



UvA-DARE (Digital Academic Repository)

Self-assembly, characterization and properties of novel poly-nuclear catalysts

Swennenhuis, B.H.G.

Publication date

2009

Document Version

Final published version

[Link to publication](#)

Citation for published version (APA):

Swennenhuis, B. H. G. (2009). *Self-assembly, characterization and properties of novel poly-nuclear catalysts*. [Thesis, fully internal, Universiteit van Amsterdam].

General rights

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

Chapter 3

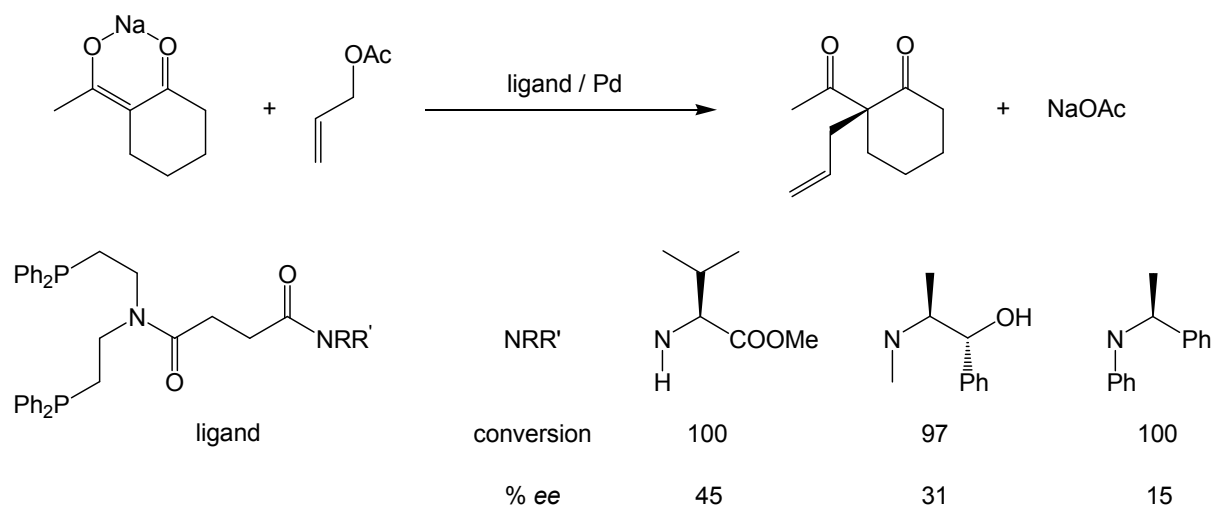
Self-Assembly of Chiral Poly-Hetero-Nuclear Catalysts

Abstract

The assembly of chiral poly-hetero-nuclear catalysts by means of metal-ligand interactions has been explored as a new approach in asymmetric catalysis. For this purpose a basic building block, containing binding sites for the coordination of a catalytically active metal and an assembly metal is combined with a chiral co-ligand. As a result of the formation of a heteroleptic assembly-metal complex, the stereo-chemical information of the chiral co-ligand is transferred to the catalytically active metal, which, if successful, results in the formation of an enantioselective catalyst. We synthesized novel chiral polypyridine building blocks and applied them as co-ligands in our approach. In both the rhodium-catalyzed hydrogenation and the palladium-catalyzed allylic substitution the assemblies proved active catalysts. The hetero-nuclear assemblies display, as proof of principle, an enantiomeric excess up to 27% in the rhodium-catalyzed hydrogenation. Studying model systems allowed us to rationalize our results and gave insight in the structure of the species present under catalytic conditions.

3.1 Introduction – chirality in catalysis and self-assembled systems

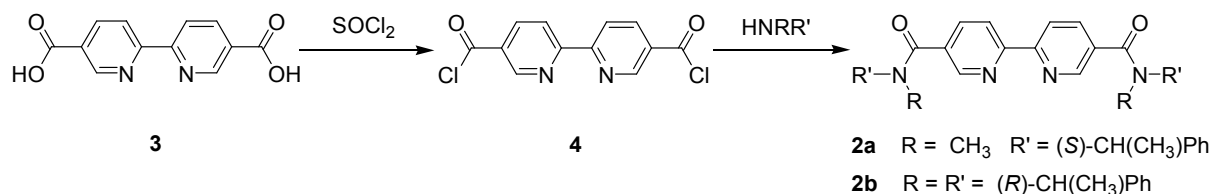
Since the discovery of molecular chirality, chemists have tried to control the stereochemistry of chemical transformations. Enantioselective catalysis has become an indispensable technique in the production of chiral compounds and numerous efficient protocols have been developed for stereoselective C-C, C-H and C-X bond formations¹. Generally the enantioselectivity originates from chiral ligand(s) coordinated to the transition-metal and consequently considerable attention has been given to the synthesis of chiral (phosphine) ligands². Initially the research mainly focused on ligand design, but more recently high-throughput experimentation and combinatorial approaches have become the main route to find enantioselective catalysts³. This can mostly be attributed to the fact that generally small structural changes of the ligand can have a large influence on the enantioselectivity of the catalyst and consequently the screening of large ligand libraries is required to find efficient catalysts⁴. Protocols that allow the formation of these libraries with only limited synthetic effort are highly desirable and (metal-mediated) assembly of catalysts has proven to be a very potent methodology^{4b,5}. Typically, the chiral moieties of the ligand are positioned very close to the catalytic center, but there are examples in which the distance between these groups is rather large. Kumada *et al.* for instance found that, despite a rather large distance between the chiral moiety and the catalytic center, the catalysts displayed enantiomeric excesses (ee) up to 45% in the palladium-catalyzed asymmetric allylic alkylation (scheme 1)⁶.



Scheme 1: Ligands containing distant chiral groups in the asymmetric allylic alkylation.

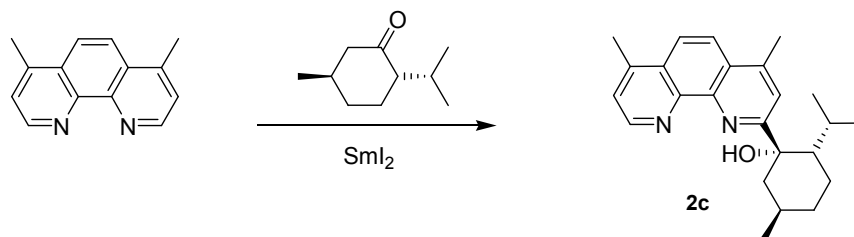
Concept In the previous chapter we reported the synthesis and coordination chemistry of a building block containing two types of binding sites (**1**, scheme 2). We applied this building block in the assembly of poly-hetero-nuclear catalysts; this method is based on the selective

manner in two steps from the commercially available 2,2'-bipyridine-5,5'-dicarboxylic acid (**3**), by converting it with SOCl_2 to the corresponding bis-acid chloride derivative (**4**), followed by reaction with enantiomerically pure (*S*)-(-)-*N*, α -dimethylbenzylamine or (-)-bis[(*S*)- α -methylbenzyl]amine, respectively (scheme 3).



Scheme 3: Synthesis of chiral bipyridines **2a** and **2b**.

A samarium(II)iodide promoted coupling¹² between 4,7-dimethyl-phenanthroline and (-)-menthone afforded chiral phenanthroline **2c** (scheme 4) in a one-step procedure. This coligand contains three chiral centers, of which two originate from the enantiomerically pure ketone reagent, while the third is formed during the C-C bond formation.



Scheme 4: Samarium-catalyzed synthesis of phenanthroline **2c**.

