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Phosphole-based ligands in catalysis

Kévin Fourmy[a,b], Duc Hahn Nguyen[a,b], Odile Dechy-Cabaret[a,b] and Maryse Gouygou[a,b*§].

[a] CNRS, LCC (Laboratoire de Chimie de Coordination), 205 route de Narbonne, BP 44099, F-31077 Toulouse Cedex 4, France; Tel: +33 534 32 35 74;

[b] Université de Toulouse, UPS, INPT, F-31077 Toulouse Cedex 4, France

* Corresponding authors: maryse.gouygou@lcc-toulouse.fr

§ dedicated to Dr. Denis Neibecker

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1. Introduction

Trivalent phosphorus compounds play a dominant role in homogeneous catalysis as ligands for transition metals through the significant progress they have helped to accomplish in terms of catalytic activities and selectivities. The advantage of soft phosphorus ligands relative to other ligands commonly used (amines, alcohols or carboxylic acids) is their special ligating properties to form stable complexes with soft metals that are catalytically active in a number of chemical transformations.[1] The ability of phosphorus ligands to act as organocatalysts was also recognized.[2]

Steric and electronic modification of the phosphorus substituents along with the structural variability of P(III) compounds enable the fine-tuning of the chemo-, regio-, and (in appropriate cases) enantio-selectivities of homogeneous catalytic reactions. Thus a wide variety of trivalent P-ligands including chiral ligands has been developed; mono-, bi- and poly-dentate ligands (even with other ligating groups).[3]

The importance of phosphorus (III) donor ligands has also contributed in both the synthesis of new phosphorus compounds and in their increasing role in homogeneous catalysis. Among them, P-heterocyclic ligands[4] have achieved impressive maturity; in particular phospholes and their derivatives.[5]

The chemistry surrounding phospholes has been developed over more than 50 years. While the first phospholes were described in the 1950s, the synthetic routes combining high yields and diversity of substitution patterns were only established in the late 1960s. The application of phospholes in homogeneous catalysis had already appeared in the early 1970s when the dibenzophospholyl moiety and various chiral skeletons of natural origin were merged resulting in ligands that showed excellent performance in asymmetric catalysis.

Phospholes exhibit a very rich chemistry due to their easy accessibility, substitution pattern variability and versatile reactivity.[6] While intensive studies have been devoted to the elucidation of their electronic structure, these heteroles are now widely used as: i) monodentate P-ligands; ii) building blocks for the design of various bi- or poly-dentate P-ligands; iii) precursors for other P-heterocycles; iv) subunits to tailor of π-conjugated systems giving recognized applications in molecular materials[7], medicine[8] and catalysis.

Initially introduced in catalytic hydroformyaltion reactions, phosphole-based catalysts were and are still being exploited in many metallo-catalyzed reactions (asymmetric or non

asymmetric reactions). More recently, the ability of phosphole compounds to act as organocatalysts was also recognized.

The present contribution intends to highlight the potential of different phosphole-based ligand families in catalysis (metal- and organo-catalyzed reactions included) and offers an overview of their applications from its discovery to the present day. This review presents a full scope of the phosphole-based ligand: monophospholes (A), multidentate hybrid phosphole ligands (B), diphosphole (C) and 2,2'-biphosphole (D) based ligands (Figure 1). Each ligand class is accompanied by its detailed and reliable synthetic procedures followed by their applications in catalysis.

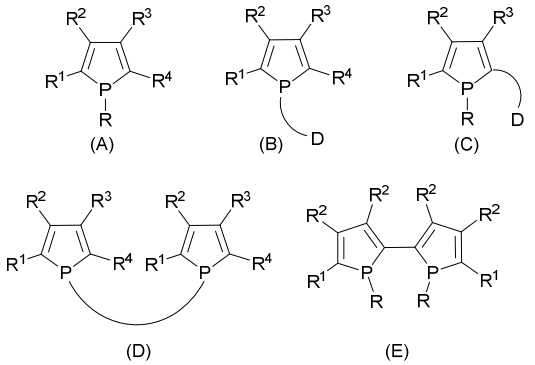


Figure 1 : Families of phosphole ligands used in catalysis

2. Monophospholes

2.1. Introduction

Up to now, monophospholes are the most investigated among the phosphole-based ligands if one considers the number of publications devoted to synthesis, structure, coordination chemistry and applications of phosphole complexes in homogeneous catalysis since their P-atom behaves as a classical two-electrons-donor toward transition metals.

Phospholes, phosphorus analogues of pyrrole, furan and thiophene, are known basically as a weakly aromatic heteroles due to two intrinsic properties: (1) the pyramidal geometry of the tricoordinated P-atom and (2) the high degree of s-character of its lone pair, which prevents an efficient interaction between this P-lone pair and the endocyclic π-system. Consequently, the phosphorus inversion barrier in phosphole is abnormally low (ca 16 kcal.mol^{-1} versus 36 kcal.mol^{-1} for the analogous saturated phospholane) leading to an inversion of phosphorus at

room temperature (Figure 2) because the aromatic stabilization provided by the electon delocalization is not sufficient to overcome the high barrier to planarity associated with the P-atom. However, a significant increase in barrier height has been observed for the fused phosphole-benzene ring (*ca* 8 and 10 kcal/mol for benzophosphole and dibenzophosphole respectively) relative to the parent phosphole.[9]

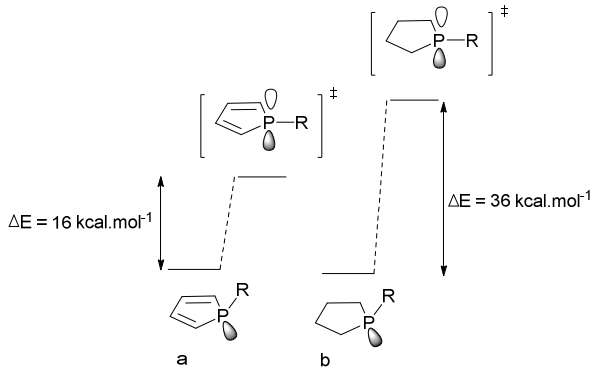


Figure 2: Inversion barrier of a phosphole (a) and a phospholane (b)

The aromaticity of phospholes has been the subject of many debates.[10] Several factors determine the degree of aromaticity, such as the substitution pattern at the carbon atoms, the pyramidalisation at the phosphorus and, most importantly, the nature of the substituent at the phosphorus.

Substituents on the phosphorus determine the amplitude of the overlap between the π-dienic system and the exocyclic P-R σ-bond (hyperconjugation effect) and thus tend to alter the aromaticity of phosphole. So it has been established that exocyclic recovery is the most contributing factor of the aromaticity. P-bulky substituent induces the flattening of the tricoordinated phosphorus which increases the hyperconjugation of the dienic system and the exocyclic P-R bond and thus increases the aromaticity and consequently the electrophilic substitution reactivity.[11] In contrast, electronegative P-substituent almost suppresses the cycle delocalization, due to a decrease in the hyperconjugation effectiveness,[12] and an increase of phosphole tendency to undergo cycloaddition reactions. On the other hand, the C-substituents in 2,5 positions, such as aromatic or vinyl, create a conjugation with the dienic system which decrease the hyperconjugation of the dienic system and the exocyclic P-R bond and thus decrease the aromaticity of phosphole.[13] This effect is also pronounced in the case of benzo-annelated ring system, such as benzophospholes, since in the fused system the π electrons are delocalized on the neighboring six-membered aromatic rings.[14] Thus, these compounds do not

display the typical electronic properties and reactivity pattern of phospholes. They have to be regarded as non-flexible diarylphosphines or as P-bridged diphenyl moieties.

According to their different electronic properties, the monophospholes could be classified into three categories: the phosphole ligands (A) and the P-bulky phospholes (B) and the fused phosphole-benzene ligands (benzo- and dibenzo-phospholes, C). Figure 3 shows the main monophosphole ligands used in catalysis (chiral ligands included).

