Chapter 3

Monodentate Phosphorus Ligands

3.1. Homogeneous catalysis using transition metal complexes

Transition metal catalysts consist of a metal center complexed with appropriate ligands. A different transformation often requires a different metal center that is responsible for the catalytic activity, due to its direct interaction with the substrate. This interaction provides the alternative pathway with lower Gibbs energy of activation, which allows the reaction to take place. However, it is the ligand which modulates the properties of the catalysts and determines the level of selectivity that can be obtained due to its electronic and steric properties. In this respect, it is noticed that the most widely exploited complexes contain the following metal and ligand classes.

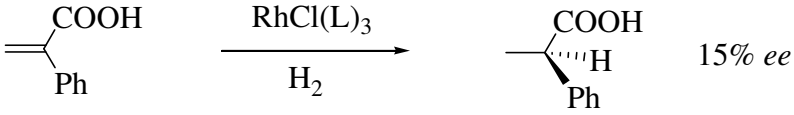
- Pd, Rh, Ru, Ir, Os, Pt and Ni are generally complexed with tertiary P and/or N containing ligands (but also Cp and CO).
- Ti, Zn, Mn and Cu are generally complexed with O and/or N containing ligands.

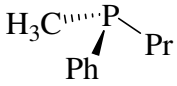
The use of transition metal catalysis allows unprecedented levels of selectivity control in terms of:

- Chemoselectivity: discrimination between different functional groups.
- Regioselectivity: discrimination between equivalent functional groups or atoms.
- Enantioselectivity: discrimination between the two faces of a prochiral substrate or enantiotopic atoms and groups, leading to a chiral compound.

Representative examples, in which these selectivity issue have been addressed, can already be found in the pioneering studies of Knowles (on olefin hydrogenation),[1] Noyori (on ketone hydrogenation)[2] and Sharpless (on olefin epoxidation),[3] who were awarded the 2001 Nobel Prize in Chemistry for their achievements in asymmetric catalysis using chiral transition metal complexes. Their pioneering work opened up the field of research known as homogeneous asymmetric catalysis. In the 1960s Knowles modified Wilkinson's homogeneous hydrogenation catalyst [$RhCl(PPh_3)_3$] with a chiral monodentate phosphane (**3.1**), which led to a chiral homogeneous catalyst for the hydrogenation pf prochiral olefins. The effectiveness of this approach was demonstrated

in a pioneering experiment where α-phenylacrylic acid was hydrogenated to phenylpropionic acid with the use of such a modified catalyst:[1a]



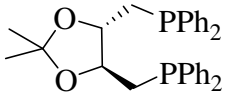


3.1

Although the enantiomeric excess is rather low by today's standards, this proof of principle inspired many others to develop highly selective ligands for asymmetric catalysis.

The low enantioselectivities were attributed to the many degrees of freedom of the rhodium complexes, particularly the rotation around the Rh-P bond was considered to be of major importance.

Dang and Kagan realized this and synthesized the first chiral bidentate phosphine **DIOP 3.2**, the first example of a chiral bidentate phosphane ligand:[4a]



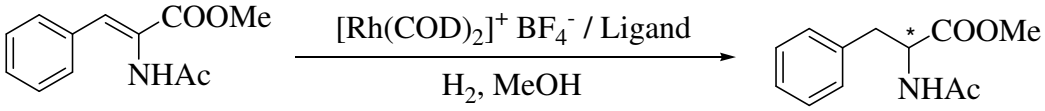
(*S*,*S*)-DIOP

3.2

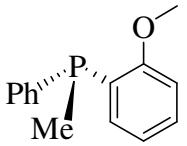
The use of a bidentate chiral ligand proved to be an effective method of increasing the enantioselectivity of the catalyst. Using DIOP as chiral ligand a remarkably high *ee* of 70% was obtained in the hydrogenation of 2-acetamidocinnamic acid.[4] Another major difference in the structure of DIOP is the fact that chirality of this C_2-symmetric ligand is found at the tartaric acid-based backbone of the ligand and not at the phosphorus atom, allowing a more facile synthesis.

Acknowledging the potential of these bidentate ligands Knowles subsequently showed that **DiPAMP** (**3.4**), which represents a dimer of the first generation ligand **PAMP**

(**3.3**), increased the enantiomeric excesses of the rhodium-catalyzed hydrogenation of methyl 2-acetamido-cinnamate from 55% to 95%.[5]

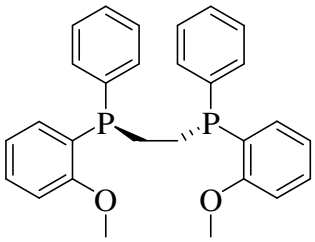


PAMP *ee* = 55%
DiPAMP *ee* = 95%



PAMP

3.3

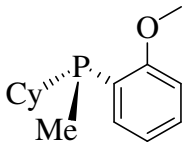


DiPAMP

3.4

The tendency to make use of non P-chiral ligands, such as DIOP, has simplified the synthesis of the chiral ligands and has lead to the discovery of several dozen of families of chiral bisphosphines.[6] Following the application of DiPAMP in the commercial process for L-DOPA the dogma of the superiority of bidentate phosphorus ligands was well established. This new bidentate phosphines set the standard for the development of chiral ligands for the asymmetric hydrogenation in the three following decades, leading to privileged bidentate ligands such as BINAP and DuPHOS which are the basis for many highly enantioselective catalysts.

This is regardless of the fact that Knowles had previously shown that the use of monodentate **CAMP** (**3.5**) led to an *ee* of 88% in the formation of *N*-acetyl-phenylalanine:[7]



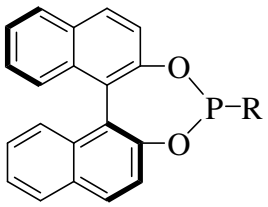
CAMP

3.5

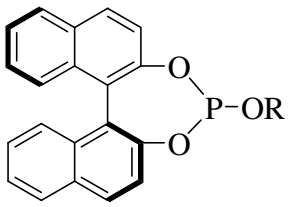
Due to the results obtained using bisphosphines this dogma remained unchallenged for many years. This can clearly be noticed from the number of monodentate phosphines described in the literature compared to the number of bidentate ligands. Just before the start of the new millennium both Zhang[8] and Kagan[9] made some interesting quotes. Zhang stated: 'There have been only a limited number of monodentate chiral phosphines reported in the literature and high enantioselectivity with monodentate phosphines is difficult to obtain.

However, there are many transition metal-catalyzed reactions that do not work with chelating bidentate ligands. *Efficient chiral monophosphines are clearly needed*.' Kagan acknowledges this by stating: 'Chelating chiral diphosphines are often used as ligands of organometallic complexes. *However monophosphines, or more generally ligands with one phosphorus linked to one or several heteroatom, may also be useful.*'

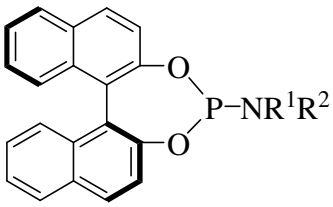
It was a surprise that three groups independently reported the use of three new classes of chiral monodentate ligands for asymmetric hydrogenation in the year 2000.[10] The use of these monodentate ligands induced remarkably high enantioselectivities, comparable to the results obtained using the best bidentate phosphines in the rhodium-catalyzed asymmetric hydrogenation. These monophosphonites, monophosphites and monophosphoramidites are all based on a BINOL backbone with an easily variable alkyl, alcohol or amine functionality:



Phosphonites
Pringle *et al*.



Phosphites
Reetz *et al*.

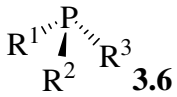


Phosphoramidites
Feringa, de Vries *et al*.

3.2. Monodentate phosphines

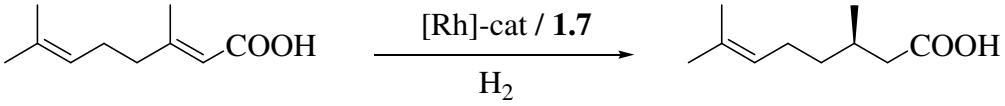
Although the focus of attention in the rhodium-catalyzed hydrogenation of olefins was on the use of chiral bidentate phosphines some monodentate phosphines were developed and tested.

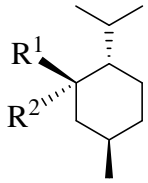
The first group of ligands were P-chiral ligands (**3.6**)[8] usually with a phenyl and a methyl moiety. The size of the third group determines to a large extent the chiral induction in the hydrogenation. Ligands belonging to this family are for example PAMP and CAMP already mentioned and presented before.



3.6

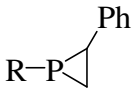
Ligands **3.7** were used in the hydrogenation of the acrylic double bond of (*E*)-3,7-dimethyl-2,6- dienoic acid.[11] They may contain a chiral phosphorus atom or not. The best result (e.e. = 79%) was obtained using a ligand which do not contain a chiral phosphorus (R^1 = H, R^2 = $P(C_6H_5)_2$):



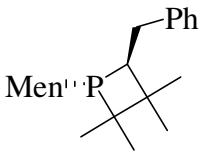


3.7

The phosphorus atom can also be part of a heterocycle as demonstrated by the diastereomeric P-chiral phosphines **3.8**[12] and **3.9**.[13]



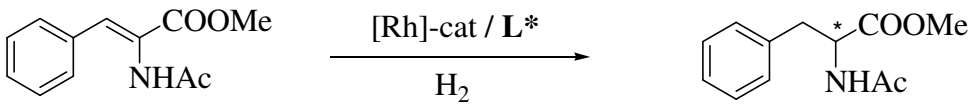
3.8

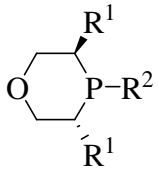


3.9

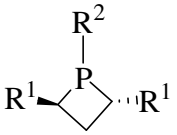
Both these ligands were used to make rhodium complexes containing two phosphine ligands. These phosphirane containing complexes were tested in the hydrogenation of 2-acetamidocinnamic acid.

Heterocyclic monodentate phosphines with C_2-symmetry with the phosphorus atom in a four, five, six and seven-membered ring, **3.10** and **3.11**[14], have been used in the following reaction:



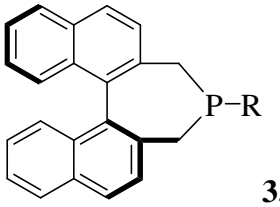


3.10



3.11

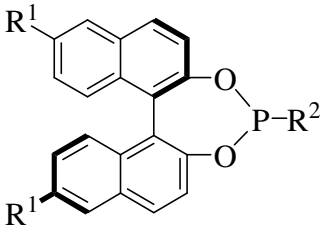
Ligands **1.12** featuring an atropisomeric moiety were also tested in the same reaction and they also display the subtle effects that the various sizes of the substituents have on the enantioselectivity of the hydrogenation.[15]



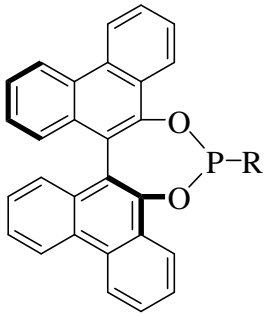
3.12

3.3. Monodentate phosphonites

Rhodium-catalyzed asymmetric hydrogenation using monodentate phosphonite ligands was first reported by Pringle *et al.*[12a] followed by Reetz *et al.*[12b]



3.13

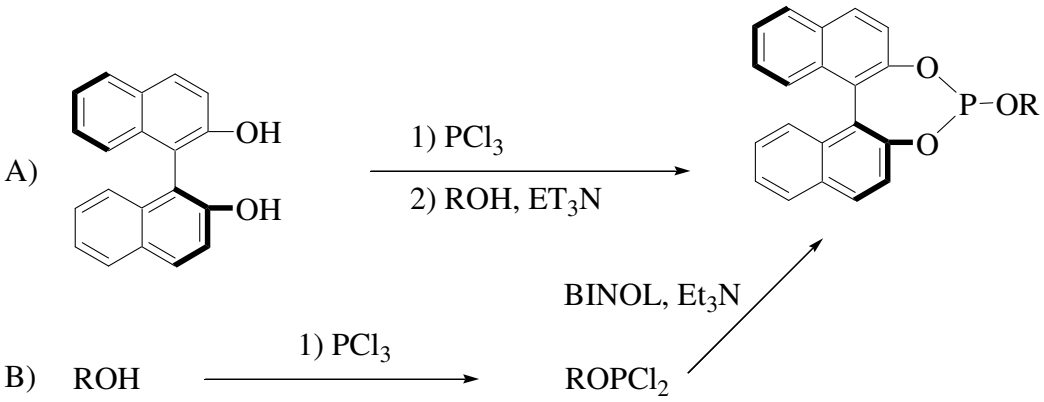


3.14

The ease of synthesis of these phosphonites makes them an interesting class of ligands for the synthesis of a ligand library. This opens the possibility to use them in high throughput experimentation (HTE). The fact that we are dealing with monodentate ligands makes it is possible to expand the diversity even further by testing mixtures of ligands (see below).