Crystals of **2c** were grown from ethylacetate and to ascertain the exact stereo-chemistry of this building block, the crystal structure was determined by X-ray diffraction. This reveals the isolated product to be (1*S*,2*S*,5*R*)-2-isopropyl-5-methyl-1-(4,7-dimethyl-1,10-phenanthrolin-9-yl)cyclohexanol. The newly formed chiral center on the cyclohexanol moiety has an *S*-chirality, corresponding with an equatorial attack of the phenanthroline on the menthone, confirming the pathway suggested by Helquist *et al.* on the basis of NMR data of a related compound^{12b}. In the solid state the menthol group is oriented in such a manner that the alcohol moiety is in close proximity of the nitrogen's with an intra-molecular N...H-O hydrogen bonding interaction. The N-H and O-H distances are, respectively, 1.90 and 0.86 Å (view **A**, figure 1). Consequently the propyl and methyl groups are placed in orthogonal positions with respect to the phenanthroline plane (view **B**). A comparable hydrogen bonding motif has been reported by Ward *et al.* in a phenol substituted phenanthroline, albeit with a considerably shorter N-H distance of 1.71 Å and a longer O-H bond of 0.92 Å¹³.

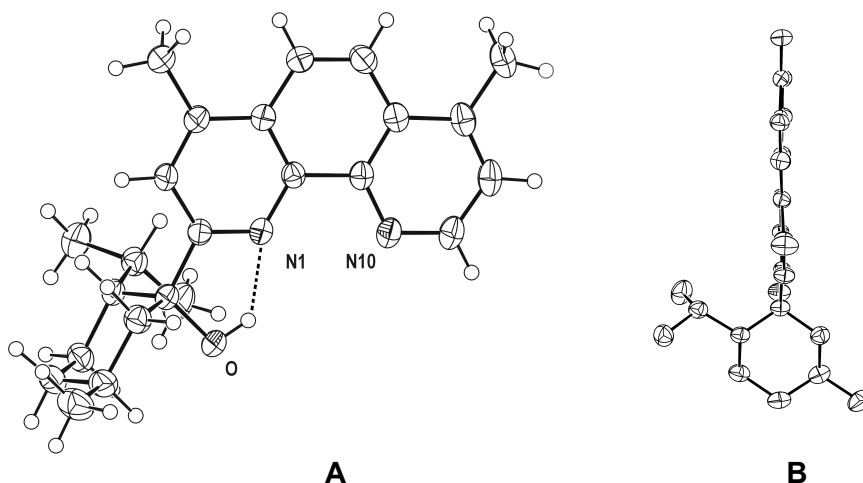


Figure 1: Molecular structure of **2c** in the solid state with a 'front' (A) and a 'side' (B) view. The ellipsoids are drawn at the 50% probability level. In the 'side' view the hydrogen atoms are omitted for clarity.

Additionally we studied the use of commercially available 2,6-bis-((*R*)-4,5-dihydro-4-isopropylloxazol-2-yl)-pyridine)¹⁴ (**2d**, figure 2) as a chiral co-ligand. This ligand provides, in combination with the diimine moiety of **1**, a penta-imine environment for the assembly metal, for which copper(II) has a high affinity¹⁵.

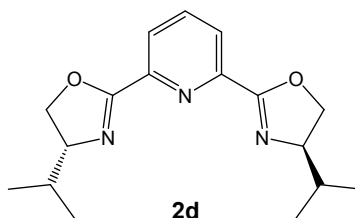
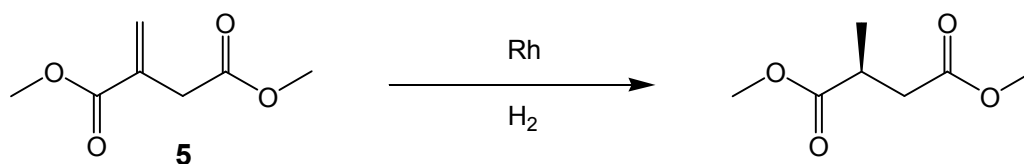


Figure 2: Terdentate chiral co-ligand **2d**.

The nitrogen-based binding sites of **2** are identical with, or closely resemble, the binding sites of the co-ligands applied in the coordination studies conducted with **1**⁸. We therefore neither studied the coordination of **2a-2d** to M_{ass} and M_{cat} , nor did we evaluate the coordination modes present in poly-nuclear assemblies with **2a-2d** as co-ligands. As a result of the mentioned resemblances of the binding sites, it can be assumed that in hetero-nuclear assemblies, rhodium and palladium will coordinate to the bidentate phosphine moieties of **1**, while zinc(II), copper(I) and copper(II) will coordinate to the nitrogen-based binding sites of **1** and **2**.

Rhodium-catalyzed asymmetric hydrogenation Catalytic asymmetric hydrogenation of unsaturated compounds has emerged as a powerful tool for the preparation of chiral

compounds¹⁶. We evaluated our approach in the rhodium-catalyzed hydrogenation of dimethyl itaconate (**5**, scheme 5).



Scheme 5: Synthesis of (*S*)-dimethyl-2-methylsuccinate by means of asymmetric rhodium-catalyzed hydrogenation.

Catalytic performance of model systems To gain insight in the effect of the co-ligands (**2**) on the catalytic performance of rhodium, we first studied several rhodium-polypyridine complexes as catalysts, of which the results are summarized in table 1. Additionally we determined the effect of polypyridine additives on the performance of a commonly applied chiral bis-phosphine rhodium catalyst.

Table 1: Polypyridines as ligands and as additives in the rhodium-catalyzed hydrogenation.

Entry	Ligand	Additive	Equivalents ^a	Yield ^b	ee (%)
1	bipyridine	-		0	-
2	2c	-		0	-
3	2d	-		0	-
4	<i>R</i> -binap	-		100	78 (<i>R</i>)
5	<i>R</i> -binap	bipyridine	1.0	0	-
6	<i>R</i> -binap	[Cu(II)(bipyridine) ₃] ²⁺	0.5	0	-
7	<i>R</i> -binap	[Cu(II)(bipyridine) ₃] ²⁺	3.0	0	-
8 ^c	<i>R</i> -binap	[Cu(II) 2d] ²⁺	0.5	100	77 (<i>R</i>)
9 ^d	<i>R</i> -binap	[2d Cu(II)(bipyridine)] ²⁺	0.5	100	78 (<i>R</i>)
10 ^c	<i>R</i> -binap	[Zn(II) 2d] ²⁺	0.5	100	76 (<i>R</i>)
11 ^d	<i>R</i> -binap	[2d Zn(II)(bipyridine)] ²⁺	0.5	100	77 (<i>R</i>)

Conditions: Solvent = DCM, T = 25 °C, 5 bar H₂, [Rh] = 3.3 mM, 4 hours, Rh/ligand/**5** 1/1/20, Rh = [(COD)Rh(I)(MeCN)₂]BF₄ (COD = 1,5-Z-cyclooctadiene), anion for M_{ass} = triflate. ^aEquivalents of additive with respect to the catalyst. ^bIn mol% based on **5**. ^c[Rh] = 4.0 mM, 5 hours. ^d[Rh] = 3.7 mM, 5 hours. *R*-Binap = (*R*)-(+)-2,2'-bis(diphenylphosphino)-1,1'-binaphthalene.

Since pyridine-based ligands generally yield inactive or only slightly active rhodium hydrogenation catalysts¹⁷, it was not surprising that no conversion was observed when bipyridine (chart 1), **2c** or **2d** were used as ligands (entries 1-3, table 1). Applying *R*-Binap (chart 1) as the ligand resulted in the formation of (*R*)-dimethyl 2-methylsuccinate with reasonable enantioselectivity (78% ee) and in good yield (entry 4). The presence of one

equivalent of bipyridine leads to the formation of inactive rhodium species (entry 5). Most likely the two types of ligands simultaneously coordinate to rhodium, yielding a coordinatively saturated metal center.