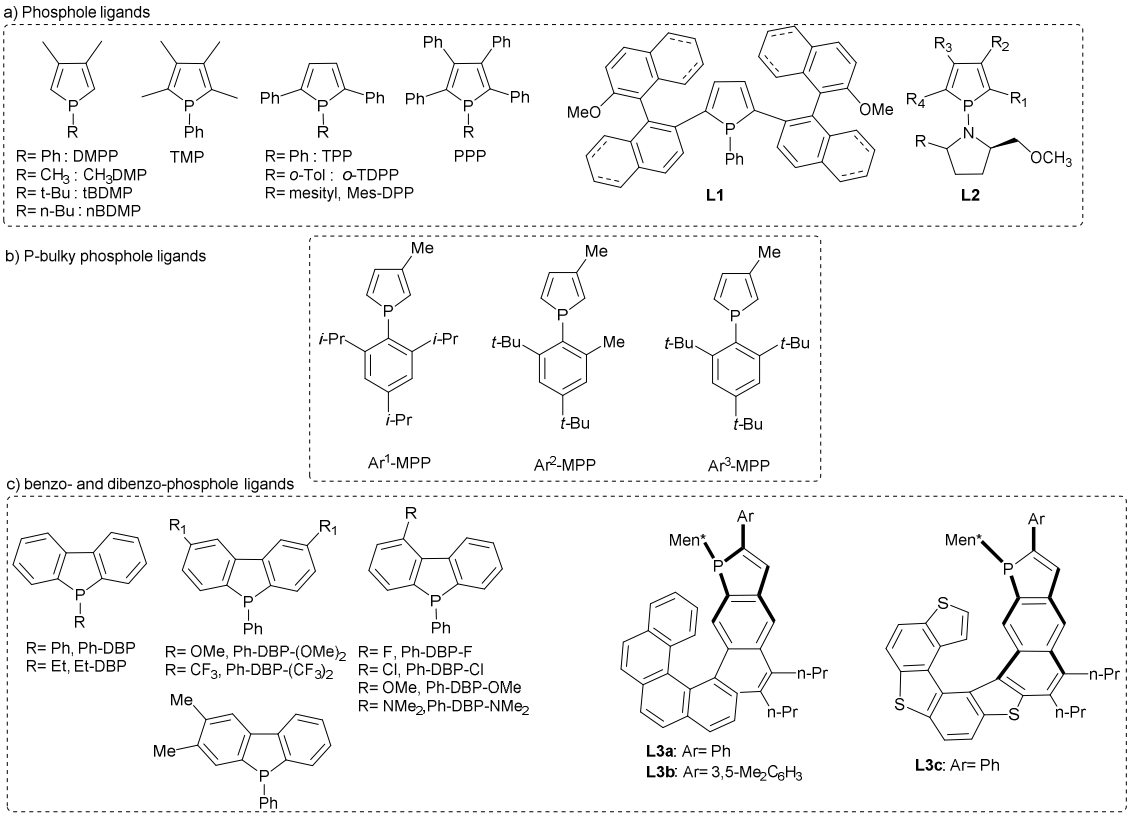


Figure 3: Monophospholes ligands used in catalysis with their abbreviations

The fundamental properties of monophospholes in coordination chemistry have been reviewed comprehensively.[15] Among the possible coordination modes, the simple η^1 mode is the preferred (σ-donor by the P-lone pair, π-acceptor by the low-lying σ*(P-R) orbital).[16] The stereoelectronic properties of the ligand play a crucial role in the metal-catalyzed reactions. However, the Tolman's parameters are only available for a very limited series of phosphole ligands (Table 1). The σ-donor/π-acceptor properties were determined by recording the IR frequencies in $[Ni(CO)_3L]$[17] or in $[RhCl(L)(CO)_2]$[18] complexes. Varying the substituents at the C-atoms or at the P-atoms of the phosphole ring gives the opportunity of fine-tuning the electronic properties of the ligands. It is interesting to note that the π-acceptor ability of **Ph-**

DBP[19], **o-TDPP**, **PPP** and **TPP** are better than that of PPh_3. On the other hand, the σ-donor ability, evaluated by measuring the magnitude of $^{1}J_{P\text{-}Se}$ in the ^{77}Se isotopomer of the corresponding selenide compounds (Table 1), indicates that introduction of methyl groups at the C-atoms of the phosphole ring increases the σ-donation, **DMPP** and **TMP** being better σ-donor ligands than PPh_3.[18]

Table 1: Stereoelectronic parameters of some phosphole ligands

Ligand	$\tilde{\upsilon}_{CO}$ (cm^{-1})	$^{1}J_{P\text{-}Se}$ (Hz)[c]	Cone angle (°)
t-BDMP	2063[a]		nd
TMP	2051[b]	708	150[d]
DMPP	2068[a]	713	nd
Mes-DPP	2068[a]		nd
PPh_3	2069[a] - 2053[b]	730	145[e]
Ph-DBP	2056[b]	748	147 [c]
o-TDPP	2070[a]		nd
PPP	2070[a]		nd
TPP	2072[a]-2058[b]	742	145[e]- 167[d]

[a] A_1 $\tilde{\upsilon}_{co}$ in $[Ni(CO)_3L]$, [b] $\tilde{\upsilon}_{CO}$ av in $[RhCl(L)(CO)_2]$, [c] ^{31}P-^{77}Se coupling constants determined in $CDCl_3$ at RT for selenide phosphole ligands, cone angles calculated from X-ray crystal structure of: [d][AuCl(L)], [e] free ligand

The steric properties of phosphole ligands can be modulated by variation of the substituents at the C-atoms of the phosphole ring.. Tollman's steric parameter first calculated from X-ray crystal structure of free ligand show that **TPP**[20] is as sterically demanding as PPh_3.[21] The classification made from cone angles calculated from X-ray crystal structure of [AuCl(L)] gave different values but allows the ranking of the selected phosphole ligands in this order : **Ph-DBP** < **TMP** < **PPP** ~ **TTP** (Table 1).[22]

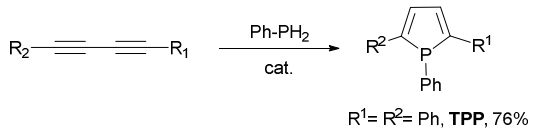
Before processing their applications in catalysis, the main synthetic routes of each category of phosphole ligands, monophospholes, P-bulky phospholes and benzophospholes, are briefly described below.

2.2. Phosphole Ligands

2.2.1. Synthesis

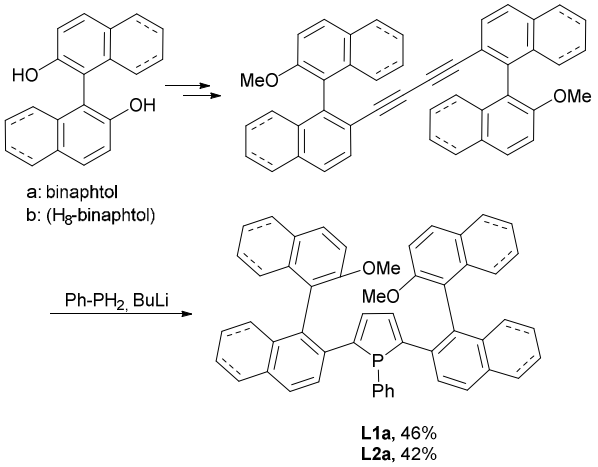
Among the great variety of available monophospholes, only a few have been involved as ligands in catalysis and for a limited number of reactions. A significant number of methods have been developed for the synthesis of phospholes but the description below will be limited to those used for the preparation of ligands involved in catalysis thereafter.

Construction of the phosphole ring, with one useful exception, is accomplished by methods that are quite different from those employed for N, S, O ring systems. The only successful method that is common to both phosphole and pyrrole ring system is the cycloaddition of 1,3-diynes with primary phosphines and amines (Scheme 1). Symmetrical and dissymmetrical diynes have been employed to create 1,2,5-trisubstituted phospholes.[23] This method developed in 1970s continues to find its uses because it is best adapted to phosphole having bulky substituents in the 2,5 positions including chiral substituents.[24] For example in presence of a base as catalyst, phenylphosphine and 1,4-diphenylacetylene yields 1,2,5-triphenylphosphole (**TPP**) in 76%.[23a]



Scheme 1

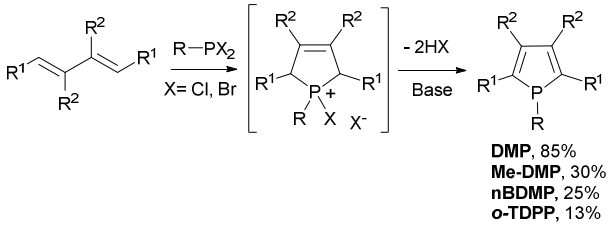
On the other hand, chiral enantiopure phospholes **L1**, bearing axially chiral biaryl substituents at the 2- and 5-positions of the phosphole ring, have been prepared by this procedure (Scheme 2).[25]



Scheme 2

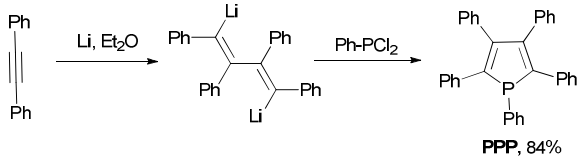
Two other major methods have been developed for the synthesis of phospholes by ring forming reactions. The first one is the reaction of dienes with $PhPX_2$ which provides a general access to various C-substituted phospholes (Scheme 3). 1,2,5-triphenylphosphole (**TPP**) was

originally synthetized by refluxing 1,4-diphenylbuta-1,3-diene in dichlorophosphine.[26] In a more convenient one pot two step procedure, the MacCormack cycloadduct is initially formed at room temperature and then dehydrohalogenated to yield phosphole (Scheme 3). This method remains the best adapted to prepare 1-phenyl-3,4-dimethylphosphole (**DMP**) and is the most general by providing more than 25 different phosphole compounds such as **Me-DMP**, **nBDMP**, **oTDPP**.[27]



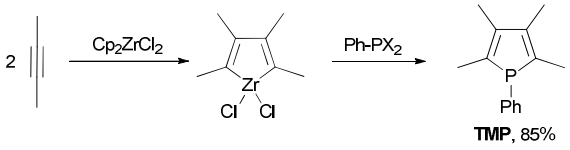
Scheme 3

The second important and versatile route to 2,3,4,5-tetrasubstituted phosphole remains the reaction of phosphorus dihalides with metalled dienes. This route involves the formation of dianionic diene intermediates prepared through metal-mediated reductive dimerization of alkynes or diyne ring-closure. The original synthesis of **PPP** involved the reaction of the dilithio derivative of tetraphenylbutadiene with $PhPCl_2$ (Scheme 4).[28]



