined using UV/Vis spectroscopy. It was found that the porphyrin with the most electron-withdrawing substituents yielded the highest binding constant (Table 2) and a linear relation between binding constants and the Hammett values[34] was observed, with a corresponding electronic dependence value of ρ = 0.285 (Figure 5).

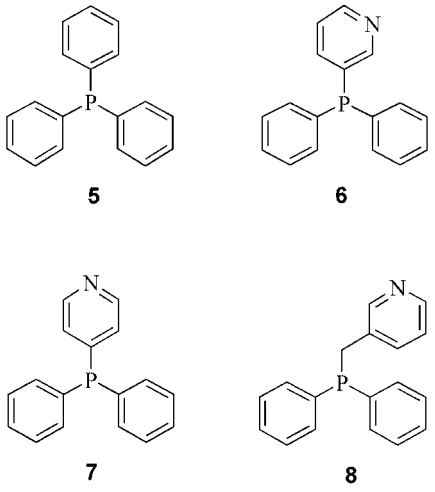


Figure 4. Various ligand building blocks used to construct supramolecular ligands.

Table 2. Binding constants observed for diphenyl(4-pyridyl)phosphane (**7**) to various zinc(II) porphyrin templates measured by UV/Vis titrations and the IR-carbonyl frequencies of the corresponding metal complexes [Rh(**7**)$_2$(CO)Cl] with the attached zinc(II) porphyrin.

Porphyrin	K [M^{-1}]	log K	4σ	$\tilde{\nu}$[a] [cm^{-1}]
1c (OCH_3-porphyrin)	2.9×10^3	3.469	–1.08	1983
1b (CH_3-porphyrin)	3.7×10^3	3.564	–0.68	1984
1a (H-porphyrin)	6.1×10^3	3.785	0	1985
1d (CF_3-porphyrin)	24.4×10^3	4.387	2.16	1986/87

[a] Measured in dichloromethane, carbonyl region.

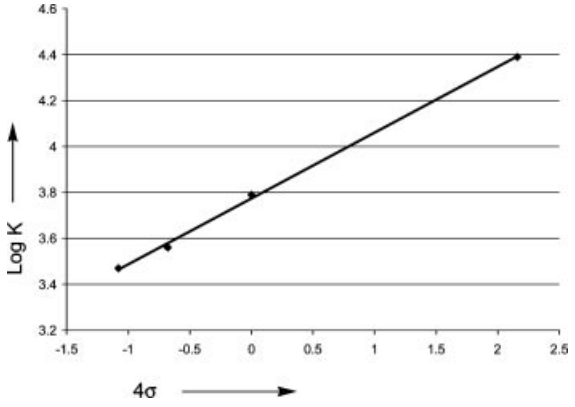


Figure 5. Plot log K vs. 4σ (sigma *para*) for the assembly of zinc(II) porphyrin complexes **1a**–**d** and diphenyl(4-pyridyl)phosphane (**7**).

The substituents on the zinc(II) porphyrin template **1a**–**d** change the π back bonding of the zinc(II) metal ion to the porphyrin macrocycle, hence influencing the electron density of the pyridine moiety ring fragment.[35] Therefore, also an effect in electron density on the phosphorus donor atom is expected. Zinc(II) porphyrins containing more electron-withdrawing substituents will increase the electron-withdrawing capacity of the pyridine ring, which will result in a lower basicity of the phosphorus donor atom. (Diphenyl)(4-pyridyl)phosphane (**7**) and [Rh(CO)$_2$(Cl)]$_2$ were mixed in a 4:1 ratio to form in situ [Rh(**7**)$_2$(CO)Cl] and subsequently a stoichiometric amount of zinc(II) porphyrin **1a**–**d** was added.[36] The IR spectra of these assembled rhodium complexes show that addition of zinc(II) porphyrin changes the shift of the carbonyl ($\tilde{\nu}_{CO}$ = 1982 cm^{-1}) of [Rh(**7**)$_2$(CO)Cl] to higher wave numbers (up to $\tilde{\nu}_{CO}$ = 1986 cm^{-1}). The $\tilde{\nu}_{CO}$ band shows a gradual shift with decreasing phosphane basicity (Table 2). The lower electron density on the rhodium leads to a decrease in back bonding from the rhodium to the carbonyl ligand and hence higher CO stretching frequencies are observed. For comparison, when the strongly electron-withdrawing tris(4-α,α,α-trifluorotoluyl)phosphane is used, the $\tilde{\nu}_{CO}$ band is at 1990 cm^{-1}, which is a shift of 12 cm^{-1} compared to triphenylphosphane, ($\tilde{\nu}_{CO}$ = 1978 cm^{-1}).[36,37] These results show that the effects induced by the zinc(II) porphyrin templates **1a**–**d** are significant. For phosphane **7**, the pyridine is directly attached to the phosphorus, and therefore changes on the nitrogen donor atom were expected to change the basicity of the phosphorus. Upon using a different spacer between the phosphorus and the nitrogen one can envisage that electronic effects on the phosphorus caused by the assembly of zinc(II) porphyrin templates **1a**–**d** will be different. Indeed, the use of diphenyl(3-pyridylmethyl)phosphane (**8**), a similar building block as **7** but with a spacer that has changed from 4-pyridine to 3-methylpyridine, shows that the carbonyl peak in the infrared spectrum of complex [Rh(**8**)$_2$(CO)Cl] hardly changes upon assembling the zinc(II) porphyrin templates **1a**–**d** ($\tilde{\nu}_{CO}$ = 1979–1980 cm^{-1}). Thus, these experiments show that electron-withdrawing substituents on the zinc(II) porphyrin that is used as a template can modify the electronic properties of the phosphane ligands, depending on the spacer between the nitrogen and phosphorus donor atom of the ligand building block.