3.4. Monodentate phosphites

The synthesis of monodentate phosphites is illustrated in the Scheme below:

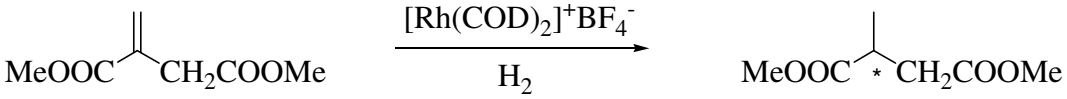


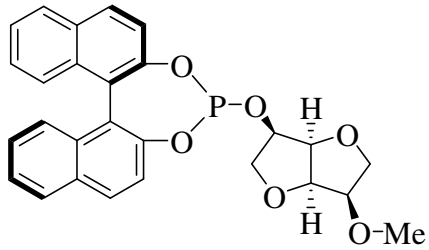
The phosphites are prepared in two steps from a diol and an alcohol. In the first approach (A) the diol, in this example BINOL, is reacted with phosphorus trichloride followed by the reaction of the phosphorus chloride with the appropriate alcohol. The intermediate phosphorus chlorides are usually oils or foams that are not easily purified. A second approach was described and it uses the reverse preparation as is illustrated in the second approach (B). This procedure results in products which have a higher purity than the products obtained using route A.

Previously, Union Carbide (now Dow Chemicals) had reported the use of monodentate phosphites for the rhodium-catalyzed asymmetric hydroformylation. The selectivities obtained with these monodentate ligands were lower than those obtained with the bidentate phosphites.[16] The use of monodentate phosphites as ligands in the rhodium-catalyzed asymmetric hydrogenation was discovered by Reetz *et al*. Originally they

were working with bidentate phosphites based on di-anhydro-D-mannite which contained two BINOL moieties.

It turned out that by substituting one of these two BINOL moieties for a methanol the enantioselectivity of the rhodium-catalyzed hydrogenation turned out to be surprisingly high:



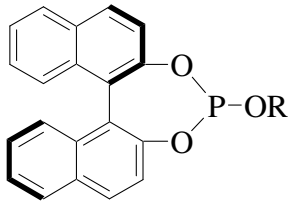


3.15

Rhodium-catalyzed hydrogenation of the starting material using ligand **3.15** containing a (*R*)-BINOL moiety resulted in the product with 95.2 % *ee* with the *R*-configuration. However, using ligand L containing a (*S*)-BINOL moiety resulted in the product with 97.8 % *ee* with the *S*-configuration. This shows that the sign of the product is predominantly determined by the sign of the BINOL moiety present in the ligand.

To elaborate on this finding a number of simple BINOL based monodentate phosphite ligands were synthesized. The use of these ligands in the rhodium-catalyzed hydrogenation revealed their excellent properties resulting in high *ee*'s in the products.[12c]

The group of Xiao reported monodentate phosphite ligands based on BINOL and L-menthol (**3.16**):[17]

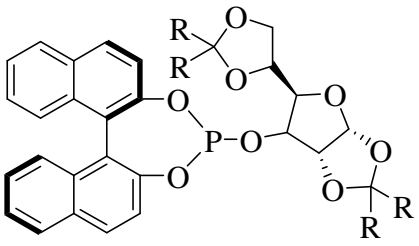


R = (*l*)-Menthyl

3.16

Rhodium-catalyzed hydrogenation with these L-menthol ligands also show, *vide supra*, that the sign of the product is predominantly determined by the sign of the BINOL moiety.

Monodentate phosphite ligands derived from carbohydrates (**3.17**) were also used in the rhodium-catalyzed hydrogenations.[18]

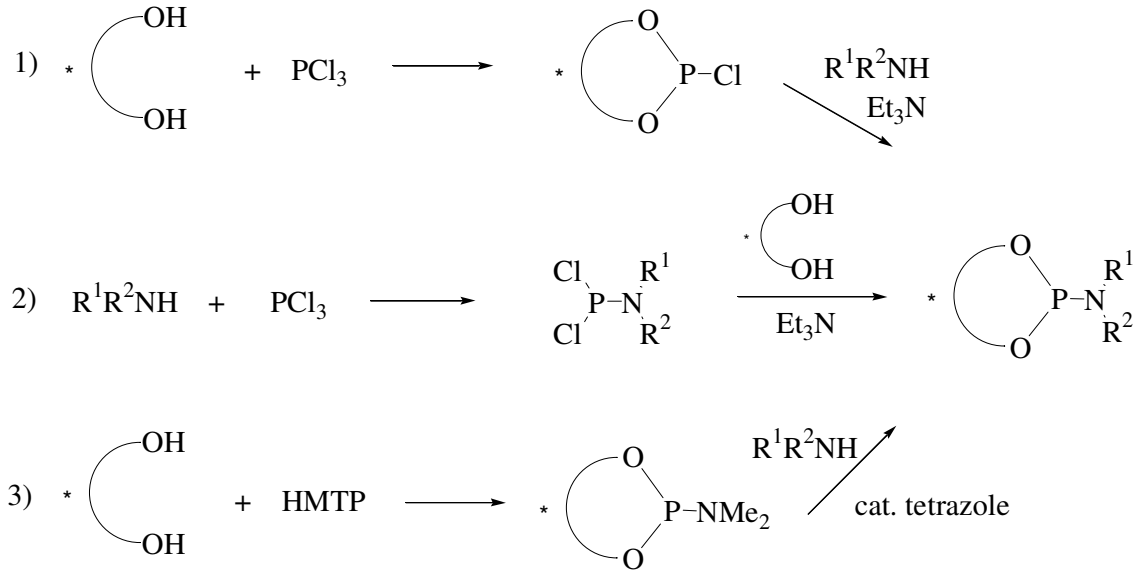


3.17

This group of ligands is based on the chiral synthons derived from the chiral pool. This could lead to the formation of a diverse group of inexpensive ligands which could be used in the hydrogenation of various functionalities.

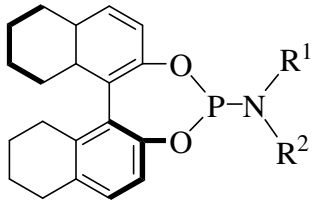
3.5. Monodentate phosphoramidites

There are several different approaches to synthesize the phosphoramidite ligands and they only require a minimum number of steps:



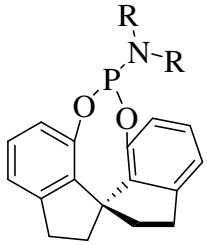
The most common route used is the first one. This is a suitable way of making relatively pure phosphoramidites from diols and amines. The second route is the method of choice for the preparation of phosphoramidites with hindered amines.[19] In the first step of the third route MonoPhos™ is prepared from BINOL and HMPT in toluene.[20] MonoPhos™, a ligand which can be used in the rhodium-catalyzed hydrogenation with excellent results, is a suitable starting material in the synthesis of other phosphoramidites. This reaction of MonoPhos™ with a primary or secondary amine in the presence of a catalytic amount of tetrazole is used to synthesize the more labile phosphoramidite ligands.

The majority of phosphoramidite ligands synthesized over the years were mainly constructed of BINOL and a diversity of readily available amines. However, other diols have also been used as building block in phosphoramidites. Both Feringa *et al.*[23,21] and Chan *et al.*[22] report phosphoramidite ligands based on octahydro-BINOL (H8-BINOL) **3.18**:



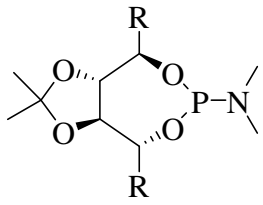
3.18

Zhou *et al.* and Zhang *et al.* reported the use of a spiro-diol moiety as the backbone in the ligands (**3.19**).[23]



3.19

Phosphoramidite ligands based on TADDOL[23] and on D-mannitol[24] have also been used (**3.20**):



3.20

However, the enantioselectivities reported for the hydrogenation of α-dehydroamino acids and itaconates were generally lower compared to the ligands based on BINOL. Furthermore, in order to synthesize these ligands usually lengthy routes are necessary.

Simultaneous with the advances in the field of asymmetric hydrogenations, catalytic asymmetric versions of conjugated additions, alkylations, reductions and epoxidations were developed and the majority of the ligands tested in the hydrogenation reaction were also tested in these transformations.

3.6. The monodentate ligand combination approach

An important breakthrough in the area of monodentate ligands was made independently by Reetz and co-workers[25] and Feringa and co-workers[26] who used a mixture of chiral monodentate P-ligands.[27]

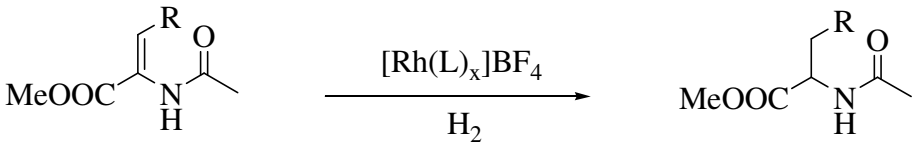
The method is relevant whenever in the transition state of the reaction at least two monodentate ligands (L) are coordinated to the metal (M) of the active catalyst ML_x. For example, in the case of a mixture of two such ligands L^a and L^b, three different catalysts exist in equilibrium with one another, namely the two homocombinations ML^aL^a and ML^bL^b as well as the heterocombination ML^aL^b:

$$ML^aL^a \rightleftharpoons ML^aL^b \rightleftharpoons ML^bL^b$$

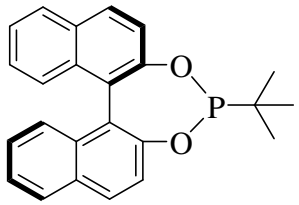
Many examples for homocombinations are known in literature and they have already been reported in the previous part of this chapter (for example, the BINOL-based modular monophosphonites, monophosphites, and monophosphoramidites, which often (but not always) lead to high enantioselectivities when used as ligands in Rh-catalyzed olefin hydrogenation).

In contrast, nothing at that time was reported about the use of heterocombinations ML^aL^b as catalysts. Since rapid ligand exchange is likely in most systems, the preparation of ML^aL^b in pure form in solution is not expected to be possible. However, the mixture of all three catalysts may well lead to enhanced enantioselectivity provided ML^aL^b is more active and more selective than either of the traditional catalysts ML^aL^a or ML^bL^b. Moreover, the relative amounts of the ligands L^a and L^b used may also influence the stereochemical outcome.

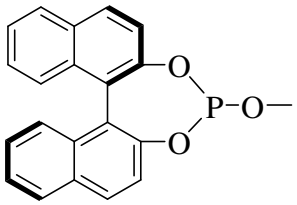
The group of Reetz studied the Rh-catalyzed hydrogenation of the acetamidoacrylate in dichloromethane as the test reaction:



It was noticed, for example, that using **3.21** and **3.22** in combination (ratio 1:1), a higher *ee* (98%) was obtained instead of using the corresponding homocombinations (*ee* = 93% with L^1 and *ee* = 76% with L^2).

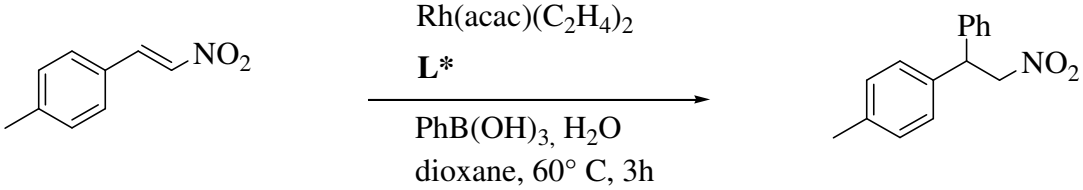


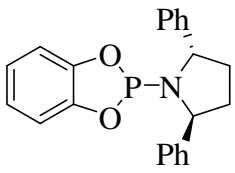
3.21



3.22

The group of Feringa and de Vries studied combinations of ligands in the asymmetric C-C bond formation. In more details they used as substrate 4-methyl-nitrostyrene in the enantioselective conjugate addition of boronic acids:





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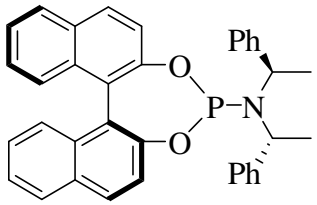
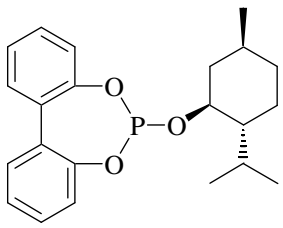


3.24

Even if the enantiomeric excesses were low, it is possible to underline that using ligands **3.23** and **3.24** in combinations, product was obtained with *ee* = 37% while with the homocombinations the values were lower (*ee* = 7% with L^3 and *ee* = 28% with L^4)

3.7. *Tropos* monodentate phosphites and phosphoramidites

Recently, a number of chiral *tropos* phosphorus ligands (see the scheme below), based on a flexible biphenol unit and a chiral P-bound alcohol (phosphites) or secondary amine (phosphoramidites), were synthesized by Gennari, Piarulli and co-workers, and used (individually or as a binary mixture) in the Rh-catalyzed asymmetric hydrogenation of functionalized olefins[28] and in the Rh-catalyzed conjugate addition of aryl boronic acids to enones and enoates:[29]



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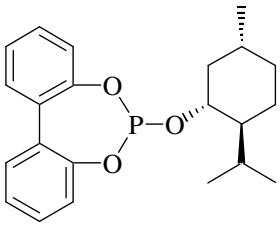