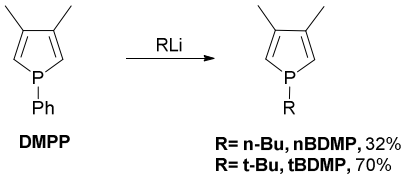
Scheme 4

Zirconacyclopentadiene, obtained by a reductive reaction of zirconocene dichloride with 2 alkynes or a diyne, can react with $PhPX_2$ to form phosphole derivatives. The method, first used to prepare **TMP**, has now been extended to various phosphole ligands (Scheme 5).[29]



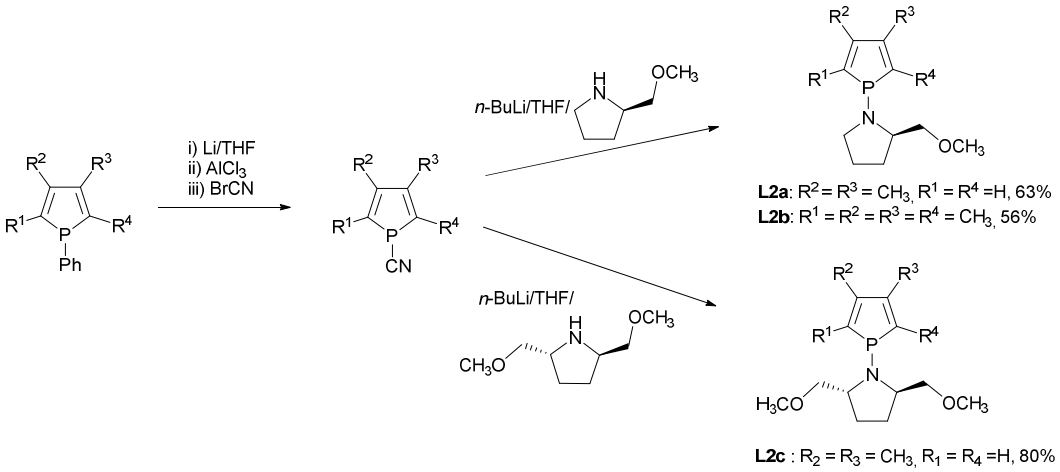
Scheme 5

Functionalization at phosphorus via electrophilic or nucleophilic substitutions represents two other important methodologies to access ligands having different steric and/or electronic properties. The most readily available P-phenyl derivatives are particularly useful for the synthesis of these new phospholes. For example, nucleophilic attacks at phosphorus could be performed with *n*-BuLi and *t*-BuLi on **DMPP** to replace the phenyl P-substituent and afford **nBDMP**[30] and **tBDMP** in moderate to high yield (Scheme 6).[31]



Scheme 6

Nucleophilic substitution reactions may also be performed on a 1-cyanophosphole due to their ease of handling, relative air-stability (contrary to 1-halogenophospholes) and good reactivity towards various nucleophilic reagents such as alkoxides and amides. A series of chiral pyrrolidino-phosphole ligands **L2** was prepared *via* a coupling reaction between cyano phosphole derivatives and methoxymethylpyrrolidino amides *in-situ* formed (Scheme 7).[32]

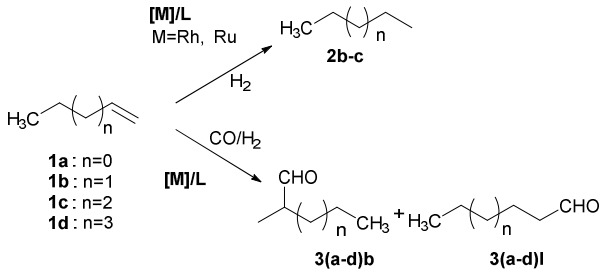


Scheme 7

2.2.2. Hydrogenation

The use of a monophosphole ligand in hydrogenation was first reported in 1972 by Hui *et al.* in the Rh-catalyzed reactions but very few applications have been subsequently developed.[33]

$[RhHCl_2(\mathbf{TPP})_2]$ complex showed its ability to hydrogenate 1-hexene **1b** at 20°C under 1 bar of H_2 in the presence of Et_3N (Scheme 8). $[RhCl(\mathbf{TPP})_3]$ also catalyzed the same hydrogenation reaction but was found to be less active than $[RhCl(PPh_3)_3]$ (for the same reaction).



Scheme 8

Some ruthenium phosphole complexes such as $[RuCl_2(\mathbf{Me\text{-}DMP})_4]$ and $[RuCl_2(\mathbf{tBDMP})_2(PPh_3)]$ have been shown to catalyze the hydrogenation of 1-heptene **1c** at ambient temperature under 1 bar of H_2 at rates comparable to $[RuCl_2(PPh_3)]$.[34]

The hydrogenation of functionalized olefins such as Z-α-acetamidocinnamic acid **4** demonstrated the performances of several $[Rh(COD)_2]PF_6$/ phosphole systems in terms of activities (Scheme 9). All phospholes tested, provided more active catalytic systems than the $[RhCl(PPh_3)_3]$, except **TPP** system. The best TOF were recorded with **nBDMP** and **tBDMP** ligands.[35]

Scheme 9

2.2.3. Carbonylation

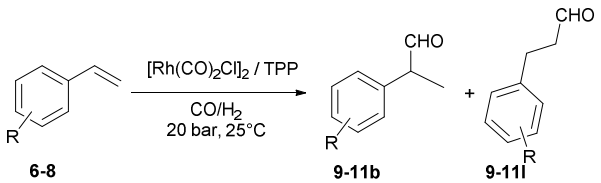
The most important work has been devoted to hydroformylation. The use of a monophosphole ligand was first reported in the Co-catalyzed hydroformylation of terminal olefin (Scheme 8). $[CoH(CO)_3(L)]$ complex with **nBu-DMP**, **DMPP** and **PPP** ligands afford similar results in the hydroformylation of 1-octene, **1d** (scheme 8) to the Shell industrial process using 9-phenyl-9-phospha-bicyclonnane.[36] Thereafter, Neibecker *et al*. developed phosphole-modified rhodium catalysts for the hydroformylation of a broad range of substrates using *in situ*

catalytic systems, generated from $[Rh(CO)_2Cl]_2$ and phosphole ligand. The reactions were conducted under mild conditions (20 bar of syngas pressure at 80°C) in presence of Et_3N to assist the formation of the active hydrido-rhodium complex and to remove HCl which is an inhibitor for the hydroformylation reaction.

For the hydroformylation of 1-hexene, **1b** (Scheme 8), a series of phospholes, **TPP**, **PPP**, **o-TDPP**, **t-BDMP**, **n-BDMP**, **DMPP**, having different steric and electronic properties has been evaluated and compared to PPh_3, known as a standard phosphine for the hydroformylation of terminal olefins. [37,38] All these phospholes produced catalytically active systems but two of them, **TPP** and **o-TDPP**, have been found to be superior to PPh_3. **TPP** was found to be better than **o-TDPP**, it furnished a more active catalytic system with a better selectivity for the linear aldehyde than the Rh-PPh_3 system (10% more selective and 18 times more active). In addition, both activity and selectivity are optimum for a P/Rh ratio of 2 contrary to PPh_3 which requires a P/Rh ratio of 5 to give the best performances. An analysis of the influence of the Rh-TPP ratio revealed the existence of a unique active species $[HRh(CO)_2(\mathbf{TPP})_2]$, evidenced by spectroscopic studies, contrasting with the case of the Rh-PPh_3 system where several species are involved. [39]

It may be mentioned that the Rh/**TPP** system (Rh/TPP ratio of 2) is also active in the hydroformylation of 2,3 and 2,5-dihydrofurans.[40]

In the hydroformylation of styrene **6a** (Scheme 10),[41,42] the $[RhCl(CO)_2]_2$/**TPP** catalytic system affords excellent aldehyde chemoselectivity (100%) and high regioselectivity in favour of branched isomer (b/l: 84:16) under mild conditions (20 bar, 25 °C, 6h). Once again, this catalyst is twice as active as the corresponding Rh-PPh_3 system with only two **TPP** per rhodium.