The electronic effect of zinc(II) porphyrin templates **1a**–**d** on diphenyl(4-pyridyl)phosphane (**7**) and diphenyl(3-pyridylmethyl)phosphane (**8**) were studied in the rhodium-catalyzed hydroformylation of 1-octene (Table 3). The assemblies of zinc(II) porphyrin **1a**–**d** and **7** show a small but distinct trend in activity (**7**·**1c**<**7**·**1b**<**7**·**1a**<**7**·**1d**). The assemblies based on more electron-withdrawing zinc(II) porphyrin templates and **7** show a small increase in conversion in the rhodium-catalyzed hydroformylation of 1-octene. From the infrared spectra we know that this effect is caused by the lower basicity of the phosphane donor atoms. In the literature a similar trend has been reported for systems in which the electronic properties of the ligands were varied in a covalent manner.[15] For the various ligand assemblies based on phosphane **8** and zinc(II) porphyrin **1a**–**d** the differences in activity are negligible. This is in line with the almost identical infrared CO stretching frequencies observed for the rhodium complexes. The catalytic results obtained for the assemblies based on zinc(II) porphyrin **1a**–**d** and ligands **7** and **8** show that the spacer between the nitrogen and phosphorus donor atoms is of great importance for the small but distinct electronic influences on the phosphorus induced by the assembly process.

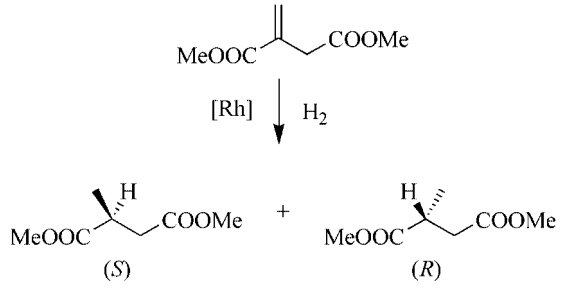
Table 3. Rhodium-catalyzed hydroformylation of 1-octene using assemblies of pyridylphosphane and zinc(II)porphyrin templates as ligands.[a]

Ligand[b]	% Conversion[c]	T.O.F.[d]	l/b[e]	% 2-Octene[f]
7·1c	56.0	2.7×10^3	2.9	1.9
7·1b	59.1	2.8×10^3	2.9	2.8
7·1a	59.6	2.8×10^3	2.9	2.9
7·1d	62.6	3.0×10^3	2.9	3.4
8·1c	74.7	3.5×10^3	2.4	1.1
8·1b	75.2	3.5×10^3	2.3	1.2
8·1a	75.1	3.6×10^3	2.3	0.7
8·1d	75.8	3.6×10^3	2.4	1.0

[a] [Rh] = 0.084 mmol/L in toluene, pressure: 20 bar (CO/H_2 = 1:1), T = 80 °C, 1-octene/rhodium = 5160. [b] [phosphorus ligand (**7** or **8**)] = 0.84 mmol/L, [porphyrin] = 0.84 mmol/L. [c] Percent total conversion of 1-octene to aldehydes and isomers. [d] T.O.F. = average turn over frequency: (mol aldehyde)(mol Rh)$^{-1}$ h^{-1}, the reaction was stopped after 1 h. [e] l/b = linear/branched. [f] Percent isomerization to 2-octene (and some 3- and 4-octene).

Application of Supramolecular Ligands in Asymmetric Hydrogenation

The supramolecular ligands were used in the asymmetric rhodium-catalyzed hydrogenation[49] of dimethyl itaconate to dimethyl methylsuccinate (Scheme 3). The ligands were based on the assembly of (*S*)-[3,3′-bis(trimethylsilyl)-1,1′-binaphthyl-2,2′-diyl] (3-pyridyl) phosphite (**3**) and zinc(II) porphyrins **1a**–**f**. Ligand **3** shows low conversion and enantioselectivity in the hydrogenation of dimethyl itaconate (Table 4). In contrast, the assemblies based on zinc(II) porphyrin template **1a**–**d** and ligand **3** give higher conversion and enantioselectivity. Electron-withdrawing substituents on the zinc(II) porphyrin **1a**–**d** have a positive effect on the activity, a twelve-fold increase for the most electron-withdrawing zinc(II) porphyrin **1d** was observed. Interestingly, the ligand based on the assembly of **1d** and **3** increases the enantioselectivity from 16% to 50% (*R*).