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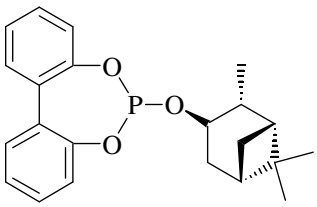

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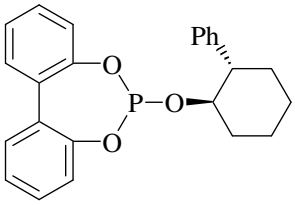

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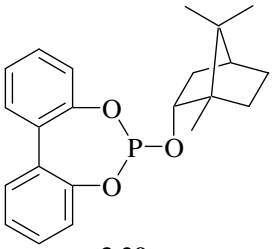

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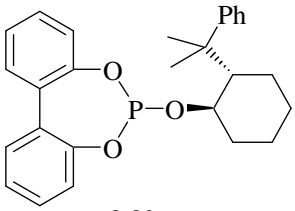

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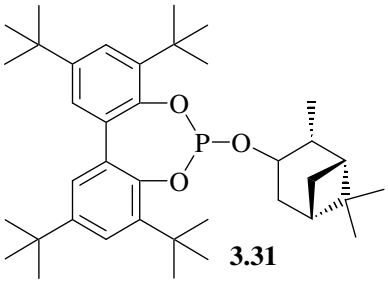

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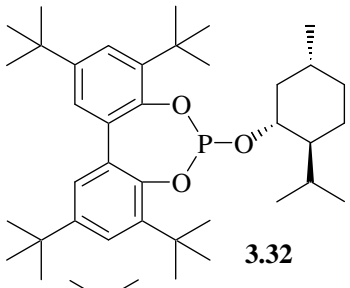

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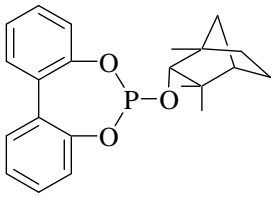

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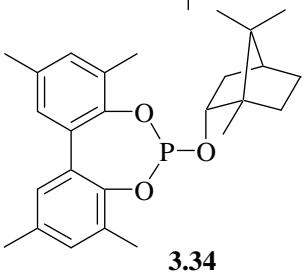

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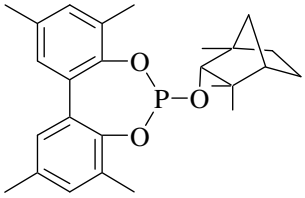

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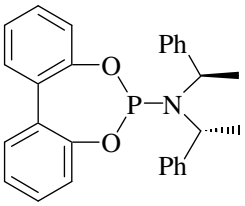

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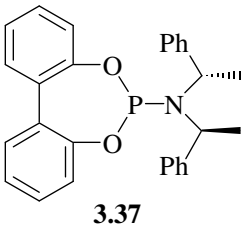

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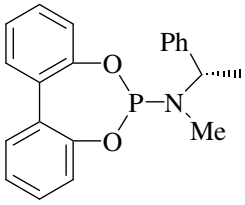

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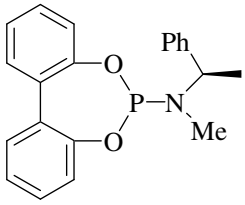

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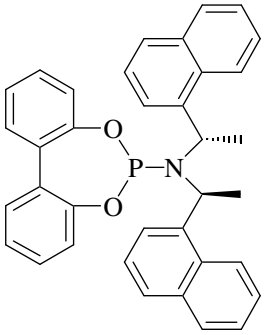

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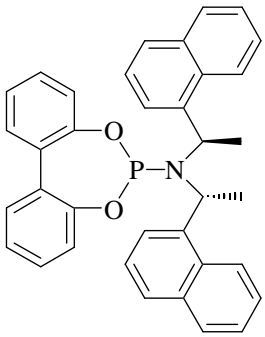

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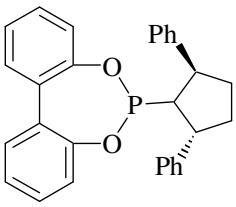

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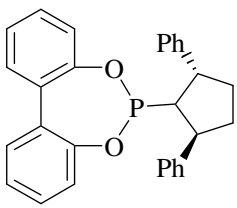
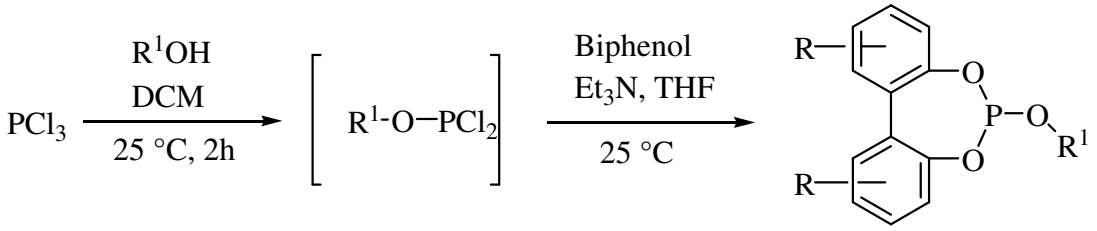
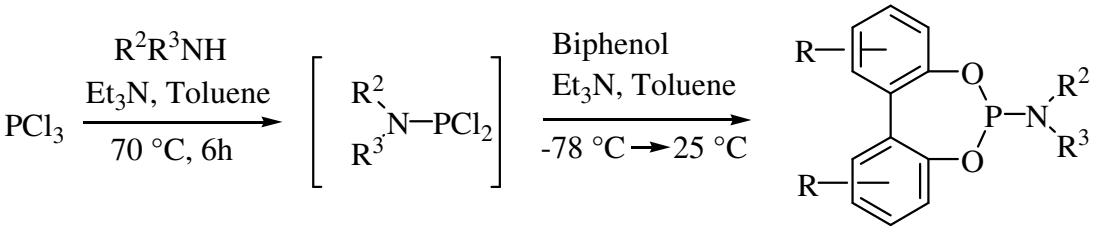


3.43

Biphenolic phosphites and phosphoramidites display several potential sites of diversity (R, R^1, R^2, R^3) and their preparation can be readily accomplished through a modular two-step synthesis.

For the synthesis (Scheme below) of phosphites [**3.25** – **3.35**], the alcohol was treated at room temperature with PCl_3 in dichloromethane, followed by the slow addition of a solution of biphenol in tetrahydrofuran. The reaction mixtures were purified by flash chromatography to give the phosphites as white foamy solids. Phosphoramidites [**3.36** – **3.43**] were synthesised by treatment of the appropriate chiral secondary amine with PCl_3 at 70°C in toluene and in the presence of triethylamine. After cooling to -78°C, a solution of biphenol in toluene was slowly added. The resulting mixtures were slowly warmed to room temperature and then purified by flash chromatography to give the phosphoramidites as white powders.

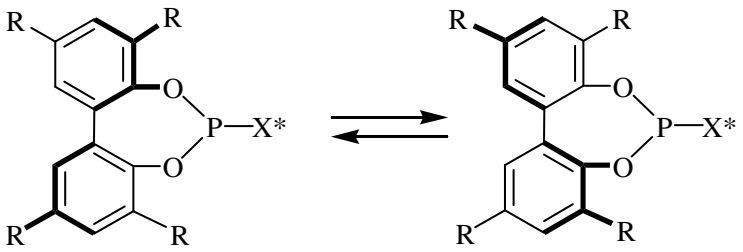




Several phosphites, namely: **3.26**, **3.27**, **3.29**, **3.31**, **3.32**, **3.33**, had previously been synthesized by Xiao and Chen.[30] However, their results were influenced by experimental problems associated with the purity of the ligands. This was not the case for the work reported by Gennari, Piarulli and co-workers where this class of compounds showed a single set of signals at room temperature by ^1H, ^{13}C and ^{31}P NMR, confirming their tropos nature. Only upon complexation with Rh, two sets of signals might possibly be observed at low temperature (-65 °C).[31] This contrasts sharply with the information contained in the Xiao and Chen paper, where the ligands were described

to display two singlets (^{31}P NMR) with the same intensity (1:1 ratio) at room temperature (without Rh).

These ligands exist, in principle, as a mixture of two rapidly interconverting diastereomers, L^a and $L^{a'}$, differing in the conformation of the biphenol unit:

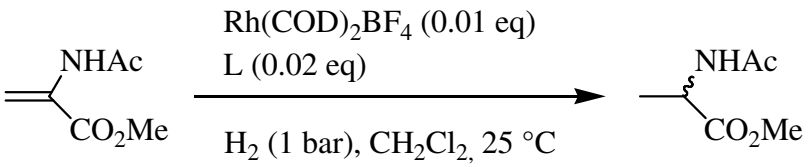


R = H, *t*Bu, Me

X* = secondary amine or alcohol, containing stereocenters

Upon complexation with Rh, the ligand (L^a in equilibrium with $L^{a'}$) should give rise to three different species, namely RhL^aL^a, $RhL^aL^{a'}$, $RhL^{a'}L^{a'}$. These three diastereomeric species, which might be interconverting, are generated in proportions which most likely differ from the statistical value (1:2:1). The novelty of this approach consisted in the use of a combination of two of these ligands (L^a in equilibrium with $L^{a'}$ and L^b in equilibrium with $L^{b'}$) resulting in the generation of a dynamic "*in situ*" library, with up to 10 different species theoretically present in solution: RhL^aL^a, $RhL^aL^{a'}$, $RhL^{a'}L^{a'}$, RhL^bL^b, $RhL^bL^{b'}$, $RhL^{b'}L^{b'}$, RhL^aL^b, $RhL^aL^{b'}$, $RhL^{a'}L^b$, $RhL^{a'}L^{b'}$.[32] Although each species could, in principle, be present and catalyse the reaction, one of them could overcome the others, determining the direction and the extent of the enantioselectivity.

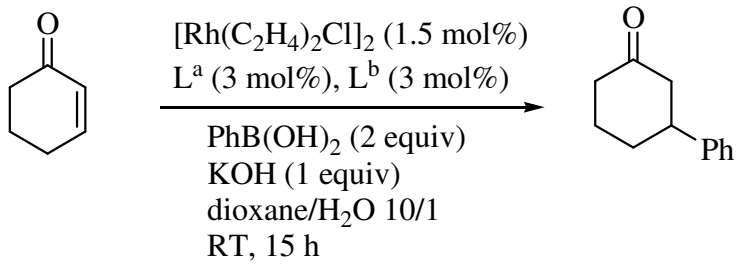
In the Rh-catalyzed asymmetric hydrogenation of functionalized olefins, methyl *N*-acetamidoacrylate was chosen as substrate:



The ligands were first screened individually (homocombinations): in general, the phosphites were much more reactive than the phosphoramidites, allowing for excellent yields (up to 100%) and moderate enantiomeric excesses [up to 55% with **3.29**].

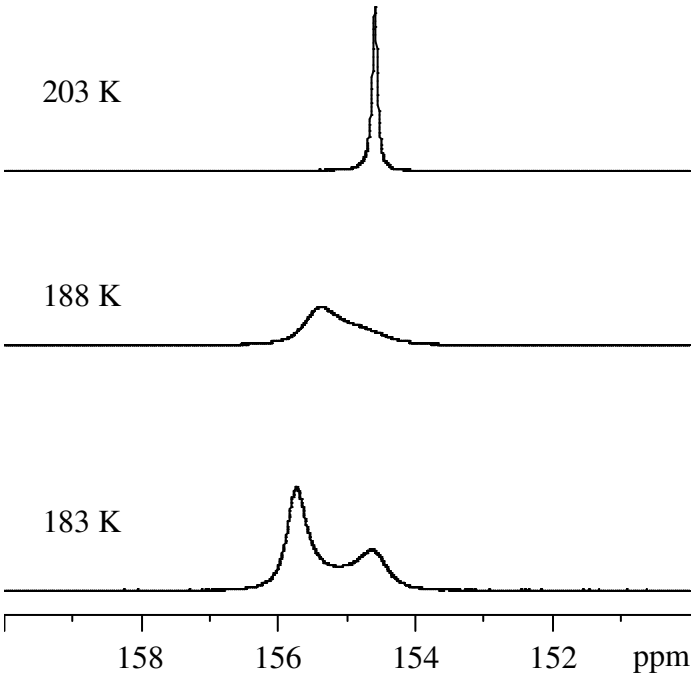
By mixing two phosphoramidite ligands, the hydrogenation product was generally obtained in moderate ee (lower than with the corresponding homocombinations), and poor conversion. The phosphite–phosphite combinations gave the product quantitatively, but with poor ee's. The phosphite–phosphoramidite combinations were the most productive, retaining the phosphite high reactivity (resulting in high conversions) and often improving the enantioselectivities compared to the homocombinations. The best combination **3.28 / 3.37** afforded the product in 87% *ee* (100% yield), while the corresponding mismatched combination [**3.28 / 3.36**] in 35% *ee* (100% yield). The amount of cooperation of these two ligands in the matched heterocombination is remarkable: the product ee is increased by some 34-35% compared to the corresponding homocombinations, which is a much more pronounced increment than those usually observed by Reetz and Feringa in their studies. Several other substrates were then tested, including other dehydroamino acid esters, dehydroamino acids, simple enamines and dimethyl itaconate. The ligand combination **3.28 / 3.37** proved highly efficient in the case of dehydroamino acid derivatives with *ee*'s of up to 98%, while in the case of enamines and dimethyl itaconate moderate enantioselectivities (up to 85% and 75% respectively) were obtained using different ligand homocombintions. Kinetic studies of the reactions with the single ligands and with the combination of phosphite [**3.28**] and phosphoramidite [**3.37**] were also performed, in the case of dehydroamino acid derivatives, by measuring the rate of hydrogen uptake. It was shown that the phosphite, despite being less enantioselective, promotes the hydrogenation of methyl *N*-acetamidoacrylate and methyl *N*-acetamidocinnamate faster than the mixture of the same phosphite with the phosphoramidite, while the phosphoramidite alone is much less active. In this way, the reaction was optimized by lowering the phosphite / phosphoramidite ratio (the best ratio is 0.25 equiv phosphite : 1.75 equiv phosphoramidite) with a resulting improvement of the product enantiomeric excess. A simple mathematical model for a better understanding of the variation of the enantiomeric excess with the phosphite / phosphoramidite ratio was also proposed.