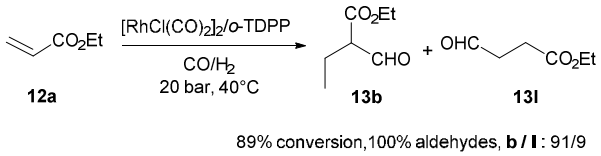
6-8 **9-11b** **9-11l**

R	conversion (%)	selectivity (%)	b/l
6a: H	64	100	84/16
7a: *p*-^{i}Bu	75	100	83/17
8: *m*-PhO	95	100	91/9

Scheme 10

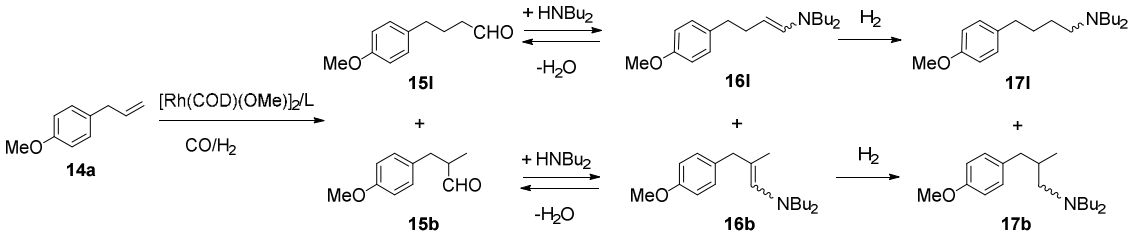
The catalytic cycle proposed from kinetic studies, involves a catalyst with two **TPP** ligands per Rh. The hydride complex $[HRh(CO)_2(\mathbf{TPP})_2]$ identified as the catalyst resting state does not seem to undergo TPP dissociation throughout the catalytic cycle.[43]

The Rh/**TPP** system was extended to the hydroformylation of vinylarenes **7a** and **8**, known as precursors of arylpropionic acids, *ie* Ibuprofen and Phenoprofen respectively, with high regioselectivity in favor of branched aldehydes, (scheme 10).[41] In addition, the regioselective hydroformylation of ethyl acrylate **12a** could be efficiently performed with rhodium-phosphole systems under mild conditions (40°C, 20 bar).[44] In this reaction, ***o*-TDPP** proved to be five times more active than **TPP** (Scheme 11).



Scheme 11

Recently, **TPP** and **PPP** phospholes have been employed for the first time as ancillaries for the rhodium-catalyzed hydroformylation and hydroaminomethylation of estragole **14a**, an allylbenzene extracted from garden plants (Scheme 12).[45] The hydroaminomethylation is a cascade reaction involving the hydroformylation, condensation of the primarily aldehyde with the added amine and hydrogenation of the enamine to generate the corresponding amine.

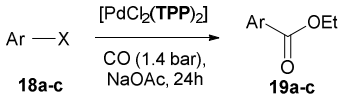


Scheme 12

In a preliminary study, phosphole-promoted systems have showed the best overall performance in hydroformylation of estragole. Under 20 bar of CO/H_2: 1/1 in toluene at 50°C for 2h with $[Rh(cod)(\mu\text{-}OMe)]_2$ as catalytic precursor, phosphole-promoted systems were more selective than the PPh_3 one. The hydroaminomethylation performed with di-n-butyl amine at 80°C under 40 bar ($CO:H_2$= 1:3) in toluene during 24h. Phosphole/[Rh(cod)(μ-

OMe)]$_2$ systems were more efficient in promoting the reductive amination and more regioselective than the standard PPh_3 based system presenting an excellent compromise to ensure high chemoselectivity and reasonably fast formation of target amines.

In addition to hydroformylation reactions, it should be noted that **TPP** was used in Pd-catalyzed carbonylation reactions of various halide derivatives **18** (Scheme 13). In all cases, the complex [$PdCl_2$(**TPP**)$_2$] was superior to the complex [$PdCl_2(PPh_3)_2$].[46]



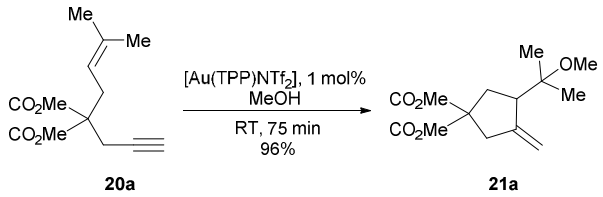
	Ar	X	Yield
18a	Ph	I	90%
18b	$PhCH_2$	Cl	65%
18c	$PhCOCH_2$	Cl	40%

Scheme 13

2.2.4 C-C coupling reactions

Monophosphole ligands have been recently used in a wide range of gold- and platinum-catalyzed alkyne activation.

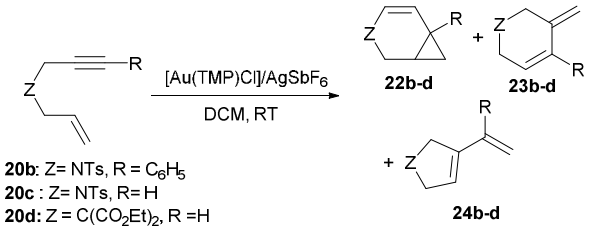
In early studies, [Au(**TPP**)(NTf_2)] complex was found to be more active than [Au(PPh_3)(NTf_2)] for the methoxycyclisation of C-tethered 1,6-enyne **20a** (complete conversion in 75 min versus 2h, Scheme 14).[47]



Scheme 14

Phospholes, **DMPP**, **TMP** and **TPP**, have been then studied in the gold-catalyzed reactions and displayed higher activities than the corresponding PPh_3-based complexes. For example, cationic gold (I) phosphole catalysts bearing **TMP** or **TPP**, generated *in situ* from 5 mol% of [Au(L)Cl] and 5 mol% of $AgSbF_6$, were active in the cycloisomerization of the model N-tethered 1,6-enyne **20b** (Scheme 15). High selectivity in the cyclopropane product **22b** (95-

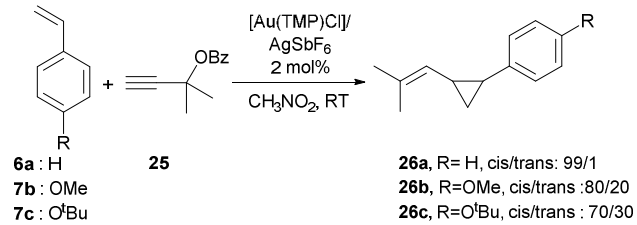
100%) was obtained[18] with an activity that increases with the σ-donor ability of the ligand (TPP < TMP). Note that **TMP** based catalyst was found more active than the PPh_3 one.



Scheme 15

The **TMP**-based complex also proved to be very efficient in the cycloisomerization of N- and C-tethered enynes bearing terminal alkynes **20c** and **20d** leading in this case to a mixture of 1,3-dienes **23** and **24**, with **23c** (90%) and **23d** (85%) as major products respectively (scheme 14).[18] A stable isolated cationic complex, [Au(**TMP**)(CH_3CN)]SbF_6, was also found to be highly active and selective especially for the **20d** cycloisomerization. Even at low catalyst loading (0.5 mol%), no loss of conversion and selectivity was observed (72% conversion in 60 min, **23d**/**24d** : 85/15).

Cationic gold (I) complexes of **TMP**, **DMPP** and **TPP** also catalyzed the cyclopropanation of olefins **6** and **7** (Scheme 16), using propargyl benzoate **25** as the gold (I) carbene precursor. A good correlation between the ligand σ-donor ability and the catalytic activity was again detected. Note the superiority of [Au(**TMP**)Cl]/$AgSbF_6$ catalytic system relative to [Au(PPh_3)Cl], which only gives undesired polymeric products under the same conditions. Even strained bicyclic norbornylene which usually requires drastic conditions, was efficiently converted into the corresponding cyclopropane less than 2h (50 min). In addition, [Au(**TMP**)Cl]/$AgSbF_6$ system provides good selectivities in *cis* diastereoisomer for the cyclopropanation of **6**, **7b** and **7c**.



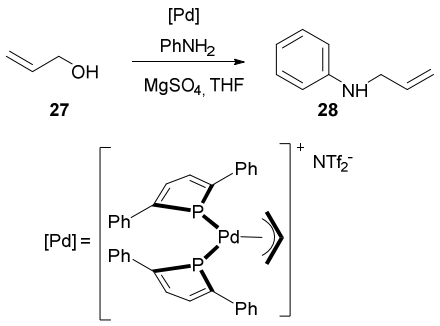
Scheme 16

The evaluation of a series of cationic platinum (II)-phosphole complexes in the cycloisomerization of various N- or C-tethered 1,6-enynes was then also reported.[48] All of these complexes proved to be more efficient than the PPh_3 counterpart. **TMP**-based complexes appeared the best catalyst of the series in terms of activity for **20c**, as already observed in Au-catalyzed cycloisomerization (Scheme 15). Interestingly, switching from **TMP**-Au catalyst to **TMP**-Pt-catalyst reverses the selectivity in favor to the diene **24c**. In addition, the influence of the nature of the counter-ion and the solvent on the chemo-selectivity has been observed. The diene formation (compound **24c**) is favored in DCE at 80°C with $AgBF_4$ or at room temperature with $AgSbF_6$, whereas the cycloisomerization is orientated towards the cyclopropane formation (compound **23c**) in toluene at 80°C with $AgBF_4$. **TMP**-Pt catalyst was also found to be efficient for the cycloisomerization of 1,6-enynes **20b** and **20d**.

$[Pt(\mathbf{TMP})_2Cl_2]/AgSbF_6$ is also able to catalyze methoxycyclization (Scheme 14) and tandem hydroarylation/cyclisation reactions of various N- or C-tethered 1,6-enynes. The regioselective addition of nucleophiles on the 5-*exo*-cyclopropyl carbene leading to five-membered ring alkoxy-compounds **21** was exclusively obtained whatever the enyne's substitution pattern and its tether Z.