Scheme 3. The rhodium-catalyzed hydrogenation of dimethyl itaconate.

After having observed a clear electronic effect, we decided to look at the effect of the size of various ligand assemblies in catalysis by changing the substituents on the zinc(II) porphyrin **1a**–**d**. The ligand assemblies **3·1a**–**3·1d** and the more bulky ligand assemblies **3·1e** and **3·1f** were tested in the rhodium-catalyzed hydrogenation of dimethyl itaconate. The different substituents on the aryl groups of the zinc(II) porphyrins **1e** and **1f** not only change the size of the ligand, but also lead to different electronic properties of the assembled ligand system. The assembled **3·1e** yielded

Table 4. Hydrogenation of dimethyl itaconate using different rhodium catalyst assemblies: variation of the zinc(II)porphyrin template.[a]

Ligand[b]	% Conversion[c]	% *ee*[d]
3	1.6	16 (*R*)
3·1a	8.1	33 (*R*)
3·1b	6.2	21 (*R*)
3·1c	4.3	31 (*R*)
3·1d	18.8	50 (*R*)
3·1e	2.5	2 (*R*)
3·1f	3.1	40 (*R*)

[a] [$Rh(nbd)_2(BPh_4)$] = 1.0 mmol/L, [dimethyl itaconate] = 100 mmol/L, pressure: 5 bar hydrogen, T = 40 °C. [b] [phosphite] = 3.0 mmol/L, [porphyrin] = 3.0 mmol/L. [c] The reaction was stopped after 17 h. [d] *ee* = enantiomeric excess.

no enantioselectivity, and a low conversion was detected in the hydrogenation. The low conversion is explained by the strong electron-donating capacity of the methoxy groups of **1e**. The more bulky ligand **3·1f** resulted in a catalyst that gave an enantiomeric excess of 40% (*R*), but at low activity.

The use of selective metal–ligand interactions to change ligand properties can be extended easily to bidentate ligands (Figure 6). The chiral (2*S*,4*S*)-(–)-4-(diphenylphosphanyl)-2-(diphenylphosphanylmethyl)pyrrolidine (**9**)[38] binds to zinc(II) porphyrins by axial coordination of the nitrogen donor atom in the pyrrolidine ring to the zinc(II) ion. ^{1}H NMR spectroscopy in [D]chloroform showed a large shift for the pyrrolidine protons of **9** on addition of one equivalent of zinc(II) porphyrin **1a**, as is typical of this type of binding. Also in the ^{31}P NMR spectra a change in chemical shifts was observed, $\Delta\delta$P(2*S*) = 4.3 ppm (Figure 7).

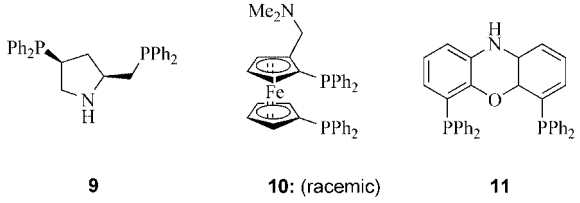


Figure 6. Various diphosphane ligand building blocks that were used to construct supramolecular ligands via nitrogen coordination to zinc(II) porphyrins.

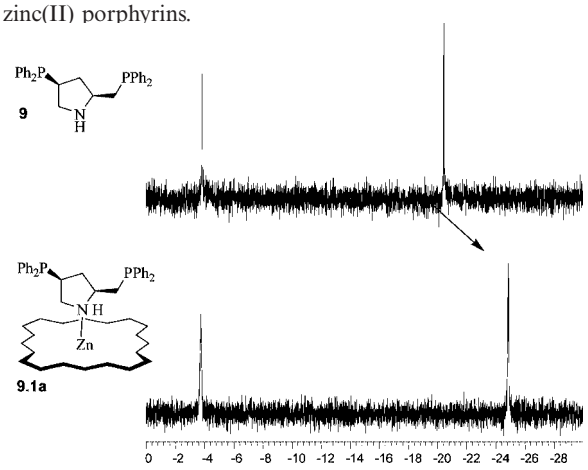


Figure 7. ^{31}P NMR spectra of (2*S*,4*S*)-(–)-4-(diphenylphosphanyl)-2-(diphenylphosphanylmethyl)pyrrolidine (**9**) in absence (above) and presence (below) of zinc(II) porphyrin **1a**.