The library of 11 biphenolic phosphites and 8 biphenolic phosphoramidites was also screened in the conjugate addition of phenylboronic acid to cyclic enones:



In general, when the chiral ligands were used individually (homocombinations) the phosphites gave catalysts more efficient and enantioselective than the phosphoramidites. However, the enantiomeric excesses were only moderate and the best *ee* was 70% with phosphite **3.31**. Mixtures of a phosphite and a phosphoramidite (heterocombinations) gave reduced yields and *ee*'s in comparison with the phosphite alone, in all combinations except those containing either phosphoramidite **3.42** or **3.43**. In these heterocombinations, considerably higher ee's and quantitative yields were obtained. In particular, (*R*)-3-phenylcyclohexanone was obtained in 95% *ee* (100% yield) with phosphoramidite **3.43** and phosphite **3.30** and in 91% *ee* (100% yield) with phosphoramidite **3.43** and phosphite **3.33**. In the latter case, the synergistic effect of the heterocombination with respect to the corresponding homocombinations is worth of an additional 55% *ee* [**3.33** 28% *ee*, **3.43** 36% *ee*]. The mismatched combinations gave (*S*)-3-phenylcyclohexanone in 70% *ee* (100% yield) with phosphoramidite **3.42** and phosphite **3.30**, and 87% *ee* (100% yield) with phosphoramidite **3.42** and phosphite **3.33**, showing that it is the phosphoramidite which determines the absolute configuration of the reaction product. Again, the synergistic effect of the heterocombination is remarkable.

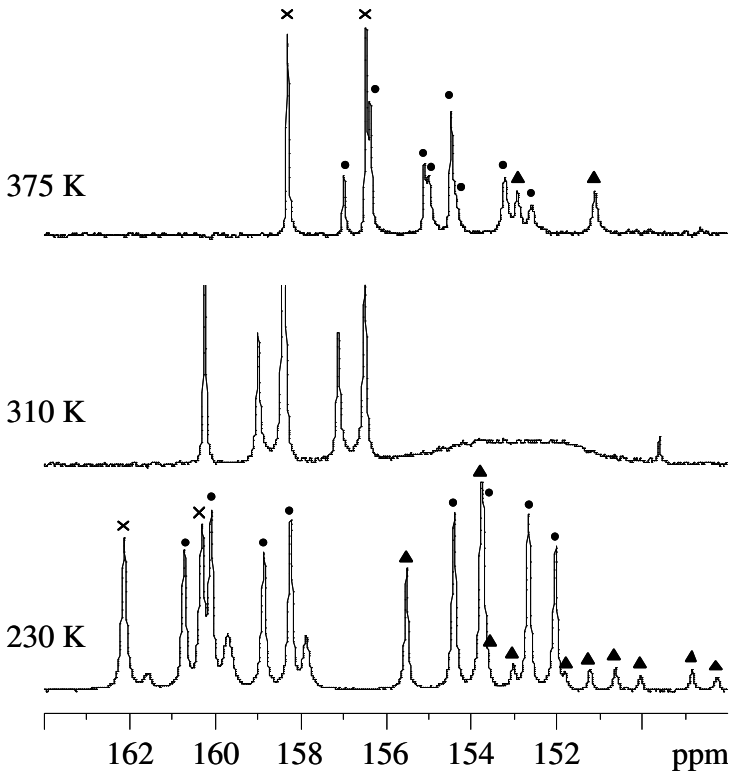
In this work[32] the *tropos*/*atropos* nature of the ligands in the rhodium complexes was also studied. Variable-temperature ^{31}P NMR studies revealed that the biphenolic phosphorus ligands are *tropos* even at low temperature (see below the variable-temperature ^{31}P-NMR spectra of ligand **3.28**. Only below 190 K was a coalescence observed; upon further cooling, two atropisomers were detected.



The composition and the dynamic behavior of the rhodium complexes containing either the single ligands (homocomplexes, $[Rh(L^a)(L^a)]^+$) or the combination of a phosphite and a phosphoramidite (heterocomplexes, $[Rh(L^a)(L^b)]^+$) were studied by variable-temperature ^{31}P NMR spectroscopy. In general, a doublet (P–Rh coupling) was observed in the case of phosphite ligands over the temperature range 380–230 K and using $[Rh(acac)(eth)_2]$ as the metal source; this demonstrates the *tropos* nature of the biphenolic phosphites in the $[L_2Rh(acac)]$ complexes even at low temperatures. The phosphoramidites showed different behaviors depending on the structure of the ligand and on the nature of the rhodium sources. In particular, two different doublets were detected by ^{31}P NMR in the homocomplexes of phosphoramidites **3.36** to **3.41** and $[Rh(acac)(eth)_2]$, which are possibly due to the presence of two species, a square-planar monomeric complex and a dinuclear complex containing bridging ligands. Homocomplexes of the same phosphoramidites **3.36** to **3.41** and either $[Rh(cod)_2][BF_4]$ or $[Rh(nbd)_2][BF_4]$ showed the presence of only one doublet and no coalescence over the 380–230 K temperature range.

Homocomplexes of phosphoramidites **3.42** and **3.43** with $[Rh(acac)(eth)_2]$ showed a single doublet at 375 K, a coalescence at 320 K, and the generation of a sharp doublet and two doublets of doublets at 230 K. This can be interpreted as the formation of three diastereomers (a*R*,a*R*; a*S*,a*S*; a*R*,a*S*) differing in the configuration at the two atropisomeric biphenols. In the most enantioselective ligand combination in the

conjugate addition reaction (that of phosphite **3.30** and phosphoramidite **3.43**, with [Rh(acac)(eth)$_2$] as the rhodium source, the biphenol-derived phosphite is free to rotate (*tropos*) while the biphenol-derived phosphoramidite shows a temperature-dependent *tropos*/*atropos* behavior (coalescence temperature=310 K). The spectrum at low temperature accounts for the presence of the signals due to four homocomplexes (total: approximately 40%) [Rh[**3.30**]$_2$], [Rh{(a*R*)-**3.43**}$_2$], [Rh{(a*S*)-**3.43**}$_2$], [Rh{(a*R*)-**3.43**}{(a*S*)-**3.43**}], and one heterocomplex [Rh{**3.30**}{(a*R*)-**3.43**}] (approximately 60%) [see in the figure below the variable-temperature ^{31}P-NMR spectra (toluene-d$_8$) of the rhodium complex resulting from the combination of ligands **3.30** and **3.43**, using Rh(acac)(eth)$_2$ as the rhodium source. At 375 K, Rh[**3.30**]$_2$ gives a doublet ×, Rh[**3.43**]$_2$ gives a doublet ▲ and Rh[**3.30**][**3.43**] gives two dd ●; at 230 K, Rh[**3.43**]$_2$ gives two dd▲ and a doublet ▲, Rh[**3.30**]$_2$ gives a doublet × and Rh[(a*R*)-**3.43**][**3.30**] gives two dd ●].

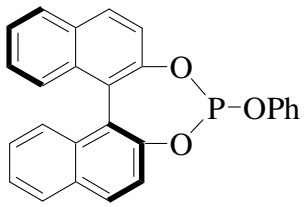


In the case of the combination of phosphite **3.30** and phosphoramidite **3.42** (the mismatched ligand combination in the conjugate addition reac reaction) with [Rh(acac)(eth)$_2$] as the rhodium source, the presence of six of the ten possible different precatalysts was detected at low temperature: the four homocomplexes (total:

approximately 28%), and two heterocomplexes (approximately 72%) [Rh[**3.30**}{(a*R*)-**3.42**}] and [Rh{**3.30**}{(a*S*)-**3.42**}] in a relative ratio 85:15 or 15:85.

From the experimental results of the Rh-catalyzed conjugate addition reactions and from the ^{31}P NMR studies of the Rh precatalysts, it is evident that: 1) the synergistic effect (resulting in notable ee enhancements) of the phosphite **3.30**/phosphoramidite **3.43** ligand heterocombination is remarkable; and 2) the flexible biphenolic P ligands outperform the analogous rigid binaphtholic P ligands. These represent emblematic cases of catalyst self-adaptation and tuning, where the heterocomplexes perform better than the homocomplexes, and the conformationally mobile systems perform better than the rigid ones.

On the basis of the results obtained with this chiral *tropos* phosphorus ligands in the Rh-catalyzed asymmetric hydrogenation of functionalized olefins and in the Rh-catalyzed conjugate addition of aryl boronic acids to enones and enoates, we decided to test them and some other ligands derived from BINOL (see below) in the enantioselective rhodium-catalysed addition of arylboronic acids to aldehydes and imines. The results abtained are presented in next chapters.



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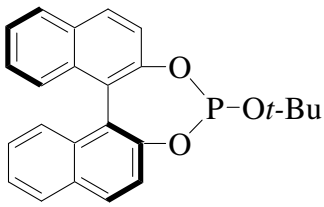

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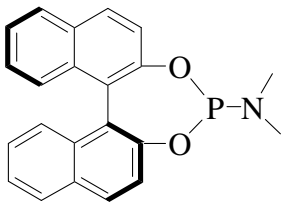

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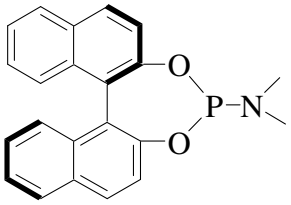

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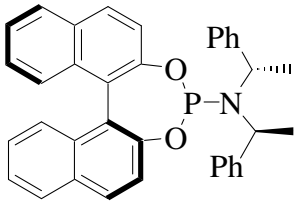
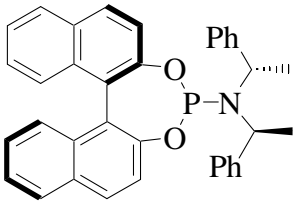
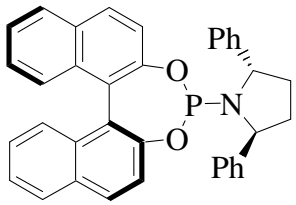


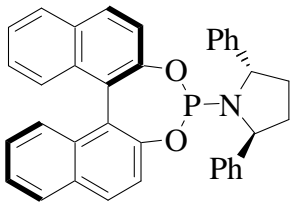
3.48



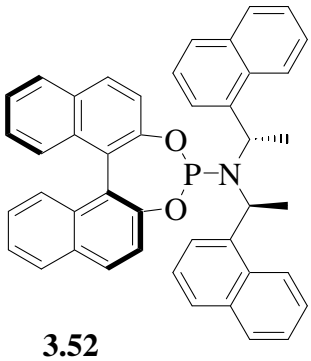
3.49



3.50

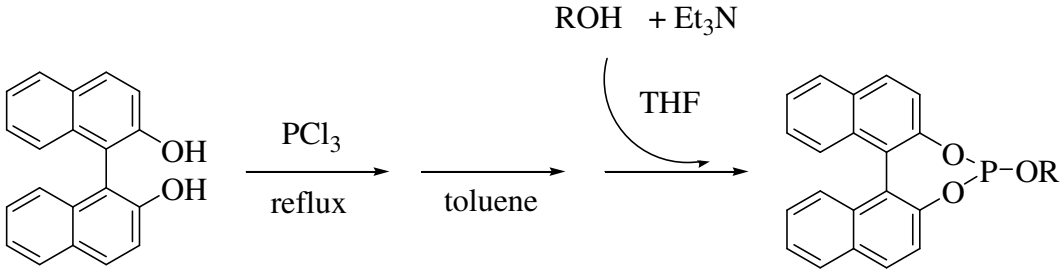


3.51



3.52

For the synthesis of phosphites [**3.44 – 3.45**], 1,1'-Bi(2-naphthol) was treated with PCl_3 at reflux, excess of PCl_3 was removed in vacuum, the foamy solid was dissolved in toluene and then alcohol and triethylamine (solution in tetrahydrofuran) were added at room temperature. The reaction mixtures were purified by flash chromatography to give the phosphites as white foamy solids.