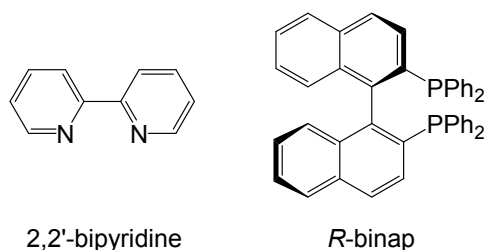
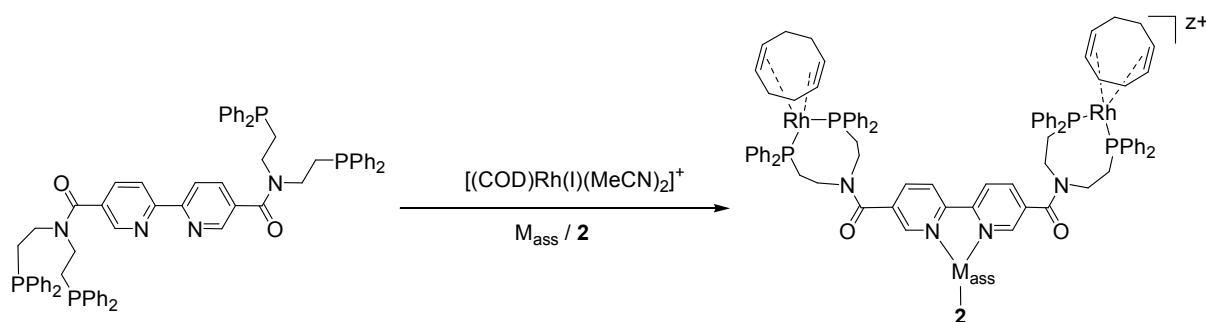


Chart 1: Bipyridine and R-binap.

The presence of $[\text{Cu(II)(bipyridine)}_3]^{2+}$ also led to a complete deactivation of the catalyst (entries 6-7), most likely due to dissociation of bipyridine from the copper. Most notable is the fact that 0.5 equivalent of $[\text{Cu(II)(bipyridine)}_3]^{2+}$ was sufficient to completely deactivate the rhodium catalyst (entry 6). On the contrary, the related $[\text{Cu(II)2d}]^{2+}$ and $[\text{2dCu(bipyridine)}]^{2+}$ complexes did not influence the yield, nor did they significantly influence the enantioselectivity of the catalyst (entries 8-9). The enantioselectivity of the catalyst was not influenced by the presence of $[\text{Zn(II)2d}]^{2+}$ or $[\text{2dZn(II)(bipyridine)}]^{2+}$ (entries 10-11) either. The above results indicate that selective coordination of M_{cat} and M_{ass} to the appropriate binding sites is essential for our approach.

Hetero-nuclear assemblies as catalysts in the asymmetric hydrogenation Next we evaluated various assemblies of **1**, with rhodium as M_{cat} , **2c** and **2d** as chiral co-ligands and Zn(II) and Cu(II) as the assembly metals, for which the results are summarized in table 2. Anticipating the formation of $[\text{2}M_{\text{ass}}\mathbf{1}(\text{Rh(I)}(\text{COD}))_2]^{x+}$ (scheme 6) species via metal directed self-assembly, M_{ass} , **1**, **2** and the rhodium precursor were allowed to react in a 1:1:1:2 ratio and the resulting assemblies were applied as catalysts without further analyses.



Scheme 6: General structure of the self-assembled chiral catalysts studied.

The assemblies studied, with **2c** or **2d** as co-ligands and Zn(II) or Cu(II) as assembly metal, all displayed good activities under the applied reaction conditions, giving the product in 78-100% yield (entries 2-4, table 2). A 1:2 mixture of **1** and the rhodium precursor yielded a poor catalyst, as racemic dimethyl 2-methylsuccinate was only formed in 13% yield (entry 1). We attribute the low conversion to the non-coordinated bipyridine moiety as a result of the absence of an assembly metal, which results in the formation of inactive diimine coordinated rhodium centers. These results also indicate that in the presence of an assembly metal and a co-ligand the rhodium is coordinated to the phosphines of **1**, while the assembly metal is coordinated to the nitrogen-based binding sites of **1** and the co-ligand.

Table 2: Chiral self-assembled catalyst in the asymmetric hydrogenation of dimethyl itaconate.

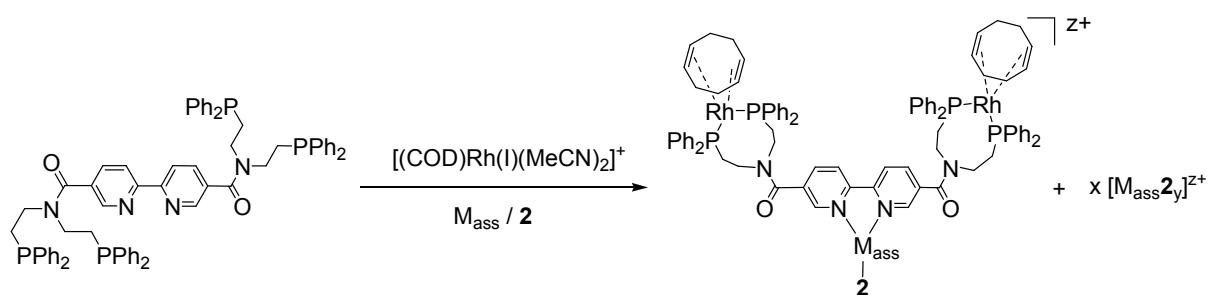
Entry	Co-ligand	M _{ass}	Solvent	Yield ^a	ee (%)
1 ^b	-	-	DCM	13	0
2	2c	Cu(II)	DCM	100	0
3	2d	Cu(II)	DCM	98	3 (R)
4	2d	Zn(II)	DCM	78	25 (R)
5 ^b	-	-	MeOH	84	0
6	2c	Cu(II)	MeOH	84	0
7	2c	Zn(II)	MeOH	100	1 (S)
8	2d	Cu(II)	MeOH	100	1 (R)
9	2d	Zn(II)	MeOH	90	1 (R)

Conditions: T = 25 °C, 24 hours, 5 bar H₂, [Rh] = 3.33 mM, Rh/1/M_{ass}/2/5 2/1/1/1/40, Rh = [(COD)Rh(I)(MeCN)₂]BF₄, M_{ass} = M(OTf)₂. ^aIn mol% based on **5**. ^bCatalyst = [1(Rh(I)(COD))₂](BF₄)₂, [Rh] = 9.99 mM.

Interestingly, for the assemblies with co-ligand **2d**, application of the Cu(II)-based species as catalyst resulted in a higher yield, than when the Zn(II)-based species was applied as the catalyst (98 versus 78%, entries 3-4). Moreover, [2dCu(II)1(Rh(I)(COD))₂]⁴⁺ catalyzed the reaction with negligible enantioselectivity (3% ee, entry 3), while [2dZn(II)1(Rh(I)(COD))₂]⁴⁺ is significantly more enantioselective (25% ee, entry 4). The enantiomeric excess may be small in comparison to conventional catalysts, but it is a proof of principle that transfer of chirality from the co-ligand to M_{cat} is possible. Moreover the effect of changing the assembly metal from zinc(II) to copper(II) is clearly evident; a decrease in conversion and an increase in enantioselectivity (entries 3-4). This result reinforces the proof of principle of our approach; as the assembly metal has a determining role in the catalytic properties of the assembly tuning of catalyst performance does not require additional synthetic steps, but merely the use of different assembly metals.