Application of Supramolecular Ligands in Asymmetric Hydroformylation

The zinc(II) porphyrins **1a**, **1e** and **1f** were used to form new ligand assemblies with the diphosphane **9**, which were applied in the asymmetric rhodium-catalyzed hydroformylation[9,50] of styrene (40 °C, toluene, 20 bar CO/H_2). As is shown in Table 5, the catalyst based on the bidentate ligand **9** resulted in moderate enantioselectivity [19% *ee*, (*S*)-product] and activity in the hydroformylation of styrene. The ligand assembly based on zinc(II) porphyrin **9·1a** resulted in small increase in enantioselectivity and a decrease in activity. Electronic changes on phosphorus caused by the assembly of the zinc(II) porphyrin template are considered to be very small, because the use of the zinc(II) *meso*-*p*-CF_3-phenylporphyrin **1d** yielded similar results as **1a**. Increasing the bulk of the porphyrin building block by using **1f**, the enantioselectivity further improved to 29% (*S*), at the cost of a lower activity and lower branched to linear ratio. These results indicate that variation of steric bulk around the catalyst introduced by supramolecular interactions using different porphyrin building blocks modifies the ligand properties and the catalytic performance of their metal complexes, both for mono- and bidentate ligands.

Table 5. Hydroformylation of styrene using assemblies based on the chiral diphosphane **9**: variation of the zinc(II) porphyrin template.[a]

Ligand[b]	% Conversion[c]	T.O.F.[d]	b/l[e]	% *ee*[f]
9	54	14.2	5.2	19 (*S*)
9·1a	25	6.7	5.6	23 (*S*)
9·1e	15	4.0	3.9	26 (*S*)
9·1f	9	2.3	2.4	29 (*S*)

[a] [Rh] = 0.33 mmol/L in toluene, pressure: 20 bar (CO/H_2 = 1:1), T = 40 °C, styrene/rhodium = 1750, in none of the reactions hydrogenation was observed. [b] [phosphane] = 1.67 mmol/L, [porphyrin] = 1.67 mmol/L. [c] Percent conversion, the reaction was stopped after 66.5 h. [d] T.O.F. = average turn over frequency: (mol aldehyde)(mol Rh)$^{-1}$h^{-1}. [e] b/l = branched/linear. [f] *ee* = enantiomeric excess.

Introducing a Chiral Environment around a Non-Chiral Catalyst

In the previous section we described the fine-tuning of catalyst properties by the introduction of steric bulk around a chiral catalyst by supramolecular interactions. An even greater challenge would be the introduction of a chiral environment around a non-chiral catalyst via a selective assembly process, resulting in a chiral catalyst assembly for asymmetric catalysis. Towards this goal, chiral zinc(II) porphyrin building blocks based on octahydro-1,4:5,8-dimethanoanthracene **12a**–**12d** were synthesized (Figure 8).[39] This type of porphyrin is known to be very selective in the ruthenium- or manganese-catalyzed epoxidation[39,40] and cyclopropanation[41] of alkenes. The crystal structure[39] of the zinc(II) porphyrin **12a** shows that the chiral moieties are highly symmetrically positioned around the core of the porphyrin and molecular modeling[42] suggests that there is enough space for axial ligand coordination to the zinc metal (Figure 9).

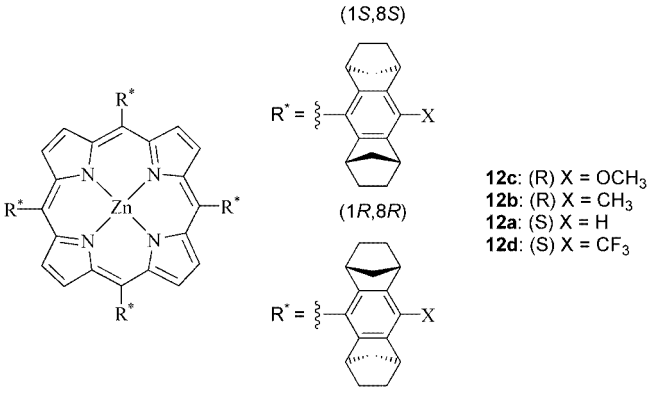


Figure 8. Various chiral porphyrin building blocks used to construct supramolecular ligands.

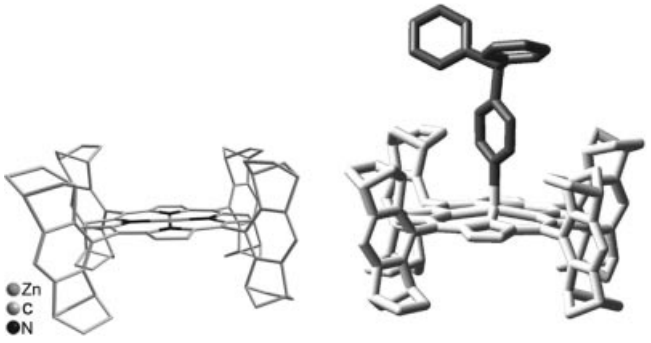


Figure 9. Crystal structure of the zinc(II) complex of *meso*,*meso*,-*meso*,*meso*-tetrakis(octahydro-1,4:5,8-dimethanoanthryl)porphyrin (**12a**) (left) and modeled structure of the assembly of **12a** (white) and diphenyl(4-pyridyl)phosphane (**7**) (dark gray, right).

Upon mixing the ligands **6**–**8** in a 1:1 ratio with the zinc(II) porphyrin **12a** supramolecular complexes were formed by complexation of the nitrogen donor atom to the axial position of zinc(II). Binding constants were determined with UV/Vis spectroscopy titrations in toluene (Table 6). Phosphane **7** has the strongest affinity for **12a** (K = 3.5×10^3 M^{-1}) and the binding constant of phosphane **6** is approximately three times smaller ($K = 8.7 \times 10^2$ M^{-1}).