2.2.5 C-N coupling reaction

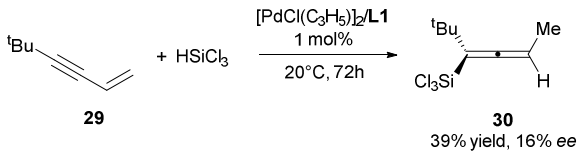
We must also mention the performance of **TPP**-palladium allyl complex in catalytic allylic amination reactions under mild conditions (Scheme 17).[16] The Pd-complex proved to be the most active catalyst (100% conversion in 1h) catalyst of the series of palladium allyl complexes in the allylation of aniline. The electronic nature of the ligand plays a crucial role in this reaction and these results clearly demonstrate that the better the ligand is a π acceptor, the more active the catalyst. **TPP**-palladium allyl complex proved also to be an efficient catalyst for the allylation of secondary amines.



Scheme 17

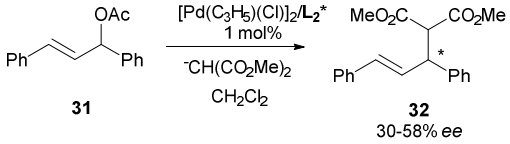
2.2.6 Asymmetric reactions

Only two chiral phosphole type ligands, **L1** and **L2**, have been reported in asymmetric catalysis. Chiral 2,5-bis(naphthyl)phospholes, **L1a-b**, have been applied to palladium-catalyzed asymmetric hydrosilylation of 5,5-dimethyl-1-hexen-3-yne **29** (Scheme 18) to give an axially chiral allenylsilane **30** with poor enantioselectivity (up to 16% **L1b**).[25]



Scheme 18

Chiral pyrrolidino-phosphole ligands **L2**, which demonstrated their tendency to behave as P-monodentate rather than P,O-bidentate ligands towards palladium (II), provided very active Pd-catalysts for asymmetric allylic substitution of 1,3-diphenylprop-2-enylacetate **31** with dimethyl malonate anion. Complete conversion of the substrate was reached within 15 to 60 min in CH_2Cl_2 (Scheme 19).[32] The asymmetric induction proved to be moderate (up to 58% for ligand **L2c**).



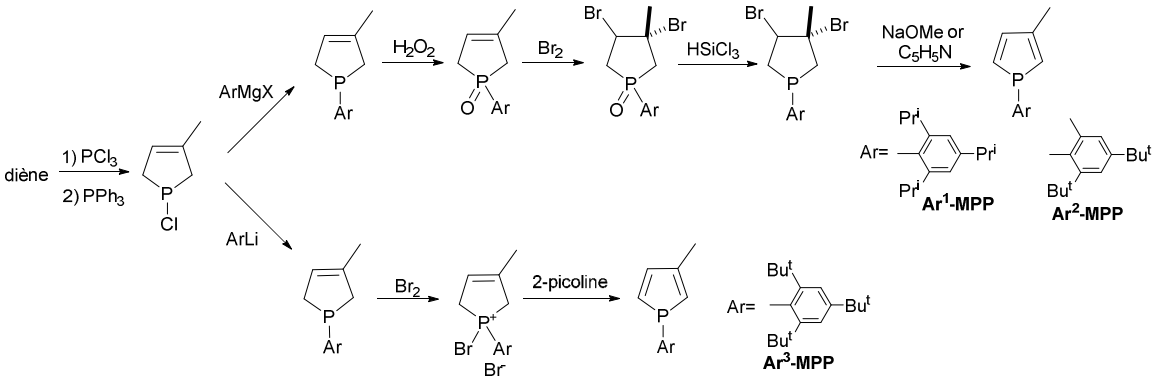
Scheme 19

2.3. Phospholes with 2,4,6-trialkyl-phenyl substituents

Sterically demanding substituents on phosphorus atom cause partial flattening of the pyramidal phosphorus and promote the overlap of its lone pair with the pz orbitals of the sp_2 carbon atoms thus increasing the phosphole aromaticity. Congested phospholes with 2,4,6-trialkylphenyl substituent on the phosphorus atom, introduced by Quin and Keglevich, possess aromatic character that depends on the size of the alkyl groups.[49]

2.3.1. Synthesis

The strategy used to prepare the 1-aryl phospholes involves the construction of the 1-chloro-phospholene in the first step followed by a sequence of conventional reactions to create the phosphole system because the direct Mc Cormack cycloaddition of diene with $ArPX_2$ is prevented by the steric hindrance of P-substituents (Scheme 20).[50]



Scheme 20

An alternative pathway was employed to synthesize the **Ar_3-MPP** phosphole with the larger 2,4,6-tri-butylphenyl substituent because the deoxygenation of the phospholene oxide was prevented by steric hindrance of this P-substituent (Scheme 20).[51]

2.3.2. Hydroformylation

These **Ar-MPP** phospholes, although hindered, could form platinum[52] and rhodium[53] complexes which have been studied in the hydroformylation of styrene **6a**. The catalysts generated *in situ* from $[PtCl_2(PhCN)_2]/2L/SnCl_2$ promoted the hydroformylation reaction with a low conversion (up to 21%) and moderate chemoselectivities (81%) and regioselectivities towards branched aldehyde **10b** (up to 63%) under 40 bar of CO/H_2 (1:1) at 100°C.[52] In contrast, in *situ* complexes obtained from $[Rh(nbd)Cl_2]$ or $[Rh(acac)(CO)_2]$ proved to be more active than platinum catalysts giving higher conversion (up to 99% at 100°C). Excellent chemoselectivities (>99%), and moderate to high regioselectivities towards branched aldehyde **9b** (up to 91% at 40°C) were reached under 50 bar of CO/H_2 (1:1).[53a]

On the other hand, a Rh(III) complex $[Rh(Cp^*)Cl_2(L)]$ could only be obtained with the phosphole **Ar_1-MPP**. This preformed complex[54] was efficient, only in presence of Et_3N, at 90°C under 50 bar of CO/H_2 (1:1), resulting in complete conversion of **6a**. Excellent chemoselectivity (99%) and moderate regiselectivity (74%) towards the branched aldehyde

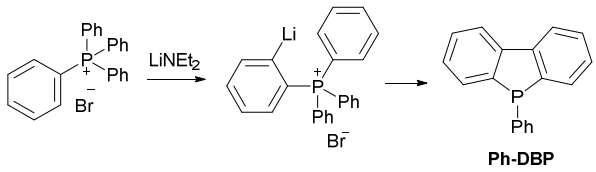
9b were obtained. The addition of triethylamine is needed to promote the reduction of Rh (III) to Rh (I) via reductive elimination of HCl from the *in situ* formed hydrido-chloro-rhodium intermediate.

2.4. Benzophospholes and Dibenzophospholes

Benzophospholes (1H-phosphindoles) and dibenzo[b,d]phospholes derivatives are not considered as classic phospholes because of the π electron delocalization in the neighboring six-membered aromatic rings. These ligands represent an independent class of monophosphole ligand classified as either phosphorus-substituted biphenyls or constrained triarylphosphines. While benzophospholes experienced only very recent applications in catalysis, dibenzophospholes were used since 1970s. Dibenzophospholes have been evaluated in hydrogenation, hydroformylation and C-C coupling reactions as monophosphole ligands. More recently, they found some application in organocatalysis.

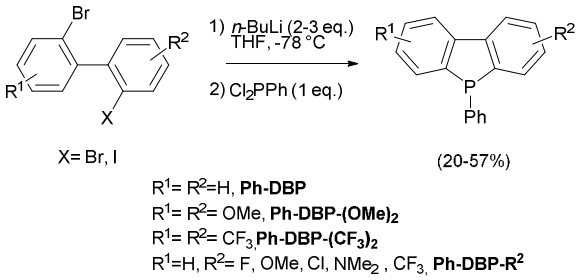
2.4.1. Synthesis

The more convenient synthetic procedure to prepare the **Ph-DBP** compound involves the tetraphenylphosphonium bromide as starting materials (Scheme 21).[55]



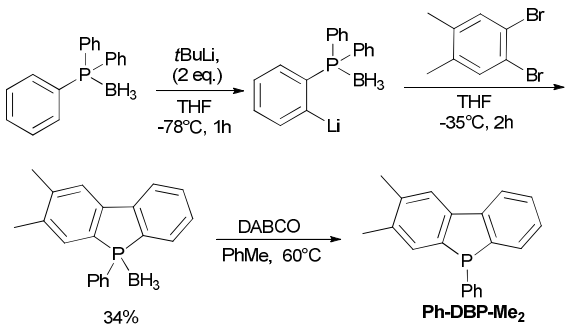
Scheme 21

For the synthesis of dibenzophosphole derivatives which are functionalized on the phosphole ring, the old and classical method based on an electrophilic trapping of 2,2′-dilithiobiphenyl with dichlorophenylphosphine,[56] continues to be used although catalytic synthesis of phospholes through C-P bond formation have been recently developed.[57] For example, dibenzophospholes **Ph-DBP-$(OMe)_2$** and **Ph-DBP-$(CF_3)_2$** were readily obtained as well as the C_1-symmetric dibenzophospholes **Ph-DBP-R^2** (Scheme 22).[58]