Since the nature of the solvent can have a determining influence on the activity and enantioselectivity of (hydrogenation) catalysts¹⁸, we also studied the catalytic performance of the assemblies in methanol. In this solvent $[\mathbf{1}(\text{Rh}(\text{I})(\text{COD}))_2]^{2+}$ led to a considerably higher yield of dimethyl 2-methylsuccinate than in dichloromethane (84 versus 13% yield, entries 1 and 5). The assemblies with **2c** or **2d** as co-ligand and Zn(II) or Cu(II) as M_{ass} also led to high conversions, although for all combinations studied no significant enantioselectivity was observed (entries 6-9). Applying $[\mathbf{2dZn}(\text{II})\mathbf{1}(\text{Rh}(\text{I})(\text{COD}))_2]^{4+}$ in dichloromethane as the solvent resulted in 25% ee, while in methanol this assembly gave almost racemic product, underlining the importance of the solvent (entries 4 and 9). Similar to the reactions performed in dichloromethane, in methanol the **2d**-Cu(II) assembly led to a higher yield than the related **2d**-Zn(II) assembly (entries 8-9). For the assemblies with co-ligand **2c** the opposite behavior was observed; the zinc(II)-based assembly resulted in a higher yield than the copper(II)-based assembly (entries 6-7). The origin of the differences in conversion observed for the different co-ligand/ M_{ass} combinations is unclear, but ligand disproportionation reactions, which can lead to inactive rhodium species, might play a role.

If ligand disproportionation were an important factor, we anticipated that changing the ratio of the different building blocks applied (**1**, M_{ass} and **2**) should affect the outcome of the catalytic reaction. We therefore studied the influence of the $\mathbf{1}/M_{\text{ass}}/\mathbf{2}$ ratio on the catalytic performance under slightly different conditions, of which the results are summarized in table 3. The applied ratios should lead to mixtures of the heteroleptic $[\mathbf{2}_x M_{\text{ass}} \mathbf{1}_y \text{Rh}_z]$ and homoleptic $[M_{\text{ass}} \mathbf{2}_x]$ complexes, which were applied as catalysts without further analyses (scheme 7). Note that the $[M_{\text{ass}} \mathbf{2}_x]$ complexes are catalytically inactive.



Scheme 7: Mixtures of hetero- and homoleptic assembly metal complexes.

For all combinations evaluated the substrate was converted quantitatively. This result indicates that coordination of the rhodium to the phosphines of **1** still takes place, even though the number of polypyridine-based binding sites significantly exceeds the number of phosphine-based binding sites. This is particularly evident for entries 3-5, where three equivalents of diimines are present per rhodium. In all but one studied combination the self-

assemblies gave the product as the racemate. Combining **2d**, zinc, **1** and rhodium in a 2:2:1:2 ratio gave the product in 27% *ee* (entry 6), only slightly higher than the 25% *ee* observed when a 1:1:1:2 ratio was applied (entry 4, table 2). The presence of an additional equivalent of the Zn(II)-**2d** complex does not significantly influence the catalytic performance, which is a strong indication that the active species is the same in both experiments.

Table 3: Application of mixtures of hetero- and homoleptic assembly metal complexes as catalysts in the asymmetric hydrogenation.

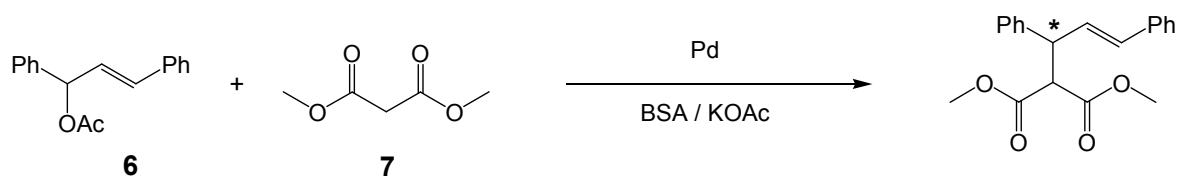
Entry	Co-ligand	M _{ass}	1:2:M _{ass}	Yield ^a	<i>ee</i> (%)
1 ^b	2a	Cu(II)	2:7:3	100	0
2 ^b	2a	Zn(II)	2:7:3	100	2 (<i>R</i>)
3 ^c	2c	Cu(II)	1:5:3	100	1 (<i>R</i>)
4 ^c	2c	Zn(II)	1:5:3	100	1 (<i>S</i>)
5 ^c	<i>S,S</i> - 2d ^d	Cu(II)	1:1:1	100	3 (<i>S</i>)
6 ^e	2d	Zn(II)	1:2:2	100	27 (<i>R</i>)

Conditions: Solvent = DCM, 20 hours, [Rh] = 0.72 mM, Rh/**5** 1/100, M_{ass} = MOTf₂. ^aIn mol% based on **5**. ^bT = 40 °C, 5 bar H₂, Rh = [(NBD)Rh(I)(THF)₂]OTf, NBD = norbornadiene. ^cT = 25 °C, 10 bar H₂, Rh = [(COD)Rh(I)(THF)₂]OTf. ^d*S,S*-**2d** = 2,6-bis-((*S*)-4,5-dihydro-4-*iso*-propyloxazol-2-yl)-pyridine. ^e5 hours, [Rh] = 2.86 mM, Rh/substrate 1/20, Rh = [(COD)Rh(I)(MeCN)₂]BF₄.

The highest enantioselectivity observed so far with the self-assembled catalyst is 27% *ee*. Most likely the rather long distance between the catalytic center and the chiral groups of the co-ligands plays an important role in this limited selectivity¹⁹. Note that Kumada and co-workers also observed moderate *ee*'s for structurally related systems (scheme 1)⁶. The current experiments, however, indicate that it is possible to transfer chiral information from the co-ligand to the catalytic center. We expect that the enantioselectivity can be drastically increased by re-designing the structure of our building blocks, so that the catalytic site and the chiral moiety are brought in closer proximity of one another. Furthermore, application of co-ligands which are structurally related to **2d** could also lead to more enantio-selective catalysts.

Palladium-catalyzed asymmetric allylic alkylation Next to rhodium-catalyzed hydrogenation, we also evaluated our assembly methodology in the palladium-catalyzed asymmetric allylic alkylation²⁰. As a model reaction we chose the alkylation of (*E*)-1,3-diphenylallyl acetate (**6**) with *in situ* generated nucleophile from dimethyl malonate (**7**) and *N,O*-bis(trimethylsilyl)acetamide (BSA) (scheme 8). Chiral bipyridines and phenanthrolines have proven to be efficient ligands for numerous transition-metal catalyzed asymmetric

reactions¹⁰, notably in the palladium-catalyzed allylic alkylation²¹. We started with control experiments, in which **2a-2d** were applied as ligands for palladium, for which the results are summarized in table 4.



Scheme 8: Palladium-catalyzed asymmetric allylic alkylation.

Table 4: Building blocks **2** as ligands for palladium in the asymmetric allylic alkylation.

Entry	Ligand	Yield ^a	ee (%)
1	2a	100	4 (S)
2	2b	100	0
3	2c	100	64 (S)
4	2d	0	-

Conditions: Solvent = DCM, T = RT, 40 hours, [Pd] = 2.50 mM, Pd/**1**/**6**/BSA/**7** 1/1/20/40/40, pinch of KOAc added, Pd = [(allyl)Pd(II)(THF)₂]OTf. ^aIn mol% based on **6**.

No product was observed when the terdentate coordinating **2d** was applied as the ligand (entry 4, table 4), while with diimines **2a-2c** full conversion to the desired product was obtained (entries 1-3). The low enantiomeric excesses obtained with **2a** and **2b** as ligands (7 and 0%, respectively) can be attributed to the relative distant position of the chiral moieties with respect to the catalytic center²². Application of **2c**, with the chiral menthol moiety in proximity of the diimine, resulted in reasonable enantiomeric pure product (64% ee). Note that phenanthrolines with comparable structures induced up to 92% ee in this reaction²¹.

Since copper complexes catalyze allylic substitution reactions²³, we also evaluated copper(II) complexes of **2a** and **2d** as catalysts. Both complexes are inactive under the reaction conditions applied (entries 1-2, table 5). Next we examined the effect of polypyridine additives on the catalytic performance of a palladium diphosphine complex. For this we applied [(dppf)Pd(II)(allyl)]⁺, which effectively catalyzes the reaction (entry 3), as a model complex for the binding of palladium to the bidentate phosphine moieties of **1** (figure 3).