Table 6. Binding constants of various pyridylphosphane ligands to zinc(II) porphyrin template **12a** (and **1a** for comparison) measured by UV/Vis titrations in toluene.

Ligand	K [M^{-1}]	Ligand	K [M^{-1}]
6·12a	0.87×10^3	**6·1a**	2.3×10^3
7·12a	3.5×10^3	**7·1a**	6.1×10^3
8·12a	1.6×10^3	**8·1a**	4.0×10^3

A similar trend for these ligands was already observed with the complexation to the zinc(II) porphyrin **1a**, and the small differences observed for **6**–**8** are likely due to electronic effects. Titrations monitored with UV/Vis spectroscopy to determine binding constants between chiral zinc(II) porphyrins **12a**–**12d** and **7** in toluene showed that electron-withdrawing substituent X on the porphyrin resulted in higher binding constant ($OMe < Me < H < CF_3$) (Table 7), which corroborates the results obtained for **7** and

zinc(II) porphyrin **1a**–**1d**. A similar linear relation between binding constants and the Hammett values is observed, with a corresponding electronic dependence value of ρ = 0.201 (Figure 10), which is comparable with results reported in literature.[43]

Table 7. Binding constants K of diphenyl(4-pyridyl)phosphane (**7**) to various zinc(II) porphyrin templates **12a**–**12d** measured by UV/Vis titrations.

Porphyrin	K [M^{-1}]	log K	4σ
(*R*)-OCH_3-porphyrin-Zn, **12c**	2.2×10^3	3.346	–1.08
(*R*)-CH_3-porphyrin-Zn, **12b**	2.8×10^3	3.444	–0.68
(*S*)-H-porphyrin-Zn, **12a**	3.5×10^3	3.545	0
(*S*)-CF_3-porphyrin-Zn, **12d**	10.0×10^3	4.000	2.16

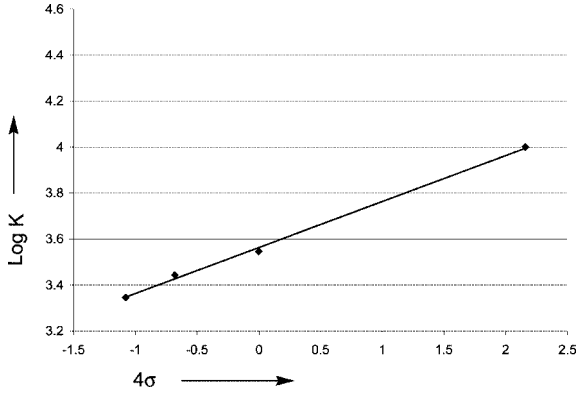
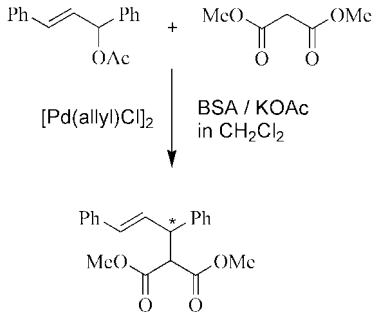


Figure 10. Plot log K vs. 4σ for the reaction of zinc(II) porphyrins **12a**–**d** and diphenyl(4-pyridyl)phosphane (**7**).

To study the effect of the "associated" chiral environment, assemblies based on zinc(II) porphyrin **12a** and **4**–**8** were tested as ligands in the asymmetric palladium-catalyzed allylic alkylation[51] using 1,3-diphenylallyl acetate as the substrate and dimethyl malonate as the nucleophile (Scheme 4). Table 8 shows that the chiral zinc(II) porphyrin **12a** was not active in the palladium-catalyzed allylic alkylation and that the palladium complexes based on triphenylphosphane (**5**) in the presence of enantiopure **12a** did not induce enantioselectivity. The assembly of the pyridine phosphite ligand **4** and chiral zinc(II) porphyrin **12a** resulted in an enantioselectivity of 8% (*S*) and a concomitant low activity. The activity was much higher upon using pyridylphosphane **6**–**8** as ligands for the assembly with **12a** and complete conversion was observed for all phosphane-based catalysts. The enantiomeric excesses for the assemblies of zinc(II) porphyrin **12a** and phosphane ligands **6**–**8** are found to be comparable with the result obtained for the assembly **4·12a**. The electronic properties of the ligand assembly were varied with the use of zinc(II) porphyrin building blocks **12a**–**12d** and phosphane **7**, but this did not affect the enantioselectivity in the palladium-catalyzed allylic alkylation. The use of the assemblies based on the other enantiomer (*R*) as zinc(II) porphyrin template (**7·12b** and **7·12c**) yields indeed the other enantiomeric product in excess. Although the chiral inductions in palladium-catalyzed allylic alkylation found for the assemblies based on monodentate phosphorus ligands **4**–**8** on the chiral zinc(II) porphyrins **12a**–**12d** do not exceed 10% yet, these first results do show that it is *possible* to create a chiral catalyst by nearby complexation of a chiral co-factor.