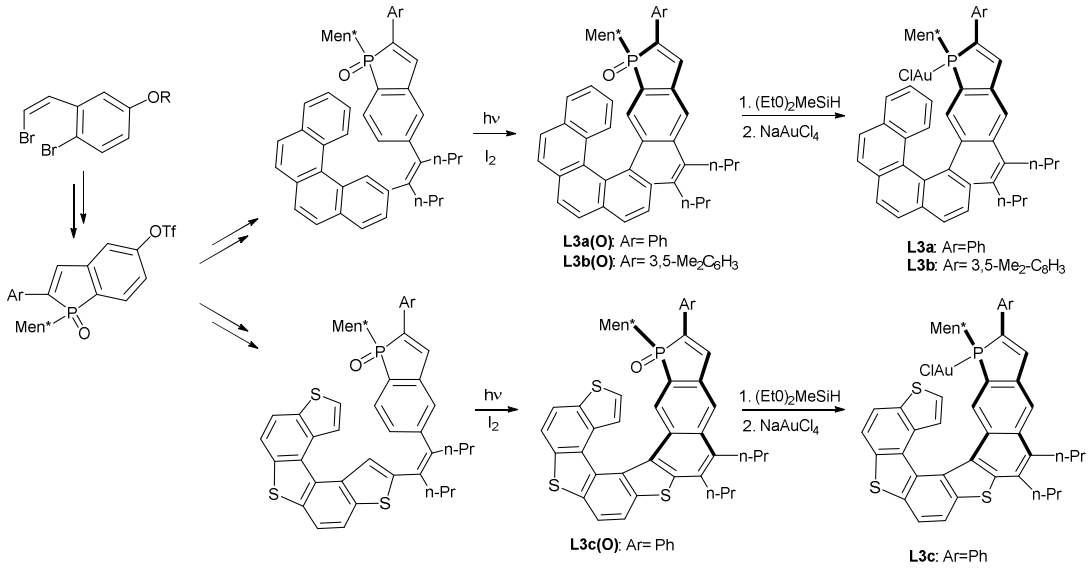
Scheme 22

On the other hand, the dibenzophosphole **Ph-DBP-Me$_2$** was synthetized by a variant of the so-called 'Aryne coupling' versions. It involves the reaction of (*ortho*-lithiophenyl) phosphine-borane complexes with *in situ* generated arynes. Ligand **Ph-DBP-Me$_2$**, obtained as its borane complex after coupling, quantitatively affords the free ligand by deprotection using DABCO (Scheme 23).[59]



Scheme 23

Very recently, α-aryl-substituted phosphindoles units have been used to prepare phosphahelicenes chiral ligands **L3**.[60,61] The synthetic procedure is based on the coupling of a diastereomerically pure P-menthyl-substituted phosphindole triflate by palladium catalysis. It is then followed by the photochemical oxidative cyclization of diaryl olefins as illustrated in Scheme 24.

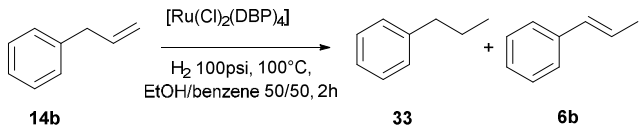


Scheme 24

These helicenes **L3** with embedded phosphole units have been isolated as phosphine oxides or gold complexes after reduction and subsequent complexation.

2.4.2. Hydrogenation

Ph-DBP was first employed in hydrogenation in 1970s. In early studies, hydrido-rhodium complex [RhH(**Ph-DBP**)$_4$], was found to be superior to [RhH(PPh_3)$_4$] in the hydrogenation of 1-hexene **1b** (Scheme 8).[62] On the other hand, [$RuCl_2$(**Ph-DBP**)$_4$] showed its ability to catalyze the hydrogenation of allylbenzene **14b** into **33**, rather than the isomerisation into methylstyrene **6b**, with higher efficiency and selectivity than [$RuCl_2(PPh_3)_4$] (Scheme 25).[63] Note that [$RuCl_2$(**Ph-DBP**)$_3$] is also an efficient catalyst for this hydrogenation reaction.



Scheme 25

2.4.3.Hydroformylation

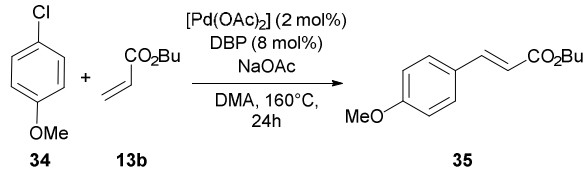
In hydroformylation, early studies showed the use of DBP ligands (**Ph-DBP** and **Et-DBP**) for cobalt-catalyzed hydroformylation of 1-pentene **1a**, using [$Co_2(CO)_8$] as a precursor. Under 20 bar of CO and 25 bar of H_2 at 160°C with P/Co ratio of 2.2, better activities and

selectivities towards the linear aldehyde (72-77%), than the corresponding catalytic systems with PPh_3 or PPh_2Et, were observed.[64] The same DBP ligands were also evaluated in Rh-catalyzed hydroformylation of styrene using $[RhCl(CO)_2]_2$ precursor with a P/Rh ratio of 4 under severe conditions (140°C, 100 bar of syngas).[64] Better results in terms of activities and selectivities (77-86% in favour to the branched aldehyde) compared to Rh-phosphines systems were obtained.

More recently, a family of non-symmetrical substituted dibenzophospholes (**Ph-DBP-F**, **Ph-DBP-Cl**, **Ph-DBP-NMe$_2$**, **Ph-DBP-OMe**, **Ph-DBP-Me$_2$**) possessing different electronic properties have been reported for rhodium-catalyzed hydroformylation reactions of styrene and 1-octene and compared to Rh-**Ph-DBP** and Rh-PPh_3 systems.[58] In the hydroformylation of styrene **6a**, the beneficial effect of these dibenzophosphole ligands was evidenced with dibenzophosphole/$[Rh(CO_2(acac)]$ systems for a Rh/P ratio of 2 under 30 bar of syngas at 60°C. Indeed, **Ph-DBP**, **Ph-DBP-NMe$_2$** and **Ph-DBP-Me$_2$** provided rhodium catalysts that are more active than the one employing PPh_3, while **Ph-DBP-F** and **Ph-DBP-Cl** proved to be the most regioselective catalyst in favor of the branched isomer **10b** (95%). For the hydroformylation of octene **1c** conducted under the same conditions, all dibenzophosphole/rhodium systems provided more active catalysts than the one obtained with PPh_3. **Ph-DBP-Cl** provides the best catalytic system regarding activity and selectivity (98% aldehyde, b/l:29/71) with a ligand/Rh ratio of 2. Note that increasing the ligand/Rh ratio (**Ph-DBP**/Rh ratio of 4) affects the regioselectivity in favor of the linear aldehyde (72% *vs* 61%). From these results, a correlation between the electronic properties of the DBP ligands and the catalytic activities and/or selectivities has been observed.

2.4.4. C-C coupling reactions

The use of the **Ph-DBP** ligand could be noted in few C-C coupling reactions but with modest to disappointing results. In the Heck vinylation of arylhalide **34** with n-butyl acrylate **13b** (Scheme 26), **Ph-DBP**/$[Pd(OAc)_2]$ catalytic system only gave 22% of conversion over 24h at 160°C in DMA.[65]

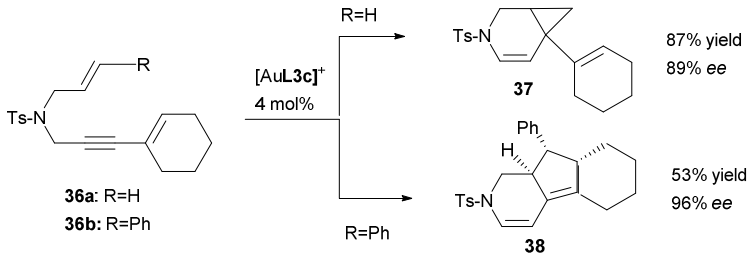


Scheme 26

In enyne cycloisomerisation reactions[18,48] (Scheme 15) and in olefin cyclopropanation[18] (scheme 16), **DBP**-catalytic systems were less efficient than those with **TMP**.

In contrast, helicenes with embedded phosphole **L3** units allowed high catalytic activity and good enantiomeric excess in the gold promoted cycloisomerization of N-tethered 1,6-enyne **20b** into cyclopropane **22b** (conversion up to 95% over 24h, *ee* up to 84%, Scheme 15).[60a,61]

The potential of the **L3** gold complexes has been established further by studies on the cycloisomerization of N-thethered dienynes. For example, the **L3c**-Au catalyst proved to be more selective than its **L3a-b** counterparts for the cycloisomerization of the dienynes **36**, with the highest *ee* attained so far (Scheme 27).[61]



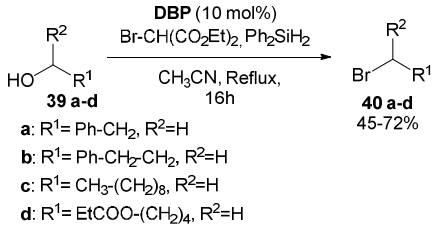
Scheme 27

2.4.5. Organocatalysis

Dibenzophospholes **Ph-DBP**, **Ph-DBP-(OMe)$_2$** and **Ph-DBP-(CF$_3$)$_2$** were found to be particularly suitable organocatalyts for catalytic variants of the Appel and Staudinger reactions. The strategy is based on a redox-driven approach, involving the formation of a pentavalent P(V)-species from the P(III) dibenzophosphole and *in situ* regeneration of the P(III)-compound by reduction of P(V) compound.