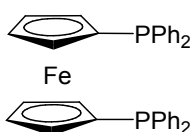


Figure 3: Structure of the bidentate phosphine dppf.

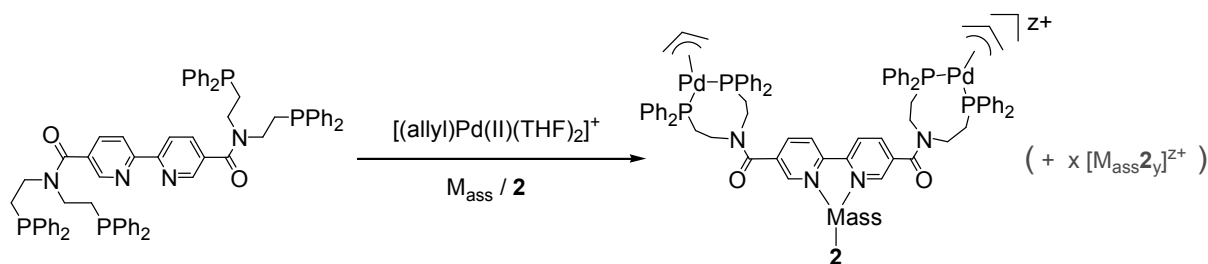
Table 5: Polypyridines as additives in the palladium-catalyzed asymmetric allylic alkylation.

Entry	Catalyst	Additive	Equivalents ^a	Yield ^b	ee (%)
1	[Cu(II) 2a] ²⁺ c,d	-		0	-
2	[Cu(II) 2a] ²⁺ c,d	-		0	-
3	[(dppf)Pd(II)(allyl)] ⁺ c	-		100	0
4	[(dppf)Pd(II)(allyl)] ⁺ c	[Cu(II) 2a] ²⁺	0.5	100	0
5	[(dppf)Pd(II)(allyl)] ⁺ c	[Cu(II) 2d] ²⁺	0.5	100	0
6	[(dppf)Pd(II)(allyl)] ⁺ e	2a	1.0	100	0
7	[(dppf)Pd(II)(allyl)] ⁺ e	2d	1.0	100	0
8	[(THF) ₂ Pd(II)(allyl)] ⁺ c	[Zn(II) 2c] ²⁺	1.0	28	0

Conditions: Solvent = DCM, T = RT, pinch of KOAc added, anion = triflate unless otherwise noted. ^aWith respect to palladium. ^bIn mol% based on **6**. ^c40 h, [Pd] = 2.5 mM, Pd/**6**/BSA/**7** 1/20/40/40. ^dNo palladium added, [Cu] = 1.25 mM. ^e18 h, [Pd] = 5.0 mM, Pd/**6**/BSA/**7** 1/12/24/24, anion = chloride. dppf = 1,1'-bis(diphenylphosphino)ferrocene.

The presence of [Cu(II)**2a**]²⁺ or [Cu(II)**2d**]²⁺ (0.5 equivalent) or **2a** or **2d** (1 equivalent) did not negatively influence the yield (entries 4-7). It must be noted that due to the long reaction time, it is difficult to comment on the structure of the palladium species present during catalysis, but the occurrence of ligand disproportionation reactions can not be excluded. An equal molar mixture of [(THF)₂Pd(II)(allyl)]⁺, Zn(II) and **2c** (entry 8) gave racemic product in low yield (28%), indicating that zinc is firmly bound to **2c** and is not displaced by the palladium²⁴. We attribute the small amount of product formed to ligand free palladium, although its activity is low. In addition, free palladium is also unstable, and indeed palladium-black formation was observed during the reaction.

Hetero-nuclear assemblies as catalysts in the asymmetric allylic alkylation Finally we studied various assemblies using **2c-2d** as chiral co-ligands, and evaluated their catalytic performance. We applied 1/*M_{ass}*/2 ratios that, after metal directed self-assembly, should yield mixtures of the heteroleptic catalyst ([*2_w**M_{ass}***1**_x(Pd(II)(allyl))_y]^{z+}) and additional equivalents of [*M_{ass}***2**_y]^{z+} (scheme 9). Note that the latter complex is inactive under the applied reaction conditions. The resulting mixtures were, without further analyses, used as catalysts.

**Scheme 9:** General structure of the chiral palladium assemblies studied as catalysts.

The homo-nuclear $[\mathbf{1}(\text{Pd}(\text{II})(\text{allyl}))_2]^{2+}$ quantitatively converted the substrate to the product (entry 1, table 6). The presence of the chiral co-ligand and Cu(II) in $[\mathbf{2aCu}(\text{II})\mathbf{1}(\text{Pd}(\text{II})(\text{allyl}))_2]^{4+}$ resulted in negligible enantioselectivity (3%), but also did not negatively affect the yield (entry 2). Similar results, thus full conversions and low *ee*'s (0-3%), were obtained with all combinations of co-ligands **2a-2d** and Cu(II) or Zn(II) as the assembly metal (entries 2-9). Apparently the chiral co-ligands **2** do not provide, when combined with Zn(II) and Cu(II), to an efficient chiral environment around palladium.

Table 6: Self-assembled chiral catalyst in the asymmetric allylic alkylation.

Entry	Co-ligand	M_{ass}	1:2:M_{ass}	Yield ^a	<i>ee</i> (%)
1 ^b	-	-	-	100	0
2	2a	Cu(II)	1:3:2	100	3 (S)
3	2a	Cu(II)	1:5:2	100	0
4	2b	Cu(II)	1:5:2	100	3 (S)
5	2c	Cu(II)	1:1:1	100	1 (S)
6	2c	Zn(II)	1:1:1	100	0
7	2d	Cu(II)	1:1:1	100	2 (S)
8	2d	Zn(II)	1:1:1	100	2 (S)
9	2d	Zn(II)	1:3:2	100	1 (S)

Conditions: Solvent = DCM, T = RT, 40 h, [Pd] = 2.50 mM, Pd/1/6/BSA/7 2/1/40/80/80, pinch of KOAc added, Pd = $[(\text{allyl})\text{Pd}(\text{II})(\text{THF})_2]^+$, anion = triflate. ^aIn mol% based on **6**. ^bCatalyst = $[\mathbf{1}(\text{Pd}(\text{II})(\text{allyl}))_2]^{2+}$.

The results obtained with co-ligand **2c** (entries 5-6) clearly indicate that under the reaction conditions the palladium is bound to **1**, as disproportionation into palladium complexes of **2c**, would have led to (some) enantio-enrichment of the product. We attribute the absence of enantioselectivity to the flexible and relative long linker between the phosphine and bipyridine moieties. As a result no efficient transfer of chirality from **2** to the palladium centers takes place. As discussed in the previous section, building blocks with shorter distances between the binding sites for M_{cat} and M_{ass} , may yield more enantioselective catalysts, but additional research is required to confirm this.