Scheme 4. Palladium-catalyzed allylic alkylation.

Table 8. Palladium-catalyzed allylic alkylation of 1,3-diphenylallyl acetate, using various ligand assemblies based on chiral zinc(II) porphyrin templates.[a]

Ligand[b]	% Conversion[c]	% *ee*[d]
12a (*S*)	0	0
4·12a (*S*)	30	9 (*S*)
5 + **12a** (*S*)	>99	0
6·12a (*S*)	>99	9 (*S*)
7·12c (*R*)	>99	8 (*R*)
7·12b (*R*)	>99	10 (*R*)
7·12a (*S*)	>99	9 (*S*)
7·12d (*S*)	>99	8 (*S*)
8·12 (*S*)	>99	5 (*S*)
10·12d (*S*)	>99	18 (*S*)
11·12d (*S*)	>99	12 (*S*)

[a] [[Pd(allyl)Cl]$_2$] = 0.100 mmol/L, T = 25 °C. [b] [phosphite] = 0.6 mmol/L, [porphyrin] = 0.6 mmol/L. [c] The reaction was stopped after 24 h. [d] *ee* = enantiomeric excess.

This approach has also been used for bidentate phosphorus ligands with nitrogen donor atoms, i.e. ligands **10** and **11** (Figure 6).[44,45] These bidentate phosphorus ligands have been assembled on zinc(II) porphyrin template **12d** with associated binding constants of ($K_{10\cdot12d}$ = 515 M^{-1}) and ($K_{11\cdot12d}$ = 150 M^{-1}), as determined by UV/Vis spectroscopy titrations in toluene. Although the binding constants are not sufficiently high to prevent the formation of non-templated ligand under the reaction conditions, these ligand assemblies were tested in the palladium-catalyzed asymmetric allylic alkylation. It was found that the supramolecular ligands **10·12d** and **11·12d** resulted in moderate enantioselectivities, up to 18%. Attempts to increase the *ee* by shifting the equilibrium from free **11** to fully assembled **11·12d**, by adding excess of **12d**, failed due to the limited solubility of this porphyrin.

Conclusions

A new class of supramolecular monodentate ligands is reported, which is based on selective metal–ligand interactions. The supramolecular ligands are obtained by just mixing simple building blocks, typically zinc(II) porphyrin tem-

plate molecules and phosphorus ligands containing nitrogen donor atoms. These unique supramolecular ligand systems provide a new tool to modify key catalyst properties, such as activity and selectivity, in a very simple manner. The major advantage of this supramolecular approach is the ease of ligand variation and accessibility of a large number of new ligand systems by variation of template molecules and phosphorus nitrogen building blocks. In the rhodium-catalyzed hydroformylation of 1-octene small but distinct changes have been observed, upon using different electron-donating and withdrawing zinc(II) porphyrin building blocks for the catalyst assemblies. Interesting changes have also been observed in the enantioselective rhodium-catalyzed hydrogenation of dimethyl itaconate. The ligand assemblies based on zinc(II) porphyrin with electron-withdrawing substituents led to a twelve fold increase of activity and an increase of enantioselectivity from 17 to 50%. We also have used, for the first time, assemblies based on non-chiral ligands and chiral zinc(II) porphyrin template molecules and used these as ligands in the asymmetric palladium-catalyzed allylic alkylation. Although the enantioselectivities observed so far are rather low (up to 18%), it demonstrates that with a chiral template a chiral environment around the metal center can be obtained. In general, the use of coordinative binding in order to construct supramolecular ligands simplifies the preparation of new (chiral) ligand systems, which enables novel (chiral) catalyst systems. We are currently expanding the scope of ligands and template molecules of which the results will be reported in due time.

Experimental Section

General Procedures: Unless stated otherwise, reactions were carried out under argon using standard Schlenk techniques. THF, hexane and diethyl ether were distilled from sodium benzophenone ketyl; CH_2Cl_2, 2-propanol and methanol were distilled from CaH_2 and toluene was distilled from sodium under nitrogen. NMR spectra (^1H, ^{31}P and ^{13}C) were measured with a Bruker DRX 300 MHz and Varian Mercury 300 MHz. $CDCl_3$ was used as a solvent, if not further specified. Mass spectra were recorded with a JEOL JMS SX/SX102A four sector mass spectrometer; for FAB-MS 3-nitrobenzyl alcohol was used as matrix. Elemental analyses were obtained with an Elementar Vario EL apparatus. Gas chromatographic analyses were run with an Interscience HR GC Mega 2 apparatus (split/splitless injector, J&W Scientific, DB-1 J&W 30 m column, film thickness 3.0 μm, carrier gas 70 kPa He, FID Detector) equipped with a Hewlett–Packard Data system (Chrom-Card). Chiral GC separations were conducted with a Chirasil-L-Val capillary column (0.25 mm × 25 m). Chiral HPLC analyses were carried out using a Daicel Chiralcel-OD column (0.46 × 25 cm).