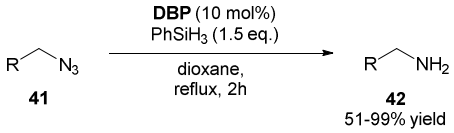
Dibenzophospholes proved to be efficient catalysts for the catalytic Appel bromination of alcohols due to their low reactivity towards alkylation by the bromo product formed and the easy *in situ* reduction of dibenzophosphole oxides by diphenylsilane under mild conditions.[66] **Ph-DBP** and **Ph-DBP-(OMe)$_2$** were found to be more active than **Ph-DBP-(CF$_3$)$_2$** for the Appel bromination of the phenylethyl alcohol because electron-withdrawing substituents (R=CF$_3$) decrease the reduction rate. In addition, **Ph-DBP** allowed high conversion of a range of primary alcohols **39** to the corresponding bromide **40** (Scheme 28) which were isolated in moderate to good yields (45 to 72%). **Ph-DBP** was also found particularly useful for the bromination of secondary alcohols such as β-chlolesterol and 1-adamantanol (ca 70% isolated

yield). Appel chlorination reaction of phenylethyl alcohol has been also achieved with a moderate conversion (40%) only using Ph-DBP-$(OMe)_2$ as catalyst.



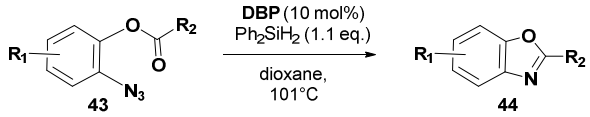
Scheme 28

Dibenzophosphole catalysts have also been applied in the Staudinger reduction of azides involving formation of a P(V)-iminophosphorane compound from addition of azide on dibenzophosphole and *in situ* reduction of the iminophosphorane intermediate with concomitant formation of amine. All catalysts, **Ph-DBP**, **Ph-DBP-$(OMe)_2$** and **Ph-DBP-$(CF_3)_2$**, allowed to decrease the reaction time for the catalytic reduction of benzyl azide (2h to reach complete conversion of the substrate *vs* 21h for PPh_3). **Ph-DBP** proved to be most suitable catalyst and displays high functional group tolerance toward nitro groups, carboxylic acids, alcohols, esters and olefins. High conversions for a range of both aromatic and aliphatic azides **41** into corresponding amines **42** (51-99 % yields) were obtained even at low catalyst loading (5 mol%) (Scheme 29).[67]



Scheme 29

The application of **Ph-DBP** has then been extended in a catalytic Staudinger/aza-Wittig tandem sequence. This process consists of the iminophosphorane formation prior to the intramolecular reaction of iminophosphorane with a carbonyl functionality and to the *in situ* reduction of the dibenzophosphole oxide by diphenylsilane. Thus, the synthesis of benzoxazoles, benzodiazepine imidates and a 2-methoxypyrrole, all from azide-containing esters, were performed using 10 mol% of **Ph-DBP** (Scheme 30).[68]



R_1= H, 5-OMe, 4-OMe, 4-NO_2, 5-Cl
R_2= Ph, 4-MeO-C_6H_4, 4-F_3CC--C_6H_4, 4-Ph-C_6H_4, Me, *t*Bu

Scheme 30

3. Multidentate hybrid phosphole ligands

Multidentate phosphorus-containing ligands display a widespread use in homogeneous transition-metal catalysis. In particular, the hybrid ligands bearing a phosphorus donor atom and other binding sites gained much attention since they introduce dissymmetry in the coordination sphere of the metal center to fit the steric and electronic requirements of the catalytic reaction. Phospholes proved to be good building blocks for the elaboration of phospholes-based ligands. Indeed, several bidentate, tridentate and tetradentate ligands possessing one phosphole P-donor and conventional N-donor or less conventional binding sites, have been developed by ring functionalization either at the phosphorus or at the carbon ring, mainly in α-position.

3.1. Bidentate phosphole/NR_2 ligands

Heteroditopic P,N-chelate ligands with two very different stereoelectronically binding sites, σ^3,λ^3-phosphorus and sp^2-hybridized nitrogen, might be the most widely studied bidendate ligands specially in asymmetric catalysis. These ligands usually behave as hemilabile ligands which could allow adapting the coordination sphere of metal center during the catalytic reaction. To tune both electronic and steric properties, the phosphole/NR_2 chelate ligand subclass has been prepared combining phosphole to pyridine, oxazoline, isoquinoline and amino-N type donor as shown in Figure 4. Few planar and axial chiral phosphole/ NR_2 ligands have also been reported.

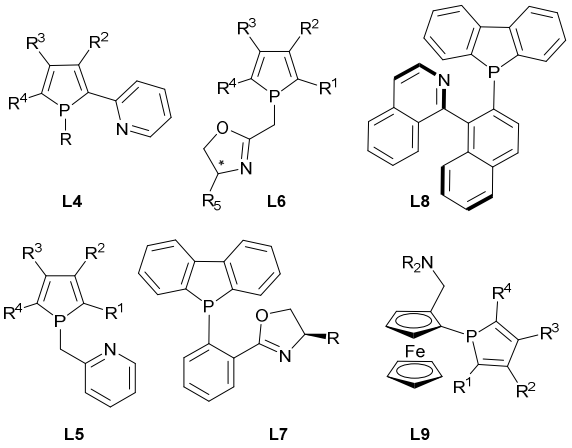
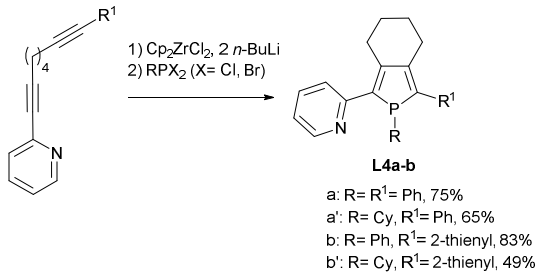


Figure 4 : Bidentate phosphole/NR_2 ligands

3.1.1. Synthesis

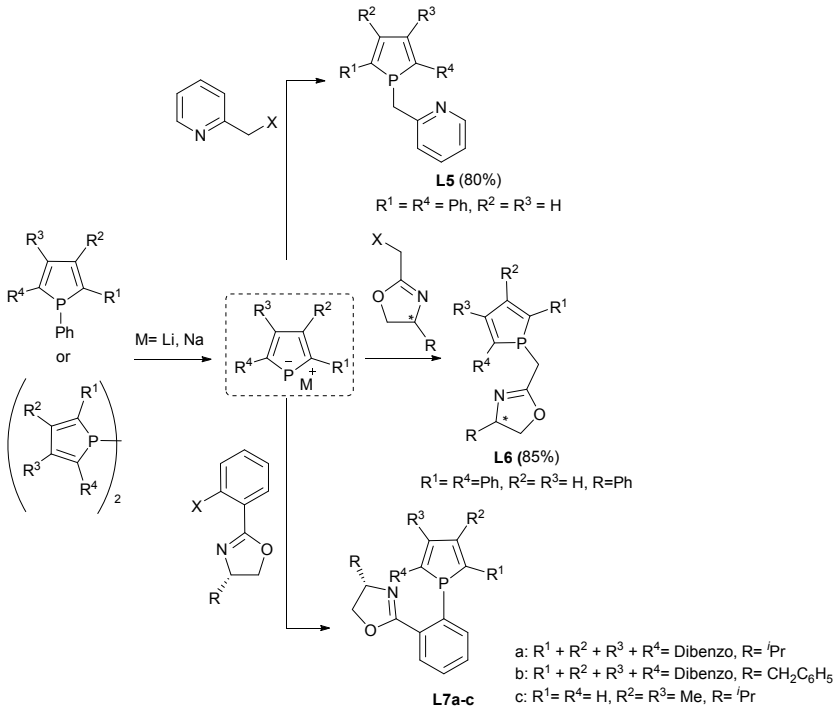
The 1,4-P,N chelates ligands **L4** have been developed by Réau *et al*.. The synthetic approach is based on an oxidative coupling between bis(2-pyridyl)octa-1,7-diyne derivatives and zirconocene, according to the well-known Fagan-Nugent method, followed by treatment with dihalide phosphine compounds RPX_2 (X= Cl or Br) to give the desired products in moderate to good isolated yield (49-83%, Scheme 31).[69]



Scheme 31

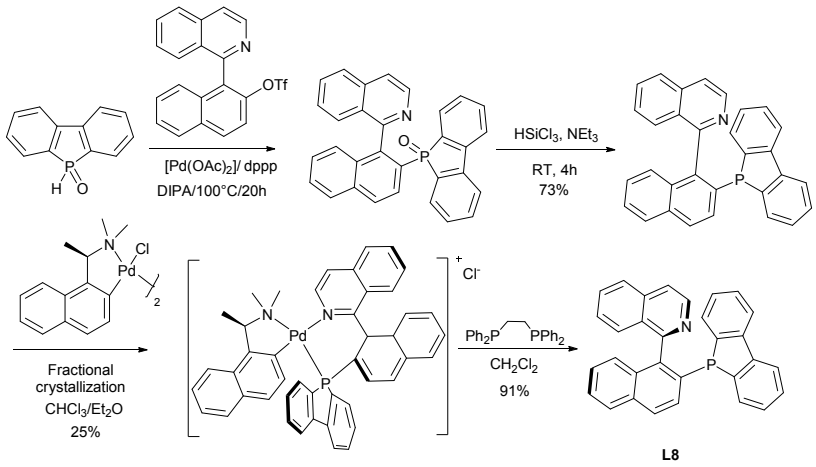
The reductive cleavage of the exocyclic phosphorus-phenyl bond of 1-phenylphosphole or phosphorus-phosphorus bond of 1,1'-diphosphole with alkali metal followed by alkylation using different N-containing electrophile reagents leads to a large variety of P,N-type ligands including chiral ones (Scheme 32).