3.3 Conclusion

We have studied a novel approach in asymmetric catalysis, in which chiral poly-hetero-nuclear catalysts are formed by means of metal-mediated self-assembly. In our approach the formation of a heteroleptic assembly metal complex brings the chiral co-ligand in proximity of the catalytic center. We synthesized novel chiral polypyridine building blocks to serve as co-ligands in our approach. We evaluated our methodology in two asymmetric reactions by

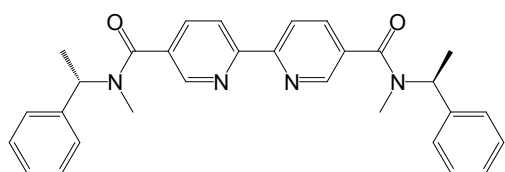
applying a variety of chiral poly-nuclear assemblies as catalysts and determined the effect of the type of assembly metal and structure of the co-ligand on the catalytic performance. The results indicate that under catalytic conditions the assembly and catalytically active metals were coordinated to, respectively, the pyridine and phosphine binding sites. In both the palladium-catalyzed allylic substitution and the rhodium-catalyzed hydrogenation the assemblies gave the products in good yield. With one hetero-nuclear hydrogenation catalyst the product was obtained with 27% enantiomeric excess, indicating the transfer of stereochemical information from the co-ligand to the catalytic center. Importantly, the assembly metal has a determining influence on the catalyst properties of the assembly, giving new handles for catalyst optimization. Currently, the enantioselectivities observed are still low, probably as a result of the flexibility and length of the linker between the bis-phosphine and bipyridine moieties. Most likely the enantioselectivity of our self-assembled catalysts can be increased by re-designing the structure of our building blocks and thereby bringing the catalytic site and the chiral moiety in closer proximity of one another.

3.4 Experimental Section

General Remarks All reactions were carried out under strictly oxygen free conditions, using standard Schlenk techniques under an atmosphere of purified nitrogen. NMR spectra were recorded on a Varian Mercury-300, a Bruker DRX-300 and a Varian Inova-500. NMR-spectra were recorded at room temperature with CDCl_3 as the solvent, unless stated otherwise. Positive chemical shifts (δ) are given (in ppm) for high-frequency shifts relative to a TMS reference (^1H and ^{13}C). ^{13}C spectra were measured with a ^1H decoupling. Data are reported as follows: (br - broad, s - singlet, d - doublet, t - triplet, q - quartet, m - multiplet; coupling constant(s) in Hz; integration; assignment). Mass spectra were recorded on a Shimadzu LCMS-2010A using APC- or ES- ionization with acetonitrile or methanol as the eluent and on a Hewlett-Packard 6890N/6973N GC-MS set-up (HP-5ms column (cross-linked phase 5% PhMe-siloxane, 30 m, 0.25 mm internal diameter, 0.25 μm film thickness), E.I. detection). Elemental analyses were carried out by H. Kolbe Mikroanalytisches Laboratorium, Mülheim an der Ruhr, Germany. Melting points were determined on a Gallenkamp melting point apparatus in open capillaries and are reported uncorrected. Optical rotations were measured on a Perkin-Elmer 241 polarimeter (with $l = 1$ dm). Gas chromatographic analysis were run on an Interscience HR GC Mega 2 apparatus (split/splitless injector, J&W Scientific DB-1 column (cross-linked phase $\text{Me}_2\text{siloxane}$, 30 m, internal diameter 0.32 mm, film thickness 3.0 μm), F.I.D. detector), on an Interscience Finnigan TraceGC ultra apparatus equipped with a RTX1 column and on a Shimadzu GC-17A apparatus (split/splitless injector, BPX35 (SGE) column (35% phenyl polysilphenylenesiloxane, 25 m, internal diameter 0.22 mm, film thickness 0.25 μm), F.I.D. detector). Dr. Martin Lutz is acknowledged for solving the crystal structure of **2c**.

Materials Chemical were purchased from Acros Chimica, Aldrich Chemical Co., Biosolve, Fluka, Merck and Strem and were used as received, unless indicated otherwise. Diethyl ether and THF were distilled from sodium/benzophenone, hexanes was distilled from sodium/benzophenone/triglyme. Acetonitrile, dichloromethane, methanol and amines were distilled from calcium hydride. SOCl_2 was freshly distilled prior to use. Deuterated solvents were distilled from the appropriate drying agents. Distilled CDCl_3 was stored on K_2CO_3 . Silica chromatography columns (silica 60, SDS Chromagel, 70-200 μm) were deactivated with 10% NEt_3 in petroleum ether (40-60), followed by several washing with petroleum ether (40-60). 5,5'-Bis(carbonylchloride)-2,2'-bipyridine⁸, 2,2'-bipyridine-5,5'-dicarboxylic acid bis-[bis-(2-diphenylphosphinoethyl)-amide] (**1**)⁸ and (*E*)-1,3-diphenylprop-2-en-1-yl acetate²⁵ were synthesized according to literature procedures. The metals were added via stock solutions of their triflate salts: Cu(II) in MeCN, Zn(II) in MeOH and $[(\eta^4\text{-COD})\text{Rh}(\text{I})(\text{MeCN})_2]\text{BF}_4$ in DCM.

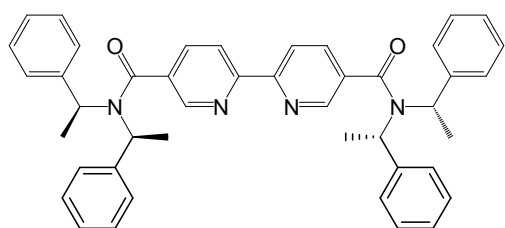
$[(\eta^4\text{-COD})\text{Rh}(\text{I})(\text{THF})_2]\text{OTf}$, $[(\eta^4\text{-NBD})\text{Rh}(\text{I})(\text{THF})_2]\text{OTf}$ and $[(\eta^3\text{-C}_3\text{H}_5)\text{Pd}(\text{II})(\text{THF})_2]\text{OTf}$ were added via DCM/THF (10:1) stock solutions⁸.



2,2'-Bipyridine-5,5'-dicarboxylic acid bis-[methyl-(1-(S)-phenyl-ethyl)-amide] (2a)

5,5'-bis-(carbonylchloride)-2,2'-bipyridine (1.35 mmol) was dissolved in 15 ml THF, followed by addition of 0.56 ml NEt_3 (4.05 mmol, 3.0 equiv.). Subsequently 0.39 ml (S)-(-)-*N*, α -dimethylbenzylamine (2.7 mmol, 2 equiv.) was added and the reaction mixture was stirred at room temperature for 14 hours. After evaporation of the solvents, the residue was dissolved in 30 ml EtOAc and washed with water (2 X 15 ml). The organic layer was dried with MgSO_4 and the solvents were evaporated *in vacuo*. Crystallization of the crude product from EtOAc/Hexanes/ Et_2O afforded **2a** as small colorless needles. Yield: 437 mg, 0.91 mmol, 68%.

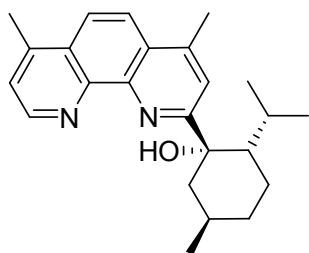
^1H NMR (25 °C): δ = 8.77 (s, 2H, Ar-*H*), 8.45 (d, 2H, J = 7.9 Hz, Ar-*H*), 7.90 (d, 2H, J = 7.9 Hz, Ar-*H*), 7.37 - 7.21 (m, 10H, Ar-*H*), 6.15/5.04 (2 br s, 2H, CHCH_3), 2.84/2.66 (2 br s, 6H, NCH_3), 1.62/1.60 (2 br s, 6H, CHCH_3); ^1H NMR (50 °C): δ = 8.75 (s, 2H, Ar-*H*), 8.45 (s, 2H, Ar-*H*), 7.86 (s, 2H, Ar-*H*), 7.30 (s, 10H, Ar-*H*), 5.62 (br s, 2H, CHCH_3), 2.75 (s, 6H, NCH_3), 1.60 (s, 6H, CHCH_3); ^{13}C NMR: δ = 169.52/169.15, 156.24, 147.87/147.23, 139.85, 136.10/136.00, 132.94, 129.00, 127.95, 127.62, 126.65, 121.26, 57.03/51.32, 32.10/28.35, 17.92/15.67; LC-MS (m/z , (rel. intensity, assignment)): 478 (31, M^+), 477 (100), 372 (12, $\text{M}-\text{C}_8\text{H}_9$); Anal. calc. for $\text{C}_{30}\text{H}_{30}\text{N}_4\text{O}_2$: C 75.29, H 6.32, N 11.71; found: C 75.08, H 6.19, N 11.59; m.p. = 160 °C; $[\alpha]_{\text{D}}^{20}$ = -205.0° (c = 0.74, DCM).