Materials: With exception of the compounds given below, all reagents were purchased from commercial suppliers and used without further purification. Diisopropylethylamine and triethylamine were distilled from CaH_2 under argon. 1-Octene was filtered through a plug of alumina. The following compound were synthesized according to published procedures: zinc(II) porphyrins **1a**–**f**,[27,28] binaphthyl or biphenyl phosphorochloridites,[26] chiral zinc(II) porphyrin **a**–**d**,[39] pyridylphosphanes **6**–**8**[46,47] and diphosphanes **9**–**11**.[38,44–45]

Synthesis of (*S*)-(1,1′-Binaphthyl-2,2′-diyl) (3-Pyridyl) Phosphite (2): 3-Hydroxypyridine (1.44 g, 15.1 mmol), azeotropically dried with toluene (3 × 5 mL), and triethylamine (2.3 mL, 16.6 mmol) were dissolved in THF (40 mL) and the solution was cooled to –40 °C. Freshly prepared (*S*)-2,2′-binaphthyl phosphorochloridite (5.3 g, 15.1 mmol) was dissolved in THF (20 mL) and added dropwise. The cooling bath was removed and the solution was warmed to room temperature, stirring was continued for 1 h. The reaction mixture was filtered and the solvent evaporated. A mixture of toluene/hexane, 1:3 (40 mL) was added to extract the product. After filtration the solvent was removed in vacuo, giving **2** (5.4 g, 13.2 mmol, 87%) as a white solid. ^1H NMR (300 MHz): δ = 8.54 (d, J = 2.4 Hz, 1 H), 8.40 (d, J = 4.2 Hz, 1 H), 8.02 (d, J = 8.7 Hz, 1 H), 7.95 (d, J = 8.7 Hz, 1 H), 7.92 (d, J = 8.7 Hz, 2 H), 7.56–7.16 (m, 10 H) ppm. ^{31}P NMR (121.5 MHz): δ = 143.05 ppm. ^{13}C NMR (75.465 MHz): δ = 148.88 (d, J_{cp} = 6.1 Hz), 147.52 (d, J_{cp} = 4.8 Hz), 146.84 (d, J_{cp} = 1.4 Hz), 145.80 (s), 142.71 (d, J_{cp} = 7.3 Hz), 133.02 (s), 132.75 (s), 132.01 (s), 131.55 (s), 130.97 (s), 130.36 (s), 129.29 (s), 128.67 (d, J_{cp} = 4.8 Hz), 128.48 (s), 127.945 (s), 127.83 (s), 127.28 (s), 127.19 (s), 126.80 (s), 126.67 (s), 125.68 (s), 125.49 (s), 124.49 (s) 121.77 (s), 121.59 (s) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{25}H_{17}NO_3P$ [MH^+]: 410.0946; obsd. 410.0952. $C_{25}H_{16}NO_3P$ (409.09): calcd. C 73.35, H 3.94, N 3.42; found C 73.20, H 4.16, N 3.25.

Synthesis of (*S*)-(3,3′-Bis(trimethylsilyl)-1,1′-binaphthyl-2,2′-diyl) (3-Pyridyl) Phosphite (3): This compound was prepared as described for **2**, using freshly prepared (*S*)-3,3′-bis(trimethylsilyl)-2,2′-binaphthyl phosphorochloridite. Yield (66%) as a white solid. ^1H NMR (300 MHz): δ = 8.30 (d, J = 2.7 Hz, 1 H), 8.27 (d, J = 5.1 Hz, 1 H), 8.08 (d, J = 2.7 Hz, 2 H), 7.92 (dd, J = 2.7, 8.1 Hz, 2 H), 7.45–7.40 (m, 2 H), 7.39–7.31 (m, 1 H), 7.26–7.09 (m, 5 H), 0.43 (s, 9 H), 0.38 (s, 9 H) ppm. ^{31}P NMR (121.5 MHz): δ = 138.99 ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{31}H_{33}NO_3PSi_2$ ([MH^+]): 554.1737; obsd. 554.1725. $C_{31}H_{32}NO_3PSi_2$ (553.2): calcd. C 67.24, H 5.82, N 2.53; found C 67.18, H 5.89, N 2.42.