Phosphoramidites [**3.46 – 3.52**] were synthesised following literature procedures (see experimental section)

3.8. Experimental section

General procedure for the synthesis of biphenolic phosphites

PCl_3 (2 eq, 6 mmol, 525 µl) was added to a solution of the alcohol (1 eq, 3 mmol) in dichloromethane (17 ml), in a Schlenk tube, under argon, at room temperature. After stirring for 2 hours, the solvent and excess PCl_3 were removed under reduced pressure. The resulting residue was dissolved in tetrahydrofuran (7 ml), and a solution of the biphenol (1 eq, 3 mmol) and triethylamine (3 eq, 9 mmol, 1.25 ml) in THF (10 ml) was slowly added. Upon addition, the formation of a white precipitate was immediately observed. The reaction mixture was stirred overnight, before filtering over a PTFE

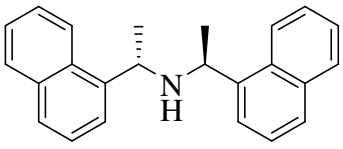
membrane filter. The solvent was removed under reduced pressure and the crude product was purified either by crystallisation, or by chromatography, to give the desired compound as a white foamy solid.

General procedure for the synthesis of biphenolic phosphoramidites

A solution of the amine (1 eq, 3 mmol) and triethylamine (1.13 eq, 3.4 mmol, 472.5 µl) in dry toluene (2.6 ml) was added to a solution of PCl_3 (1 eq, 3 mmol, 262 µl) in toluene (38 ml), in a Schlenk tube, under argon. The reaction mixture was heated to 70°C for 6 hours, and allowed to cool to room temperature. Triethylamine (2.26 eq, 6.78 mmol, 945 µl) was added, and the mixture was cooled to –78°C. A solution of 1,1'-biphenol (1 eq, 3 mmol) in a mixture toluene : THF = 4 : 1 (7.5 ml) was slowly added. The reaction mixture was left under stirring overnight, allowing to slowly warm to room temperature. The mixture was filtered over a pad of celite, and the solvent removed under reduced pressure. The crude product was purified either by crystallisation, or by chromatography, to give the desired compound as a white powder.

Bis-[(*S*)-1-naphth-1-yl-ethyl]amine and bis-[(*R*)-1-naphth-1-yl-ethyl]amine,[32] (*R*,*R*)-1,2-diphenylpyrrolidine and (*S*,*S*)-1,2-diphenylpyrrolidine were prepared following literature procedures which have been reported here.[33]
3,3',5,5'-tetramethyl-biphenol[34] and 3,3',5,5'-*tert*-butyl-biphenol[35] were prepared following the reported procedures.

Bis-(1-naphthalen-1-yl-ethyl)-amine



A mixture of 1-acetonaphthone (1 eq, 6.2 mmol, 940µL), (*R*)-(+)-alpha-(1-Naphthyl)ethylamine (1 eq, 6.2 mmol, 1 mL) and titanium(IV) isopropoxide (3 eq, 18.6 mmol, 5.5 mL) was stirred at room temperature for 1 h. The mixture was then washed with KOH 1 M, until TiO_2 was completely precipitated, and extracted with AcOEt. The

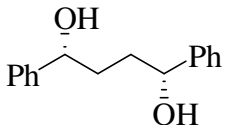
organic phase was washed again with KOH 1 M, dried over Na_2SO_4, and concentrated in vacuo.

The mixture was then hydrogenated in methanol (7 mL) at 1 atm with 10% palladium-on-charcoal (0.5 mol%) under vigorous stirring at room temperature. The reaction course was monitored by TLC. At complete conversion, the reaction was filtered over Celite, the solvent was evaporated and the crude was purified by flash chromatography (CH_2Cl_2/diysopropylether = 10/0.5) affording the product as a pale yellow oil (357 mg, 20% yield).

^{1}HNMR (400 MHz, $CDCl_3$): 7.93-7.85 (m, 8H), 7.62 (t, 2H, *J* = 7.8 Hz), 7.47 (t, 2H, *J*= 7.3 Hz), 7.28 (t, 2H, *J* = 7.3 Hz), 4.63 (q, 2H, *J* = 6.6 Hz), 2.02 (brs, 1H), 1.57 (d, 6H *J* = 6.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): 142.1, 134.1, 131.7, 128.9, 127.3, 125.9, 125.6, 125.4, 123.3, 122.9, 51.4, 24.7. $[\alpha]_D$ = +34.4 (*c* 0.80, $CHCl_3$). MS (EI mode) *m/z* (%) : 325 (13), 310 (18), 170 (16), 155 (100). HRMS (ES) calculated for $C_{24}H_{24}N$ ($[M+H]^+$) 326.1909, found 326.1902.

1,2-diphenylpyrrolidine

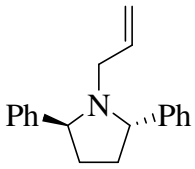
(1*R*,4*R*)-1,4-Diphenylbutan-1,4-diol



To a stirred solution of α,α-diphenyl-2-pyrrolidine methanol (0.17 eq, 0.36 mmol, 91 mg) in THF (3 mL) at room temperature, trimethyl borate ($B(OMe)_3$) (0.21 eq, 0.44 mmol, 50 μL) was added and stirred for an hour. Borane-dimethyl sulphide complex (2.12 eq, 4.45 mmol, 420 μL) was then added, and a solution of the diketone 1,2-dibenzoylethane (1 eq, 2.10 mmol, 500 mg) in THF (8 mL) (warm water bath) was added over an hour by means of a cannula. After a further hour, the resulting mixture was slowly quenched with 2N HCl. The aqueous layer was extracted with r ether before the combined organic extracts were washed with H_2O and brine, dried over Na_2SO_4 and concentrated in vacuo. The resulting oil (white solid in the fridge) was used without any further purification (508 mg, 95% yield), IR (thin film): ν_{max} = 3339, 3025, 1207, 990; ^{1}H-NMR (300 MHz)): δ = 7.3-7.1 (m, 10H, Ph), 4.58 (br s, 2H, C**H**OH), 3.0 (br s, 2H,

O**H**), 1.84-1.6 (4H, m, C**H**$_2$); ^{13}C-NMR (75 MHz): δ = 144.6, 128.1, 127.0, 125.6, 74.3, 35.1; $[\alpha]_D$ = 58.0 (c 1.02, $CHCl_3$); m/z (EI); 242 (M+), 224, 118 (100%), 107, 79.

(2*S*,5*S*)-N-Allyl-2,5-diphenylpyrrolidine

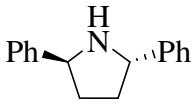


To a solution of methanesulfonyl chloride (2.6 eq, 5.40 mmol, 420 μL) in DCM (20 mL) at -20 °C was added a solution of (1*R*,4*R*)- 1,4-Diphenylbutan-1,4-diol (1 eq, 2.10 mmol, 508 mg) and triethylamine (3 eq, 6.30 mmol, 880 μL) in DCM (21 mL) by means of a canula. The mixture was stirred for 2 h and then quenched with satd NH_4Cl. The mixture was warmed to room temperature and solvent reduced in vacuo to approximately 17 mL. The solution was then diluted with AcOEt (80 mL) and washed with water (4 × 20 mL), brine (6 × 20 mL) and satd $NaHCO_3$ (6 × 20 mL), before being dried over Na_2SO_4, filtered through Celite and concentrated in vacuo to approximately 8 mL. The solution was the cooled to 0 °C, set to stir and the crude dimesylate was precipitated out by dropwise addition of hexane (80 mL). The resulting solid, almost unstable, was used directly in the next step.

Allyl amine (196 eq, 270 mmol, 20 mL) was added to a cooled flask (0 °C) containing the dimesylate and the resultant solution was stirred at this temperature overnight. After warming to room temperature, the excess of allyl amine was removed in vacuo, and the residue dissolved in ether and washed with satd $NaHCO_3$ (2 × 40 mL) and brine (40 mL), dried over Na_2SO_4, and concentrated in vacuo to afford the crude product as a yellow oil. Flash chromatography (Hexane/Et_2O = 98/2) yielded the pure product (293 mg, 55% yield). IR (thin film): ν_{max} = 3070, 2967, 2817, 1640, 1071, 916; ^{1}H-NMR (300 MHz): δ = 7.41-7.20 (m, 10H, Ph), 5.7-5.55 (m, 1H, C**H**=CH_2), 4.92-4.87 (m, 2H, CH=C**H**$_2$), 4.32-4.30 (m, 2H, C**H**Ph), 2.95-2.68 (m, 2H, NC**H**$_2$), 2.60-2.45 (br m, 2H, 3,4-C**H**), 2.01-1.90 (br m, 2H, 3,4-C**H**'); ^{13}C-NMR (75 MHz): δ = 144.6, 137.2, 128.5, 128.2, 127.1, 115.9, 65.9, 50.2, 33.5; $[\alpha]_D$ = -115 (c 0.56, $CHCl_3$); $C_{19}H_{21}N$ calcd: C

86.65; H 8.04; N 5.32; found: C 86.38; H 7.93; N 5.57; m/z (EI); 263 (M+, 30%), 262, 186 (100%), 91.

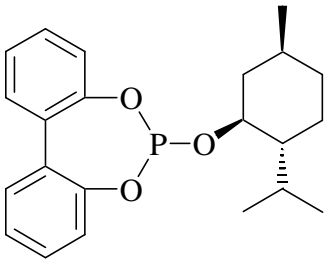
(2*S*,5*S*)-2,5-Diphenylpyrrolidine



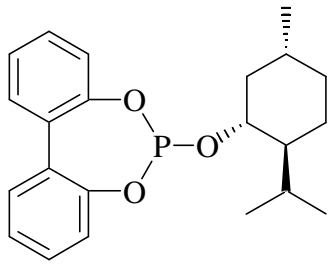
In a flask flushed with nitrogen, (*S,S*)-N-Allyl-*trans*-2,5-diphenylpyrrolidine (1 eq, 1.11 mmol, 293 mg) and $(Ph_3P)_3RhCl$ (0.5% mol) (Wilkinson's catalyst) were dissolved in 2.8 mL of 84:16 w/w acetonitrile:water mixture previously degased. The mixture was heated to 85 °C and stirred at this temperature for 5 h. The reaction was then cooled to room temperature and diluted with ether . The layers were separated and the organic layer washed with brine (2 × 2 mL), and the combined aqueous washes were back extracted with ether (3 mL). The combined organic extracts were dried over Na_2SO_4, and concentrated in vacuo. The resulting yellow oil was purified by flash chromatography (Hexane/AcOEt = 8/2) to yield the desired amine as a yellow oil, which solidified upon standing overnight (203 mg, 81% yield), m.p. = 43 °C. IR (thin film): ν_{max} = 3360, 3055, 2962, 2867, 1598, 1489, 1450, 1402; ^{1}H-NMR (200 MHz): δ = 7.5-7.1 (m, 10H, Ar), 4.5 (t, 2H, PhC**H**N), 2.4-2.3 (m, 2H, 3,4-C**H**), 2.3 (br, 1H, N**H**), 1.9-1.8 (m, 2H, 3,4-C**H**'). ^{13}C-NMR (75 MHz): δ = 145.7, 128.2, 126.5, 126.1, 62.1, 35.3; $[\alpha]_D$ = -108.2 (c 0.45, $CHCl_3$); $C_{16}H_{17}N$ calcd: C 86.05; H 7.67; N 6.27; found: C 86.23; H 7.63; N 6.17; m/z (EI); 223 (M+, 31%), 222, 195 (100%).

3.25, **Biphenol / (1*S*, 2*R*, 5*S*)-(+)-menthol**: 97% yield; $[\alpha]_D$ = + 17.4 (c 1.00, $CHCl_3$)

3.26, Biphenol / (1*R*, 2*S*, 5*R*)-(-)-menthol: 88% yield; $[\alpha]_D$ = - 17.4 (c 1.00, $CHCl_3$)



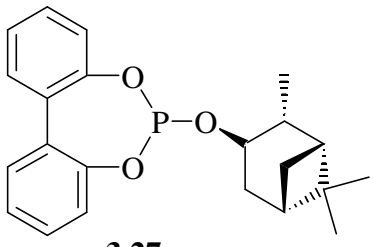
3.25



3.26

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 7.6 Hz, 2H, Ar**H**), 7.37 (t, *J* = 7.6 Hz, 2H, Ar**H**), 7.30 (t, *J* = 7.5 Hz, 2H, Ar**H**), 7.22-7.20 (m, 2H, Ar**H**), 4.20-4.16 (m, 1H, C**H**), 2.32-2.27 (m, 1H, C**H**), 2.25-2.18 (m, 1H, C**H**), 1.73-1.69 (m, 2H, C**H**), 1.51-1.35 (m, 2H, C**H**), 1.08-1.04 (m, 3H, C**H**), 0.99 (d, *J* = 6.5 Hz, 3H, C**H**$_3$), 0.96 (d, *J* = 7.0 Hz, 3H, C**H**$_3$), 0.88 (d, *J* = 6.9 Hz, 3H, C**H**$_3$); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 156.0, 149.8, 131.8, 130.3, 129.4, 128.1, 125.4, 122.5, 120.3, 118.5, 76.7 (d, $J_{C,P}$ = 17.4 Hz), 48.9, 44.6, 34.5, 32.2, 25.7, 23.3, 22.5, 21.4, 16.0; ^{31}P-NMR (162 MHz, $CDCl_3$): δ = 152.8; m.p. = 98°C; IR (CCl_4): ν_{max} = 3068, 3030, 2958, 2871, 1943, 1910, 1600, 1570, 1556, 1545, 1499, 1476, 1438, 1386, 1370, 1271, 1249, 1210, 1187, 1097, 1013, 992, 900 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{22}H_{27}NaO_3P]^+$: 393.1595 $[M+Na]^+$; found: 393.1579; $C_{22}H_{27}O_3P$ calcd. C 71.33, H 7.35; found: C 71.23, H 7.32.