2,2'-Bipyridine-5,5'-dicarboxylic acid bis-[bis-(1-(R)-phenyl-ethyl)-amide] (2b)

This compound was prepared analogously to the synthesis of **2a** by quenching 5,5'-bis(carbonylchloride)-2,2'-bipyridine (**2**, 0.22 mmol) with (-)-bis-[(S)- α -methylbenzyl]-amine (0.1 ml, 0.44 mmol, 2.0 equiv.). After work-up the crude product was purified by column chromatography (neutral alumina, DCM) to afford **2b** as an off-white solid. Yield: 114 mg, 0.17 mmol, 79%.

^1H NMR: δ = 8.67 (d, J = 2.4 Hz, 2H, Ar-*H*), 8.39 (d, J = 8.4 Hz, 2H, Ar-*H*), (dd, J = 8.4 Hz, J = 2.4 Hz, 2H, Ar-*H*), 7.19 (m, 12H, Ar-*H*), 7.05 (m, 8H, Ar-*H*), 4.98/4.96 (2 br s, 4H, CHCH_3), 1.82/1.80 (2 s, 12H, CH_3); ^{13}C NMR: δ = 168.95, 155.35, 146.39, 140.27, 134.98, 134.67, 129.25, 128.39, 128.05, 127.73, 125.52, 121.232, 55.51 (br, CHCH_3), 19.05 (CH_3); LC-MS (m/z , (rel. intensity, assignment)): 659 (100, M^+), 555 (5), 452 (5), 338 (12); m.p. = 94 °C; $[\alpha]_{\text{D}}^{20}$ = -248.5° (c = 0.14, DCM).

**(2R,5S,1S)-2-iso-propyl-5-methyl-1-(4,7-dimethyl-1,10-**

phenanthroline-9-yl)-cyclohexanol (2c) 834 mg 4,7-dimethyl-1,10-phenanthroline (4.00 mmol) was azeotropically dried by dissolving it in 10 ml toluene followed by evaporation *in vacuo* of the solvent (2 times). It was dissolved in 30 ml THF and 1.51 ml (–)-menthone (1.34 g, 8.7 mmol, 2.2 equiv.) was added. After 20

minutes 10 mmol SmI_2 was added (100 ml 0.1 M in THF, 2.5 equiv.) The dark blue suspension was stirred for 48 hours and subsequently the reaction was quenched by addition of 100 ml aqueous saturated NH_4Cl . The THF was partially evaporated and the resulting solution was extracted with 300 ml EtOAc (3 times). The combined organic fractions were dried with MgSO_4 , filtered and the solvent was evaporated *in vacuo*. The crude yield was determined by ^1H NMR spectroscopy to be roughly 40%. Purification by column chromatography (silica) with hexanes/EtOAc 1:3 gave unreacted menthone as the first fraction, while a mixture of 4,7-dimethyl-1,10-phenanthroline and the target compound was obtained when the eluent was changed to DCM/MeOH 95:5. Enantiomeric pure **2c** was obtained as small colorless cubic crystals, by crystallization from EtOAc. Yield: 280 mg, 0.77 mmol, 20%.

^1H NMR: δ = 9.00 (d, J = 4.7 Hz, 1H, Ar-*H*), 8.01 (s, 2H, Ar-*H*), 7.48 (s, 1H, Ar-*H*), 7.44 (d, J = 4.7 Hz, 1H, Ar-*H*), 6.24 (br s, 1H, OH), 2.81 (s, 3H, phen- CH_3), 2.78 (s, 3H, phen- CH_3), 2.10 (m, 1H), 1.60-2.00 (m, 5 H), 1.20-1.45 (m, 2H), 1.11 (m, 1H), 0.89 (d, J = 4.8 Hz, 3H), 0.86 (d, J = 4.8 Hz, 3H), 0.68 (d, J = 7.2 Hz, 3H); ^{13}C NMR: δ = 165.57, 150.12, 145.76, 145.37, 144.46, 143.94, 128.40, 126.84, 124.06, 122.11, 121.96, 120.08, 51.19, 49.73, 35.63, 31.17, 28.72, 28.04, 24.112, 22.67, 22.45, 19.89, 19.86, 19.39, 19.15; GC-MS (m/z , relative intensity): 362 (20, M^+), 347 (25, M- CH_3), 319 (40, M- C_3H_7), 277 (100), 251 (84), 222 (41), 208 (70, M- $\text{C}_{10}\text{H}_{19}\text{O}$); Anal. calc. for $\text{C}_{24}\text{H}_{30}\text{N}_2\text{O}$: C 79.52, H 8.34, N 7.73; found: C 79.47, H 8.06, N 8.59; m.p. = 209 °C; $[\alpha]_{\text{D}}^{20}$ = -23.7° (c = 0.43, DCM).

General procedure for the hydrogenation of dimethyl itaconate A Schlenk-tube, equipped with a magnetic stirring bar, was charged in the following order with **2**, the assembly metal, **1** and $[(\text{COD})\text{Rh}(\text{I})(\text{THF})_2]\text{OTf}$ in the appropriate amounts. After stirring for approximately 60 minutes, the solvents were evaporated *in vacuo* and the complex was re-dissolved in dichloromethane. Vessels equipped with Teflon stirring bars, were charged with the self-assembled catalyst (0.6 μmol rhodium), 24 μmol dimethyl itaconate and 25 μmol decane (as internal standard) via dichloromethane stock solutions (tot volume = 1.8 ml). The vessels were transferred into a stainless steel 150 ml autoclave and the autoclave was flushed with hydrogen gas (3 x 3 bar) and pressurized to 5 bar. After stirring for 24 h at 25 °C the autoclave was depressurized and the reaction mixtures were filtered over silica and

eluted with dichloromethane. Conversions were determined by GC and enantiomeric purities were determined by chiral GC (Carlo Erba Vega 6000 gas chromatograph, equipped with a Beta-Dex 325 (Supelco) column (30 m, 0.25 mm internal diameter, 0.25 μm film thickness), He 150 kPa, H₂ 50 kPa, air 100 kPa, isothermal; T = 70 °C, T_R(R) = ~ 33 min., T_S(S) = ~ 34 min.). All catalytic runs were performed at least in duplo and the results were reproduced within GC error limits.

General procedure for the palladium-catalyzed asymmetric allylic alkylation A Schlenk-tube, equipped with a magnetic stirring bar, was charged in the following order with **2**, the assembly metal, **1**, the palladium allyl precursor ([allyl]Pd(II)(THF)₂]OTf or [(C₃H₅)Pd(II)Cl]₂) (0.01 mmol) and KOAC (1 mg) in the appropriate amounts via stock solutions. After stirring for approximately 30 minutes, the solvents were evaporated *in vacuo* and the complex was re-dissolved in dichloromethane (2 ml). 1,3-diphenylallyl acetate (0.20 mmol) and *n*-decane (0.20 mmol, internal standard for GC measurement) were added via freshly prepared stock-solutions in DCM. After 15 minutes the reaction was started by addition of a mixture of 0.40 mmol dimethylmalonate and 0.40 mmol *N,O*-bis(trimethylsilyl)acetamide (BSA) via freshly prepared stock-solutions in DCM (total volume = 4 ml). After 40 hours the reaction was stopped by the addition of Et₂O (5 ml) and a saturated aqueous ammonium chloride solution (5 ml). The organic layer was subsequently dried over MgSO₄ and an aliquot was analyzed by GC to determine the yield, while the rest was evaporated to dryness. The crude product was further purified by flash column chromatography (SiO₂, EtOAc/PE 40-60 1:5) to yield a yellowish oil. The enantiomeric purity was determined by chiral HPLC (Daicel OD; *n*-hexane/2-propanol 99.5:0.5; flow 0.5 ml/min; ν = 254 nm. t_R (R) = 42.1 min., t_R (S) = 45.8 min.). All allylic alkylation experiments were performed at least in duplo and the results were reproduced within GC and HPLC error limits.