Synthesis of (3,3′-5,5′-Tetra-*tert*-butyl-1,1′-biphenyl-2,2′-diyl) (3-Pyridyl) Phosphite (4): 3-Hydroxypyridine (0.95 g, 10 mmol), azeotropically dried with toluene (3 × 2 mL), and triethylamine (1.4 mL, 10 mmol) were dissolved in THF (20 mL) and the solution was cooled to 0 °C. Freshly prepared 3,3′,5,5′-tetra-*tert*-butyl-1,1′-biphenyl phosphorochloridite (4.75 g, 10 mmol) was dissolved in THF (20 mL) and added dropwise, stirring was continued for 10 min. The cooling bath was removed and the solution was warmed to room temperature, stirring was continued for 1 h. The reaction mixture was filtered and the solvent evaporated. A mixture of toluene/hexane, 1:3 (40 mL) was added to extract the product. After filtration the solvent was removed in vacuo, giving **4** (3.4 g, 6.4 mmol, 64%) as a white solid. ^1H NMR (300 MHz): δ = 8.39 (d, J = 2.4 Hz, 1 H), 8.31 (dd, J = 2.4, 4.2 Hz, 1 H), 7.45 (d, J = 2.7 Hz, 2 H), 7.22–7.19 (m, 1 H), 7.18 (d, J = 2.7 Hz, 2 H), 7.16–7.12 (m, 1 H), 1.47 (s, 18 H), 1.35 (s, 18 H) ppm. ^{31}P NMR (121.5 MHz): δ = 137.49 ppm. ^{13}C NMR (75.465 MHz): δ = 147.34 (C), 145.72 (CH), 142.92 (CH), 140.37 (C), 132.86 (C), 127.95 (CH), 127.90 (C), 126.94 (CH), 125.29 (CH), 124.74 (C), 124.16 (CH), 35.66 (C), 34.93 (C), 31.75 (CH), 31.39 (CH) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{33}H_{45}NO_3P$ ([MH^+]): 534.3137; obsd. 534.3147; $C_{33}H_{44}NO_3P$ (533.3): calcd. C 74.27, H 8.31, N 2.62; found C 74.35, H 8.27, N 2.75.

Catalysis: The hydroformylation experiments were performed as follows. A stainless steel 25 mL autoclave, equipped with a Teflon stirring bar, was charged with 0.42 μmol of [Rh(acac)$(CO)_2$], 10.4 μmol of phosphane (and 1 equiv. of porphyrin template) and

0.017 mL of diisopropylethylamine, as a base, in 4.0 mL of toluene. The solution was stirred for 1 h under 20 bar CO/H_2 (1:1) at 80 °C. The pressure was reduced to 1 bar and a mixture of 0.34 mL 1-octene (styrene) and 0.17 mL of decane in 0.67 mL of toluene was added. Subsequently the CO/H_2 pressure was adjusted to 20 bar. The mixture was stirred for 1 h (80 °C or 120 °C) and 18 h (40 °C). Then the autoclave was cooled to 0 °C in ice and the pressure was reduced to 1.0 bar. The products were analyzed by GC. A sample was taken and the conversion was checked by GC measurement of the crude product after filtration through a plug of silica to remove the catalyst. In none of the reactions hydrogenated side-products were observed. The crude product mixture of styrene was subjected to reduction with $NaBH_4$ by stirring in 5.0 mL methanol for 30 min. Quenching with water, extraction with a mixture of ethyl acetate/hexane = 1:1, drying of the organic layer, filtrations and removal of solvent gave the corresponding alcohols, for which the enantiomeric purities were determined by chiral GC (Cyclosil-B, isothermal; T = 90 °C, t_R (*R*) = 63.5 min. and t_S (*S*) = 64.8 min.).

The allylic alkylation experiments were performed as follows. Under Schlenk conditions 0.50 μmol of $[Pd(allyl)Cl]_2$, 3.0 μmol phosphite and 3.0 μmol phosphane were dissolved in 5.0 mL of CH_2Cl_2 and stirred for 30 min. Then 50 μmol of 1,3-diphenylallyl acetate, 150 μmol of dimethyl malonate, 150 μmol of BSA and 50 μmol of decane and a catalytic amount of KOAc were added. The mixture was stirred for 24 h at 25 °C and the reaction was subsequently stopped by adding saturated aq. ammonium chloride. Subsequently, 5.0 mL of petroleum ether was added and the solution was washed once more with a saturated NH_4Cl solution. The organic phase was dried with Na_2SO_4, filtered and the conversion was checked by GC measurement. The solution was chromatographed (SiO_2; petroleum ether/CH_2Cl_2 = 1:1) to give analytically pure products.[48] Enantiomeric purities were determined by chiral HPLC (OD column, eluent 0.5% 2-propanol in hexane t_R (*R*) = 33.2 min. and t_S (*S*) = 34.9 min.).

Asymmetric hydrogenation reactions were performed as follows. A 150-mL stainless-steel autoclave, equipped with 15 vessels and teflon stirring bars, was charged with 0.5 μmol of $[Rh(nbd)_2(BPh_4)]$, 1.5 μmol of phosphane, 1.5 μmol of porphyrin, 1.0 μL of dipea, 50 μmol dimethyl itaconate and 50 μmol of decane in 0.5 mL of toluene. The H_2 pressure was adjusted to 5 bar and the mixture was stirred, for 17 h at 40 °C. Then the autoclave was cooled to 0 °C and the pressure was reduced to 1.0 bar. The conversion was checked by GC measurement of the crude product after filtration through a plug of magnesium sulfate and subsequently silica. Enantiomeric purities were determined by chiral GC (Chirasil-L-Val, isothermal; T = 70 °C, t_R (*R*) = 34.4 min. and t_S (*S*) = 35.2 min.).

Acknowledgments

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