3.27, **Biphenol / (1*R*, 2*R*, 3*R*, 5*S*)-(-)-isopinocampheol**: 76% yield

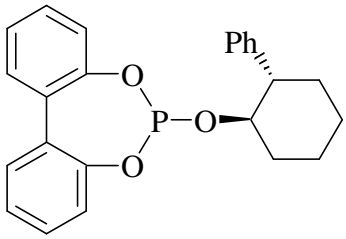


3.27

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 7.6 Hz, 2H, Ar**H**), 7.38 (t, *J* = 7.6 Hz, 2H, Ar**H**), 7.29 (t, *J* = 7.6 Hz, 2H, Ar**H**), 7.21 (t, *J* = 7.6 Hz, 2H, Ar**H**), 4.77-4.69 (m, 1H, C**H**), 2.59-2.52 (m, 1H, C**H**), 2.41-2.36 (m, 1H, C**H**), 2.27-2.23 (m, 1H, C**H**), 2.10-2.03

(m, 1H, C**H**), 1.99-1.97 (m, 1H, C**H**), 1.87-1.84 (m, 1H, C**H**), 1.25 (s, 3H, C$\mathbf{H}_3$), 1.20 (d, J = 7.2 Hz, 3H, C$\mathbf{H}_3$), 1.15 (d, J = 10 Hz, 1H, C**H**), 0.91 (s, 3H, C$\mathbf{H}_3$); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 150.0, 130.4, 129.4, 125.4, 122.6, 122.4, 76.1 (d, $J_{C,P}$ = 15 Hz), 48.2, 46.1, 42.0, 38.8, 38.2, 34.4, 28.0, 24.3, 20.4; ^{31}P-NMR (162 MHz, $CDCl_3$): δ = 147.7; m.p. = 106°C; IR (CCl_4): ν_{max} = 3069, 3029, 2959, 2910, 2872, 1943, 1911, 1601, 1567, 1553, 1499, 1476, 1437, 1386, 1370, 1260, 1249, 1210, 1187, 1097, 996, 942, 897, 857 cm^{-1}; $[\alpha]_D$ = - 17.0 (c 1.00, $CHCl_3$); HRMS (ESI) *m/z* calcd for $[C_{22}H_{27}NaO_4P]^+$: 409.1545 $[M+Na+H_2O]^+$; found: 409.1538; $C_{22}H_{25}O_3P$ calcd. C 71.72, H 6.84; found: C 71.80, H 6.86.

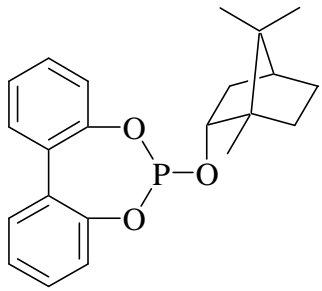
3.28, Biphenol / (1R,2S)-(-)-*trans*-2-phenyl-1-cyclohexanol: 63% yield



3.28

^{1}H-NMR (400 MHz, C_6D_6): δ = 7.46-6.90 (m, 12H, Ar**H**), 6.50-6.40 (m, 1H, Ar**H**), 4.50-4.38 (m, 1H, Cy**H**), 2.80-2.65 (m, 1H, Cy**H**), 2.35-2.20 (m, 1H, Cy**H**), 2.10-1.20 (m, 7H, Cy**H**); ^{13}C-NMR (100 MHz, C_6D_6): δ = 149.9, 143.9, 130.4, 130.1, 129.5, 129.4, 129.1, 129.0, 128.4, 127.3, 125.5, 125.4, 122.8, 122.7, 79.3 (d, $J_{C,P}$ = 17 Hz), 52.2, 36.0, 34.5, 26.3, 25.7; ^{31}P-NMR (162 MHz, $CDCl_3$): δ = 151.5; m.p. = 117°C; IR (CCl_4): ν_{max} = 3066, 3031, 2961, 2936, 2859, 1942, 1911, 1604, 1556, 1498, 1476, 1437, 1260, 1250, 1210, 1187, 1097, 1025, 901, 855, 831 cm^{-1}; $[\alpha]_D$ = - 53.6 (c 1.00, $CHCl_3$); HRMS (ESI) *m/z* calcd for $[C_{24}H_{25}NaO_4P]^+$: 431.1388 $[M+Na+H_2O]^+$; found: 431.1370; $C_{24}H_{23}O_3P$ calcd. C 73.83, H 5.94; found: C 71.15, H 6.16.

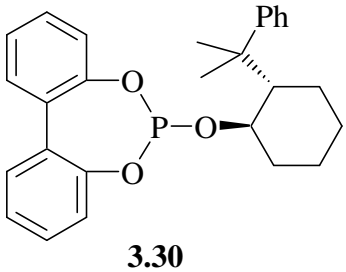
3.29, **Biphenol / (-)-borneol**: 82% yield



3.29

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 7.6 Hz, 2H, Ar**H**), 7.40-7.36 (m, 2H, Ar**H**), 7.30-7.26 (m, 2H, Ar**H**), 7.20 (d, *J* = 8.0 Hz, 2H, Ar**H**), 4.62-4.56 (m, 1H, C**H**), 2.26-2.18 (m, 1H, C**H**), 2.06-2.00 (m, 1H, C**H**), 1.87-1.62 (m, 2H, C**H**), 1.32-1.24 (m, 3H, C**H**), 0.94 (s, 3H, C**H**$_3$), 0.88 (s, 3H, C**H**$_3$), 0.77 (s, 3H, C**H**$_3$); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 150.2, 131.6, 131.5, 130.3, 129.4, 129.3, 125.3, 122.5, 81.5, 50.2, 48.1, 45.4, 38.4, 28.5, 26.9, 20.4, 19.0, 13.8; ^{31}P-NMR (162 MHz, $CDCl_3$): δ = 145.4; m.p. = 88°C; IR (CCl_4): ν_{max} = 3069, 3030, 2961, 2881, 2453, 1943, 1601, 1499, 1476, 1438, 1264, 1210, 1188, 1097, 891, 858 cm^{-1}; $[\alpha]_D$ = - 5.5 (c 1.00, $CHCl_3$); HRMS (ESI) *m/z* calcd for $[C_{22}H_{25}NaO_3P]^+$: 391.1439 $[M+Na]^+$; found: 391.1427; $C_{22}H_{25}O_3P$ calcd. C 71.72, H 6.84; found: C 71.78, H 6.87.

3.30, **Biphenol / (1R,2S)-(-)-*trans*-(1-methyl-1-phenylethyl)cyclohexanol**: 79% yield

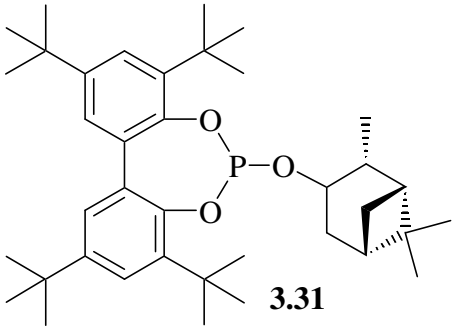


3.30

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.58-7.10 (m, 13H, Ar**H**), 4.32-4.24 (m, 1H, C**H**), 2.28-2.24 (m, 1H, C**H**), 1.99-1.92 (m, 1H, C**H**), 1.76-1.56 (m, 3H, C**H**), 1.50 (s, 3H, C**H**$_3$), 1.46 (s, 3H, C**H**$_3$), 1.38-1.19 (m, 1H, C**H**); 1.19-0.88 (m, 3H, C**H**); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 150.3, 149.6, 131.4, 129.9, 129.4, 129.0, 127.9, 126.0, 125.3, 124.9, 124.8, 122.2, 122.0, 121.0, 117.0, 77.5 (d, $J_{C,P}$ = 16 Hz), 52.6, 40.8, 36.8, 30.4,

27.6, 25.6, 24.8, 24.6; ^{31}P-NMR (162 MHz, $CDCl_3$): δ = 153.4; m.p. = 128°C; IR (CCl_4): ν_{max} = 3065, 3031, 2935, 2859, 1943, 1553, 1499, 1476, 1437, 1260, 1210, 1187, 1098, 1016, 900, 847, 830 cm^{-1}; $[\alpha]_D$ = - 12.6 (c 1.00, $CHCl_3$); HRMS (ESI) *m/z* calcd for $[C_{27}H_{29}NaO_3P]^+$: 455.1752 $[M+Na]^+$; found: 455.1743; $C_{27}H_{29}O_3P$ calcd. C 74.98, H 6.76; found: C 72.39, H 6.90.

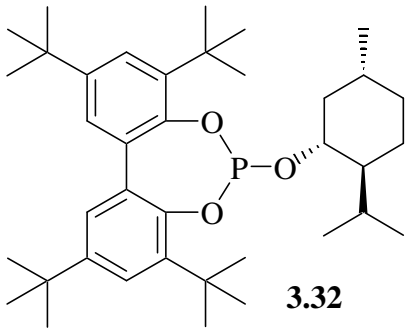
3.31, **3,3',5,5'-*tert*-butyl-biphenol / (1*R*, 2*R*, 3*R*, 5*S*)-(-)-isopinocampheol**: 87% yield



3.31

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.53-7.51 (m, 1H, Ar**H**), 7.45-7.43 (m, 1H, Ar**H**), 7.28-7.26 (m, 1H, Ar**H**), 7.19-7.17 (m, 1H, Ar**H**), 4.75-4.57 (m, 1H, C**H**), 2.59-2.52 (m, 1H, C**H**), 2.41-2.36 (m, 1H, C**H**), 2.27-2.23 (m, 1H, C**H**), 2.10-1.94 (m, 2H, C**H**), 1.87-1.84 (m, 1H, C**H**), 1.50 (s, 18H, *t*Bu), 1.45 (s, 3H, C**H**$_3$), 1.36 (s, 18H, *t*Bu), 1.20 (d, *J* = 7.2 Hz, 3H, C**H**$_3$), 1.06 (d, *J* = 10 Hz, 1H, C**H**), 0.89 (s, 3H, C**H**$_3$); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 127.0, 126.9, 125.4, 124.5, 76.7, 48.2, 46.0, 45.7, 42.0, 38.2, 33.9, 31.9, 31.8, 31.6, 27.9, 24.3, 20.5; ^{31}P-NMR (162 MHz, $CDCl_3$): δ = 146.7; m.p. = 75°C; IR (CCl_4): ν_{max} = 2963, 2907, 2871, 2448, 1945, 1595, 1556, 1545, 1475, 1440, 1397, 1363, 1260, 1229, 1094, 1018, 937, 879 cm^{-1}; $[\alpha]_D$ = + 5.3 (c 1.00, $CHCl_3$); HRMS (ESI) *m/z* calcd for $[C_{38}H_{57}NaO_3P]^+$: 615.3943 $[M+Na]^+$; found: 615.3935; $C_{38}H_{57}O_3P$ calcd. C 76.99, H 9.69; found: C 77.02, H 9.71.

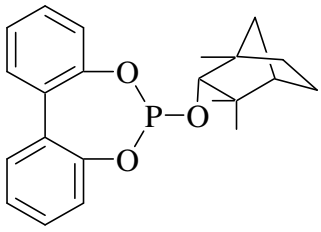
3.32, **3,3',5,5'-*tert*-butyl-biphenol / (1*R*, 2*S*, 5*R*)-(-)-menthol**: 84% yield



3.32

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.44 (s, 1H, Ar**H**), 7.43 (s, 1H, Ar**H**), 7.19 (s, 1H, Ar**H**), 7.18 (s, 1H, Ar**H**), 4.11-4.06 (m, 1H, C**H**), 2.25-2.15 (m, 1H, C**H**), 2.10-1.80 (m, 2H, C**H**), 1.70-1.55 (m, 2H, C**H**), 1.50 (s, 18H, 2 x *t*Bu), 1.50-0.60 (m, 4H, C**H**), 1.36 (s, 18H, 2 x *t*Bu), 0.87-0.84 (m, 6H, 2 x C**H**$_3$), 0.73 (d, *J* = 6.9 Hz, 3H, C**H**$_3$); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 150.0, 131.7, 130.3, 129.4, 125.4, 122.5, 79.1, 76.7, 76.6, 58.3, 48.9, 44.5, 34.5, 32.2, 25.7, 23.3, 22.5, 21.4, 16.0; ^{31}P-NMR (162 MHz, $CDCl_3$): δ = 147.0; m.p. = 140°C; IR (CCl_4): ν_{max} = 2962, 2870, 1595, 1558, 1547, 1456, 1413, 1396, 1362, 1093, 1017 cm^{-1}; $[\alpha]_D$ = - 17.3 (c 1.00, $CHCl_3$); HRMS (ESI) *m/z* calcd for $[C_{38}H_{59}NaO_3P]^+$: 617.4099 $[M+Na]^+$; found: 617.4093; $C_{38}H_{59}O_3P$ calcd. C 76.73, H 10.00; found: C 76.69, H 9.97.