3.5 References and Notes

- ¹ For reviews on asymmetric catalysis see: *Chem. Rev.* **2003**, *103*, no. 8.
- ² See for instance: Pietrusiewicz, K. M.; Zablocka, M. *Chem. Rev.* **1994**, *94*, 1375.
- ³ For reviews see for instance: a) Gennari, C.; Piarulli, U. *Chem. Rev.* **2003**, *103*, 3071; b) Reetz, M. T. *Angew. Chem., Int. Ed.* **2001**, *40*, 284; c) A. Hoveyda in *Handbook of Combinatorial Chemistry*, Vol. 2 (Eds.: K. C. Nicolaou, R. Hanco, W. Hartwig), Wiley-VCH, Weinheim, **2002**, 991; d) V. Murphy, H.W. Turner, T. Weskamp in *Applied Homogeneous Catalysis with Organometallic Compounds*, Vol. 2 (Eds.: B. Cornils, W. A. Herrmann), second edition., Wiley-VCH, Weinheim, **2002**, 740.
- ⁴ See for instance: a) Lefort, L.; Boogers, J. A. F.; de Vries, A. H. M.; de Vries, J. G. *Org. Lett.* **2004**, *6*, 1733-1735; b) Jiang, X.-B.; Lefort, L.; Goudriaan, P. E.; de Vries, A. H. M.; van Leeuwen, P. W. N. M.; de Vries, J. G.; Reek, J. N. H. *Angew. Chem., Int. Ed.* **2006**, *45*, 1223-1227.
- ⁵ a) Slagt, V. F.; Kaiser, P.; Berkessel, A.; Kuil, M.; Kluwer, A. M.; van Leeuwen, P. W. N. M.; Reek, J. N. H. *Eur. J. Inorg. Chem.* **2007**, 4653; b) Kuil, M.; Goudriaan, P. E.; van Leeuwen, P. W. N. M.; Reek, J. N. H. *Chem. Commun.* **2006**, 4679; c) Reek, J. N.H.; Röder, M.; Goudriaan, P. E.; Kamer, P. C.J. van Leeuwen, P. W. N. M.; Slagt, V. F. *J. Orgmet. Chem.* **2005**, *690*, 4505; d). Takacs, J. M.; Reddy, D. S.; Moteki, S. A.; Wu, D.; Palencia, H. *J. Am. Chem. Soc.* **2004**, *126*, 4494.
- ⁶ Hayashi, T.; Kanehira, K.; Tsuchiya, H.; Kumada, M. *Chem. Commun.* **1982**, 1162.
- ⁷ In the remainder of this chapter bipyridine and phenanthroline indicate, respectively, the 2,2'-bipyridine and 1,10-phenanthroline isomers.
- ⁸ See chapter 2 for details.
- ⁹ Metals have been applied successfully as 'transporters' of stereo-chemical information: a) Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F.; Woods, C. R.; Siegel, J. S. *Eur. J. Org. Chem.* **2001**, 173; b) Nabeshima, T.; Hashiguchi, A.; saika, T. Akine, S. *Angew. Chem.* **2002**, *114*, 499.
- ¹⁰ For reviews on the synthesis and use of chiral polypyridines, see: a) Schoffers, E. *Eur. J. Org. Chem.* **2003**, 1145; b) Fletcher, N. C. *Perkin Trans. 1* **2002**, 1831; c) Malkov A.V.; Kosovsky, P. *Curr. Org. Chem.* **2003**, *7*, 1737; d) Chelucci, G.; Thummel, R. P. *Chem. Rev.* **2002**, *102*, 3129.
- ¹¹ Chiral polypyridines have been applied to assemble chiral superstructures. See: a) Mamula, O.; von Zelewsky, A. *Coor. Chem. Rev.* **2003**, *242*, 1-2, 87; b) Albrecht, M. *Chem. Rev.* **2001**, *101*, 3457.
- ¹² a) O'Neil, D. J.; Helquist, P. *Org. Lett.* **1999**, *1*, 1659-1662; b) Weitgenant, J. A.; Mortison, J. D.; O'Neil, D. J.; Mowery, B.; Puranen, A.; Helquist, P. *J. Org. Chem.* **2004**, *69*, 2809-2815.
- ¹³ Jeffrey, J. C.; Moore, C. S. G.; Psillakis, E.; Ward, M. D.; Thornton, P. *Polyhedron* **1995**, *14*, 5, 599.
- ¹⁴ Desimoni, G.; Faita, G.; Quadrelli, P. *Chem. Rev.* **2003**, *103*, 8, 3119-3154.
- ¹⁵ This coordination motif has been applied frequently in supramolecular systems, see for instance: Hasenknopf, B.; Lehn, J.-M.; Baum, G.; Fenske, D. *Proc. Natl. Acad. Sci. U.S.A.* **1996**, *93*, 1397-1400.
- ¹⁶ Knowles, W. S. *Advanced Synthesis & Catal.* **2003**, *345*, 3-13.
- ¹⁷ By preventing rhodium-pyridine coordination, pyridylphosphines have been successfully applied in rhodium catalyzed hydrogenation reactions: Chan, A. S. C.; Chen, C.-C.; Cao, R.; Lee, M. R.; Peng, S. M.; Lee, G. H. *Organometallics* **1997**, *16*, 3469.
- ¹⁸ See for instance: van den Berg, M.; Minnaard, A. J.; Haak, R. M.; Leeman, M.; Schudde, E. P.; Meetsma, A.; Feringa, B. L.; de Vries, A. H. M.; Maljaars, C. E. P.; Willans, C. E.; Hyett, D.; Boogers, J. A. F.; Henderickx, H. J. W.; de Vries, J. G. *Adv. Synth. Catal.* **2003**, *345*, no. 1-2, 308-322.
- ¹⁹ Test experiments in the rhodium-catalyzed hydrosilylation gave comparable results; the products were formed in good yield, albeit as racemates.
- ²⁰ For reviews on (palladium-) catalyzed (asymmetric) allylic substitutions see: a) *Palladium-Catalyzed Allylic Substitutions*, Heumann, A. In *Transition Metals for Organic Synthesis*; Beller, M.; Bolm, C. Eds.; Wiley-VCH, Weinheim, **2008**; b) Pfaltz, A.; Lautens, M. *Comprehensive Asymmetric Catalysis II*; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H. Eds.; Springer: Berlin, **1999**; c) Trost, B. M. *J. Org. Chem.* **2004**, *69*, 5813.
- ²¹ Pona-Carbera, E.; Norby, P. O.; Sjorgen, M.; Vitagliano, A.; De Felice, V.; Oslob, I.; Ishii, S.; O'Neill, D.; Akermark, B.; Helquist, P. *J. Am. Chem. Soc.* **1996**, *118*, 4299.
- ²² Closely related ligands have been applied in stereoselective conversions: Sakaki, S.; Ishikura, H.; Kuraki, K.-I.; Tanaka, K.-J.; Satoh, T.; Arai, T.; Hamada, T. *Dalton Trans.* **1997**, 1815.
- ²³ a) Baruah, J. B.; Samuelson, A. G. *J. Organomet. Chem.* **1989**, *361*, C57-C60; Malda, H; b) Van Zijl, A. W.; Arnold, L. A.; Feringa, B. L. *Org. Lett.* **2001**, *3*, 1169-1171.
- ²⁴ Copper displacing palladium from chiral diimine ligands has been observed by others: Zhang, Y.; Sigman, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 3076-3077.
- ²⁵ Auburn, P. R.; Mackenzie, P. B.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2033.