3.33, **Biphenol / (1*R*)-endo-(+)-fenchol**: 78% yield

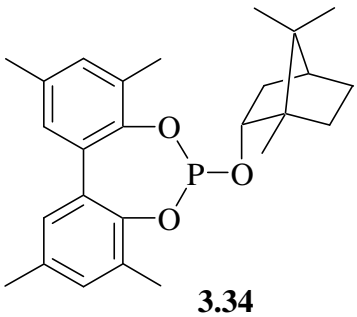


3.33

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.50 (d, *J* = 7.6 Hz, 2H, Ar**H**), 7.44-7.21 (m, 6H, Ar**H**), 3.96 (d, *J* = 11.6 Hz, 1H, C**H**), 1.85-1.67 (m, 4H, C**H**), 1.58-1.40 (m, 3H, C**H**), 1.24 (s, 3H, C**H**$_3$), 1.04 (s, 3H, C**H**$_3$), 0.96 (s, 3H, C**H**$_3$); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 130.5, 129.6, 125.6, 125.5, 122.9, 89.2 (d, $J_{C,P}$ = 12.0 Hz), 50.1, 48.8, 41.8, 40.4, 30.6, 26.7, 26.5, 22.2, 20.2; ^{31}P-NMR (162 MHz, $CDCl_3$): δ = 148.6; m.p. = 104°C; IR

(CCl_4): ν_{max} = 3069, 3030, 2962, 2873, 1944, 1911, 1602, 1569, 1556, 1499, 1476, 1437, 1260, 1210, 1187, 1098, 1015, 904, 857 cm^{-1}; $[\alpha]_D$ = + 9.8 (c 1.00, $CHCl_3$); HRMS (ESI) *m/z* calcd for $[C_{22}H_{25}NaO_3P]^+$: 391.1439 $[M+Na]^+$; found: 391.1423; $C_{22}H_{25}O_3P$ calcd. C 71.72, H 6.84; found: C 69.42, H 7.07.

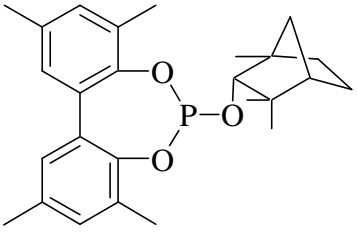
3.34, 3,3',5,5'-tetramethyl-biphenol / (-)-borneol: 76% yield



3.34

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.13 (s, 2H, Ar**H**), 7.08 (s, 2H, Ar**H**), 4.65-4.60 (m, 1H, C**H**), 2.40 (s, 12H, 4 x C**H**$_3$), 2.27-2.20 (m, 1H, C**H**), 2.07-2.00 (m, 1H, C**H**), 1.76-1.67 (m, 2H, C**H**), 1.33-1.23 (m, 3H, C**H**), 0.96 (s, 3H, C**H**$_3$), 0.91 (s, 3H, C**H**$_3$), 0.86 (s, 3H, C**H**$_3$); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 134.2, 131.6, 130.6, 128.6, 81.8 (d, $J_{C,P}$ = 12.0 Hz), 50.5, 48.4, 45.7, 38.5, 28.9, 27.3, 21.6, 20.8, 19.4, 17.5, 14.1; ^{31}P-NMR (162 MHz, $CDCl_3$): δ = 145.7; m.p. = 81°C; IR (CCl_4): ν_{max} = 2957, 2880, 1557, 1478, 1260, 1245, 1214, 1188, 1154, 1119, 1030, 866, 830 cm^{-1}; $[\alpha]_D$ = + 2.5 (c 1.01, $CHCl_3$); HRMS (ESI) *m/z* calcd for $[C_{26}H_{35}NaO_4P]^+$: 465.2171 $[M+Na+H_2O]^+$; found: 465.2141; $C_{26}H_{33}O_3P$ calcd. C 73.56, H 7.84; found: C 72.15, H 8.06.

3.35, 3,3',5,5'-tetramethyl-biphenol / (1*R*)-endo-(+)-fenchol: 78% yield

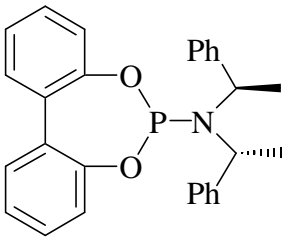


3.35

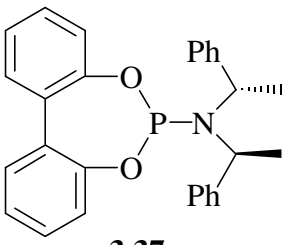
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.13 (d, *J* = 7.2 Hz, 2H, Ar**H**), 7.08 (s, 2H, Ar**H**), 3.94 (dd, J_1 = 12.0, J_2 = 1.6 Hz, 1H, C**H**), 2.41 (s, 6H, 2 x C**H**$_3$), 2.40 (s, 6H, 2 x C**H**$_3$), 1.84-1.69 (m, 4H, C**H**), 1.59-1.43 (m, 3H, C**H**), 1.21 (s, 3H, C**H**$_3$), 1.09 (s, 3H, C**H**$_3$), 0.90 (s, 3H, C**H**$_3$); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 146.9, 146.4, 134.3, 132.0, 131.7, 131.5, 130.7, 128.6, 88.8 (d, $J_{C,P}$ = 15.0 Hz), 50.0, 48.7, 41.9, 40.4, 30.8, 26.9, 26.4, 22.4, 21.6, 20.1, 17.7, 17.5; ^{31}P-NMR (162 MHz, $CDCl_3$): δ = 149.7; m.p. = 91°C; IR (CCl_4) ν_{max} 2962, 2872, 1945, 1557, 1478, 1260, 1214, 1187, 1154, 1098, 1012, 871, 831 cm^{-1}; $[\alpha]_D$ = - 27.5 (c 1.01, $CHCl_3$); HRMS (ESI) *m/z* calcd for $[C_{26}H_{35}NaO_4P]^+$: 465.2171 $[M+Na+H_2O]^+$; found: 465.2153; $C_{26}H_{33}O_3P$ calcd. C 73.56, H 7.84; found: C 72.39, H 7.98.

3.36, **Biphenol / [*R*(*R**,*R**)]-bis(α-methylbenzyl)amine**: 89% yield; $[\alpha]_D$ = + 238.0 (c 1.00, $CHCl_3$)

3.37, **Biphenol / [*S*(*R**,*R**)]-bis(α-methylbenzyl)amine**: 80% yield; $[\alpha]_D$ = - 238.0 (c 1.00, $CHCl_3$)



3.36

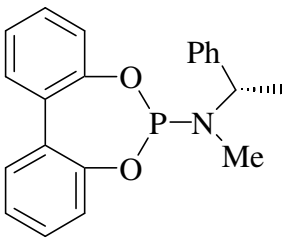


3.37

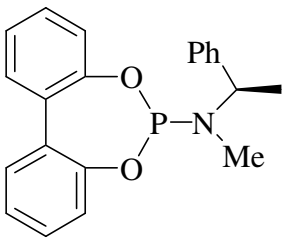
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.49-7.56 (m, 2H, Ar**H**), 7.22-7.41 (m, 6H, Ar**H**), 7.11-7.20 (m, 10H, Ar**H**), 4.58-4.66 (m, 2H, 2 x **H**-benzyl), 1.77 (d, *J* = 7.2 Hz, 6H, 2 x C**H**$_3$-benzyl); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 151.5, 143.4, 131.6, 130.4, 130.2, 129.5, 129.4, 128.3, 128.2, 127.0, 125.0, 124.4, 122.9, 122.4, 53.1, 53.0, 22.7; ^{31}P-NMR (162 MHz, $CDCl_3$): δ = 147.6; m.p. = 105°C; IR (CCl_4): ν_{max} = 3065, 3030, 2963, 2905, 1943, 1911, 1602, 1546, 1497, 1476, 1436, 1375, 1261, 1211, 1194, 1098, 1015, 889, 830 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{28}H_{26}NNaO_2P]^+$: 462.1599 $[M+Na]^+$; found: 462.1574; $C_{28}H_{26}NO_2P$ calcd. C 76.52, H 5.96, N 3.19; found: C 76.60, H 5.97, N 3.21.

3.38, **Biphenol / (*S*)-(-)-*N*,α-dimethylbenzylamine**: 55% yield; $[\alpha]_D$ = + 23.0 (c 1.00, $CHCl_3$)

3.39, **Biphenol / (*R*)-(+)-*N*,α-dimethylbenzylamine**: 40% yield; $[\alpha]_D$ = - 23.0 (c 1.00, $CHCl_3$)



3.38

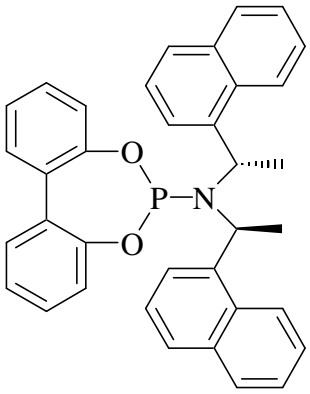


3.39

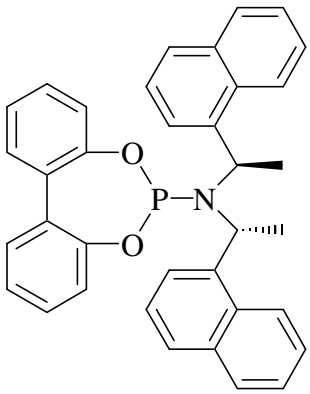
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.54-7.09 (m, 13H, Ar**H**), 4.92-4.84 (m, 1H, C**H**), 2.23 (d, *J* = 4.8 Hz, 3H, C**H**$_3$), 1.69 (d, *J* = 7.2 Hz, 3H, C**H**$_3$); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 152.3, 142.7, 131.6, 130.3, 129.8, 129.0, 128.0, 127.7, 125.1, 125.0, 122.6, 56.3, 55.9, 27.7, 19.2; ^{31}P-NMR (162 MHz, $CDCl_3$): δ = 149.6; m.p. = 109°C; IR (CCl_4): ν_{max} = 3067, 3030, 2963, 2905, 1603, 1564, 1556, 1498, 1476, 1436, 1260, 1208, 1194, 1098, 1013, 934 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{21}H_{20}NNaO_2P]^+$: 372.1129 $[M+Na]^+$; found: 372.1112; $C_{21}H_{20}NO_2P$ calcd. C 72.20, H 5.77, N 4.01; found: C 72.31, H 5.79, N 3.98.

3.40, Biphenol / bis-[(*S*)-1-naphth-1-yl-ethyl]amine: 60% yield; $[\alpha]_D$ = + 204.8 (c 0.53, $CHCl_3$)

3.41, Biphenol / bis-[(*R*)-1-naphth-1-yl-ethyl]amine: 71% yield; $[\alpha]_D$ = - 204.8 (c 0.53, $CHCl_3$)



3.40

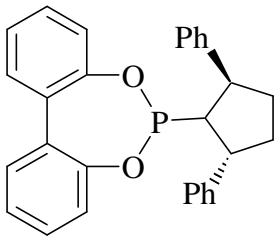


3.41

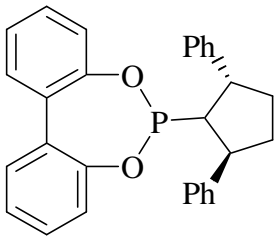
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.62-7.22 (m, 18H, Ar**H**), 6.86 (t, *J* = 7.6 Hz, 2H, Ar**H**), 5.61-5.53 (m, 2H, 2 x C**H**), 1.83 (d, *J* = 7.2 Hz, 6H, 2 x C**H**$_3$); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 139.1, 133.8, 131.5, 130.9, 130.8, 129.9, 129.8, 129.0, 127.6, 125.9, 125.5, 125.3, 125.2, 124.7, 123.9, 123.1, 123.0, 51.5, 51.4, 23.7, 23.6; ^{31}P-NMR (162 MHz, $CDCl_3$): δ = 150.1; m.p. not determined due to decomposition; IR (CCl_4): ν_{max} = 3053, 2964, 2905, 2876, 1943, 1912, 1600, 1566, 1499, 1476, 1435, 1396, 1373, 1262, 1212, 1194, 1175, 1142, 1098, 1016, 960, 891, 850 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{36}H_{30}NNaO_2P]^+$: 562.1912 $[M+Na]^+$; found: 562.1910; $C_{36}H_{30}NO_2P$ calcd. C 80.13, H 5.60, N 2.60; found: C 80.15, H 5.63, N 2.59.

3.42, **Biphenol / (*R*,*R*)-2,5-diphenylpyrrolidine**: 67% yield; $[\alpha]_D$ = + 111.4 (c 1.03, $CHCl_3$)

3.43, **Biphenol / (*S*,*S*)-2,5-diphenylpyrrolidine**: 73% yield; $[\alpha]_D$ = - 111.4 (c 1.03, $CHCl_3$)



3.42

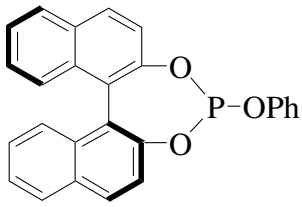


3.43

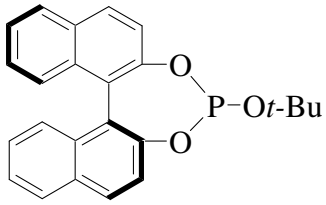
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.50-6.96 (m, 18H, Ar**H**), 5.10 (d, *J* = 5.6 Hz, 2H, C**H**), 2.51-2.38 (m, 2H, C**H**), 1.89-1.78 (m, 2H, C**H**); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 144.1, 130.4, 129.9, 129.6, 129.2, 128.9, 127.5, 125.0, 124.4, 122.7, 122.2, 63.4, 63.1, 34.3, 33.0; ^{31}P-NMR (162 MHz, $CDCl_3$): δ = 149.2. ; m.p. = 101°C; IR (CCl_4): ν_{max} = 3065, 3029, 2963, 2904, 1943, 1603, 1546, 1497, 1476, 1436, 1261, 1211, 1097, 1019, 829 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{28}H_{24}NNaO_2P]^+$: 460.1442 $[M+Na]^+$; found: 460.1431; $C_{28}H_{24}NO_2P$ calcd. C 76.87, H 5.53, N 3.20; found: C 76.70, H 6.00, N 3.21.

3.44, 4-Phenoxy-3,5-dioxa-4-phospha-cyclohepta[2,1-a;3,4-a']dinaphthalene[36]

3.45, 4-tert-Butoxy-3,5-dioxa-4-phospha-cyclohepta[2,1-a;3,4-a']dinaphthalene



3.44

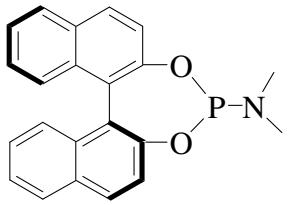


3.45

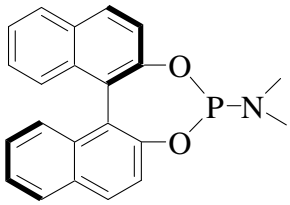
In a flask flushed with nitrogen, (-)-(*S*)-1,1'-Bi(2-naphthol) (1 eq, 1.05 mmol, 300 mg) was dissolved in PCl_3 and the mixture was heated to reflux for 8 hours. Excess of PCl_3 was removed by distillation. The residual oil was subjected to azeotropic distillation with dry toluene (3 times) and dried under vacuum until a white solid was formed. This solid was dissolved in 2 mL of dry toluene and a solution of alcohol (1 eq, 1.05 mmol) and Et_3N (2 eq, 2.1 mmol, 290 μL) in THF (3 mL) was added by means of a canula. The resulting suspension was stirred under nitrogen overnight. The solid was filtered over a PTFE membrane, solvent was evaporated and the resulting oil was washed with hexane affording a white solid (201 mg, 78%); ^{1}H-NMR ($CDCl_3$): δ = 8.12–7.87 (m, 5H), 7.55–7.28 (m, 12H); ^{31}P NMR ($CDCl_3$): δ = 145.88.

3.46, (*S*)-MONOPHOS[37]

3.47, (*R*)-MONOPHOS



3.46



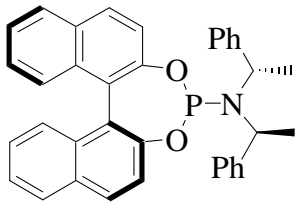
3.47

1,1'-Bi(2-naphthol) (1 eq, 1.4 mmol, 400 mg), hexamethylphosphorustriamide (HMTP) (1.27 eq, 1.77, 322 μL) and NH_4Cl (2.7%) were dissolved in dry toluene (2.5 mL) and the resulting mixture was heated to reflux for 12 h. The reaction was then cooled to room temperature and solvent removed in vacuum affording a pale yellow oil. Dry

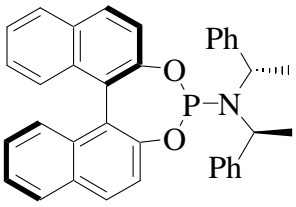
diethylether was added and the mixture was stirred overnight forming a white precipitate. The solid was filtered and washed with diethylether. The white powder was finally recristallized from dry diethylether giving the pure product (401 mg, 88%); mp 190–191°C; ^{1}H-NMR ($CDCl_3$): δ = 7.37–7.92 (m, 12H), 2.53 (d, $^{4}J_{P-H}$ = 9.32 Hz, 6H); ^{31}P NMR ($CDCl_3$): δ = 148.72; $[\alpha]_D$ = -565.1 (c 0.5, $CHCl_3$).

3.48 *O-O'*-(*S*)-(1,1'-dinaphthyl-2,2'-diyl)-N,N'-di-(*S*,*S*)-1-phenylethylphosphoramidite (*S*,*S*,*S*)[38]

3.49, *O-O'*-(*R*)-(1,1'-dinaphthyl-2,2'-diyl)-N,N'-di-(*S*,*S*)-1-phenylethylphosphoramidite (*R*,*S*,*S*)



3.48



3.49

In a flask flushed with nitrogen PCl_3 (1 eq, 1.75 mmol, 153 μL) was dissolved in dry toluene (25 mL). A solution of Bis(1-phenylethyl)amine (1 eq, 1.75 mmol, 400 μL) and triethylamine (1.13 eq, 1.98 mmol, 276 μL) in toluene (15 mL) was added by the mean of a canula. The mixture was heated to 70 °C and stirred for 6 h. The system was allowed to cool to room temperature, triethylamine (2.26 eq, 3.97 mmol, 555 μL) was added and then the solution was cooled to -78 °C. A solution of (±)-BINOL (1 eq, 1.75 mmol, 500 mg) in toluene/THF (6 mL, 4/1) was added via canula. The mixture was allowed to warm to room temperature during the night.

The reaction was filtered through celite, solvent evaporated and the crude purified by flash chromatography (Hexane/CH_2Cl_2 = 7/3), obtaining the two diastereomers .

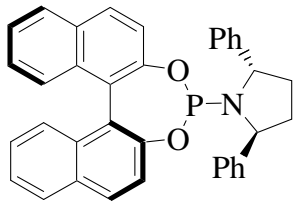
O-O'-(*S*)-(1,1'-dinaphthyl-2,2'-diyl)-N,N'-di-(*S*,*S*)- 1-phenylethylphosphoramidite (*S*,*S*,*S*) 53% yield; ^{1}H NMR ($CDCl_3$): δ = 8.08-7.78 (m, 4H), 7.65-7.24 (m, 18H), 4.47 (q, *J* = 7.2 Hz, 2H), 1.75 (d, *J* = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ = 150.45, 150.20, 149.80, 143.13, 132.77, 131.38, 130.47, 129.60, 129.25, 128.33, 128.06, 127.99,

127.79, 127.26, 126.71, 126.05, 125.87, 24.80, 124.36, 122.54, 54.55, 54.34, 23.07, 22.83; ^{31}P NMR ($CDCl_3$): δ = 150.4. $[\alpha]_D$ = 202.1 (c 0.79, $CHCl_3$); HRMS calcd for $C_{36}H_{30}NO_2P$: 539.201, found 539.208.

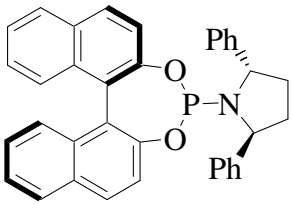
O-O'-(*R*)-(1,1'-dinaphthyl-2,2'-diyl)-N,N'-di-(*S*,*S*)-1-phenylethylphosphoramidite (*R*,*S*,*S*) 15% yield; ^{1}H-NMR ($CDCl_3$): δ = 7.95 (m, 4H), 7.61 (d, *J* = 4.8 Hz, 1H), 7.42 (m, 4H), 7.20 (m, 3H), 7.11 (m, 10H), 4.51 (m, 2H), 1.85 (d, *J* = 7.2 Hz, 6H); ^{13}C-NMR ($CDCl_3$): δ = 149.9, 149.5, 142.7, 132.7, 131.3, 130.4, 130.2, 129.4, 129.1, 128.2, 128.0, 127.9, 127.8, 127.7, 127.1, 127.0, 126.6, 125.9, 124.7, 124.4, 124.0, 122.3, 121.7, 52.3, 52.1, 21.9; ^{31}P-NMR ($CDCl_3$): δ = 144.7; $[\alpha]_D$ = 490.5 (c 0.79, $CHCl_3$); HRMS calcd for $C_{36}H_{30}NO_2P$: 539.201, found 539.208.

3.50, *O-O*'-(*S*)-(1,1'-dinaphthyl-2,2'-diyl)-4-((*S*,*S*)-2,5-diphenylpyrrolidine)-(*R*)-dinaphthodioxaphosphephine (*S*,*S*,*S*)[39]

3.51, *O-O*'-(*R*)-(1,1'-dinaphthyl-2,2'-diyl)-4-((*S*,*S*)-2,5-diphenylpyrrolidine)-(*R*)-dinaphthodioxaphosphephine (*R*,*S*,*S*)



3.50



3.51

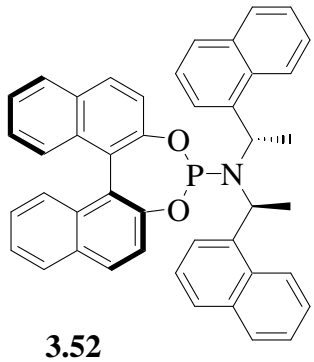
In a flask flushed with nitrogen, (2*S*,5*S*)-2,5-Diphenylpyrrolidine (1 eq, 0.2 mmol, 45 mg) was dissolved in THF (2 mL). The system was cooled to -78 °C and BuLi (1.12 eq, 0.23 mmol, 140 μL) was added dropwise, the yellow solution became brown. After an hour and a half stirring, PCl_3 (10 eq, 2.2 mmol, 176 μL) was suddenly added. The solution became red.

The mixture was warmed to room temperature and stirred for 2 h. The solvent was evaporated in vacuum affording a yellow oil. Toluene (2 mL) was added and the system was cooled to 0 °C. A solution of (*S*)-BINOL (1 eq, 0.2 mmol, 58 mg) and triethylamine

(5 eq, 1.1 mmol, 140 μL) in toluene (2 mL) was slowly added by the mean of a canula and the reaction was let to warm to room temperature and stirred overnight.

The mixture was filtered over Celite and the solvent evaporated. The resulting product was purified by flash chromatography (Hexane/AcOEt = 9/1) to yield the desired ligand as a white solid (65 mg, 60% yield), ^{1}H-NMR ($CDCl_3$): δ = 7.9-7.1 (m, 22H), 5.1-5.0 (m, 2H), 2.4-2.3 (m, 2H), 1.7-1.6 (m, 2H); ^{13}C-NMR ($CDCl_3$): δ = 144.6, 144.5, 132.8, 131.1, 130.6, 129.9, 128.1, 127.1, 126.8, 126.0, 125.8, 124.5, 121.9, 121.4, 63.4, 63.2, 34.2; $[\alpha]_D$ = -556.2 (c 1.0, $CHCl_3$); HRMS observed mass = 537.1906 (calculated mass = 537.1858)

3.52, O,O'-(*S*)-1,1'-dinaphthyl-2,2'-diyl)-N,N'-di-(*S*,*S*)-(1naphthalen-1-yl)-ethylphosphoramidite[40]



3.52

(*R*)-bis-β-naphthol (1 eq, 0.24 mmol, 79 mg) were dissolved in 0.8 mL of PCl_3 and heated at reflux for 6 h. Excess of PCl_3 was removed by distillation. The residual solid was subjected to an azeotropic distillation with toluene (2 mL) and dried under vacuum until a white foam was obtain. This solid was dissolved in 1 mL of toluene. In a second flask flushed with nitrogen, 1-naphthyl-amine (1 eq, 0.24 mmol, 90 mg) was dissolved in THF (1.5 mL) and the solution cooled to -78 °C. n-BuLi (190 μL) was added dropwise and the red mixture was warmed to 0 °C and stirred at this temperature for half an hour. The red solution at 0 °C was added dropwise to BINOL-PCl in toluene at – 78°C by the mean of a canula, then warmed to room temperature and stirred overnight. The day after, solvent was evaporated, 1 mL of toluene was added, LiCl precipitated, and the solution was filtered under nitrogen, toluene evaporated obtaining a yellow oil which was washed with hexane, affording a yellow solid. The crude was purified through a bit of silica, obtaining a pale yellow solid; yield : 13 %. ^{1}H NMR

(300 MHz, $CDCl_3$) : 8.10 (d, 1H, *J* = 8.9 Hz), 8.01 (d, 1H, *J* = 8.2 Hz), 7.79-7.09 (m, 24H), 5.54 (quint, 2H, *J* = 7.1 Hz), 1.77 (d, 6H, *J* = 7.1 Hz). ^{13}CNMR (75 MHz, $CDCl_3$): 151.0, 149.6, 139.2, 139.1, 133.3, 133.1, 132.8, 131.5, 130.8, 130.5, 130.3, 129.7, 128.5, 128.4, 128.2, 127.2, 127.1, 126.1, 125.9, 125.5, 125.0, 124.9, 124.6, 124.5, 124.3, 123.1, 122.4, 122.1, 121.6, 53.1, 53.0, 23.4, 23.2. ^{31}P NMR (122 MHz, $CDCl_3$) : 154.7. $[\alpha]_D$ = +235.7 (*c* 0.79, $CHCl_3$).

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