According to this strategy, Le Floch *et al.* prepared the 1-(2-methylpyridine)-2,5-diphenylphosphole ligand **L5** and the chiral phosphole-oxazoline ligand **L6**[70] while Helchem[71] and Marinetti[72] reported other phosphole-oxazoline ligands **L7** (Scheme 32), equivalent to diphenylphosphinoxazoline class of ligand (PHOX).



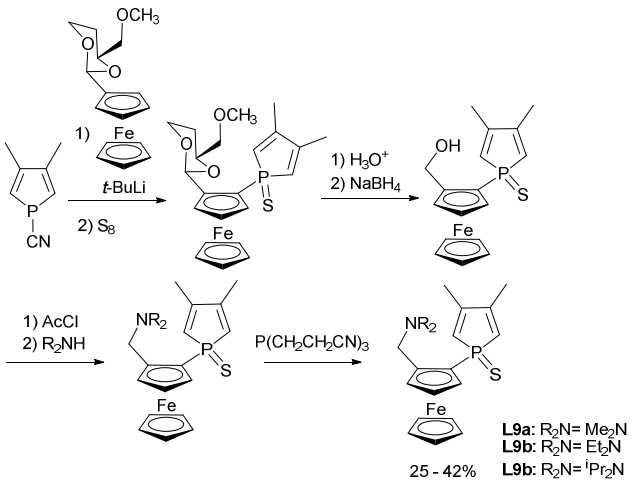
Scheme 32

On the other hand, Brown prepared the 1'-(2-P-dibenzophospholyl-1-naphthyl) isoquinoline ligand **L8**, phosphole ligand equivalent to 1-(2-diphenylphosphino-1-naphthyl)isoquinoline, QUINAP. A multistage synthesis from 1-triflate isoquinoline and the secondary dibenzophosphole oxide followed by reduction with trichlorosilane and its resolution were reported (Scheme 33).[73]



Scheme 33

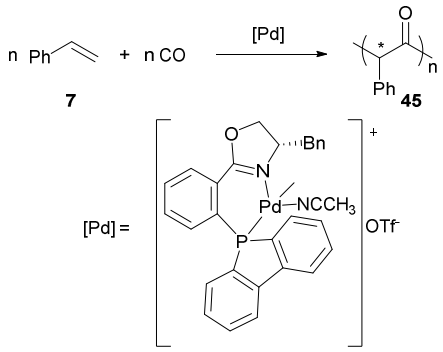
Chiral planar ferrocenylamine phosphole ligands **L9** with planar chirality as only element of chirality (Scheme 34) were prepared by Gouygou and coworkers[74] using the highly diastereoselective ortho-lithiation of Kagan's acetal followed by the introduction of the appropriate 1-cyanophosphole as electrophile.



Scheme 34

3.1.2. Polymerization/Copolymerization

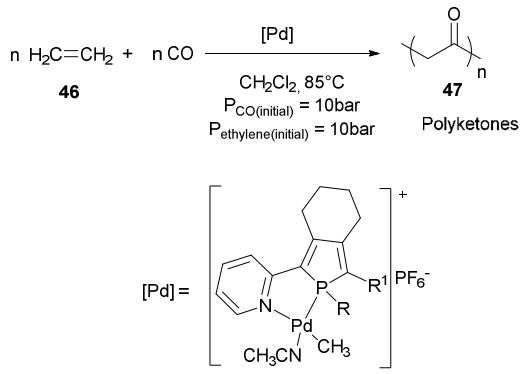
In early studies, Consiglio *et al.* investigated the copolymerization and terpolymerisation with a cationic palladium (II) complex bearing (*S*)-**L7b** ligand.[75] In the copolymerization of styrene with CO at 320 bar (Scheme 35), this catalyst showed twofold increase activity than the corresponding diphenylphosphino complex, with a productivity of 130.0 mmol (g Pd h)$^{-1}$). In addition, highly isotactic *R*-copolymer (M_n=7500 gmol^{-1}) was obtained.



Scheme 35

The terpolymerization of styrene, ethene and CO at 300 bar was performed in the two olefins, similar concentrations. (*S*)-**L7b**-Pd complex showed a productivity of 38.8 mmol (g Pd h)$^{-1}$ closer to that for ethene/CO copolymerization (14.8 mmol (g Pd h)$^{-1}$) which is indicative of an easier enchainment of ethene than styrene in terpolymers consistent with their composition (C_2H_4CO:C_8H_8CO 81:19, M_n= 8000 gmol^{-1}). Furthermore, based on the chiroptical properties, the styrene enantioface selection is similar in both the ter- and co-polymerisation processes.

In 2002, Réau *et al.* published the application of 2-(2-pyridyl)phospholes **L4** in Pd-catalyzed copolymerization of different olefins.[76] All the palladium complexes of **L4** catalyzed the copolymerization of CO and ethylene in CH_2Cl_2 at 85°C in 6h (Scheme 36). The nature of both substituents on the phosphorous atom and on the C^5 atom have an impact on the productivity of the Pd catalysts, since P-cyclohexylphosphole ligands **L4a'-b'** are more efficient ligands than their P-phenyl analogues **L4a-b**. This trend is more pronounced for 5-phenyl phosphole **L4a'** than for 5-(2-thienyl)-phosphole **L4b'**. The catalytic activities, expressed in grams of polyketone formed per grams of palladium (varying from 135 to 279), and TOF values, varying from 43 to 113 h^{-1}, are among the highest obtained for P,N chelates.

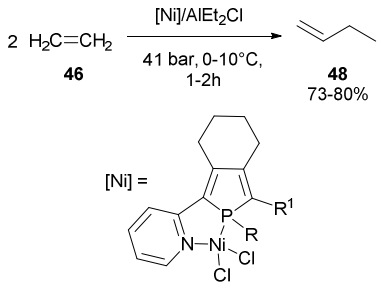


Scheme 36

L4b-Pd(II) complex catalyzes the copolymerization of CO and norbornene at 85°C affording white solid soluble co-oligomers with a molecular weight of 4 094 and a low molecular weight distribution (M_w/M_n =1.18) that suggests the living polymerization nature of the catalyst.

The same group also evaluated the 2-pyridylphosphole ligands **L4** in nickel-catalyzed oligomerisation of ethylene.[77] **L4**-nickel complexes, obtained by reacting **L4** with one equivalent of [$NiCl_2$(DME)], are highly efficient for dimerization of ethylene (Scheme 37). They exhibit good to high catalytic activities (TOF ranging from 1.9 to 3.4 s^{-1}) under mild

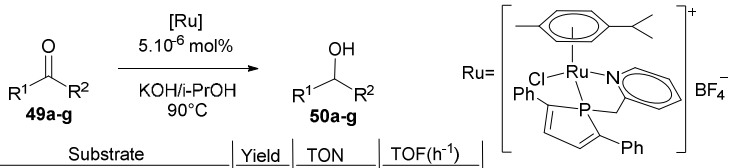
conditions (1.1 bar, 0°C) in the presence of Et_2Al as cocatalyst affording butenes as major product (71-89%). In these cases, the catalytic activities are not influenced by the nature of P-substituent but vary with the nature of the R substituent, the highest catalytic activities being observed when R is a thienyl group. In addition, **L4**-nickel complexes exhibit unusually high selectivites in 1-butene (80%) for high C4 fraction contents (up to 97%) at higher ethylene pressure (41 bar) (Scheme 37).



Scheme 37

3.1.3. Hydrogen transfer/ Hydrosilylation/ Hydroboration

Le Floch *et al.* reported the use of the ligand **L5** in Ru-catalyzed transfer hydrogenation of ketones.[70] Isolated air-stable cationic ruthenium complex, obtained in very good yield by reaction of **L5** with $[Rh(\eta^6\text{-}C_{10}H_{14})Cl_2]_2$ in the presence of chloride abstractor $AgBF_4$ has been found to be remarkably active at very low loading (5.10^{-6} mol%) for the conversion of both aliphatic and aromatic ketones **49** to the corresponding secondary alcohols **50** (Scheme 38). The highest TON and TOF values obtained for cyclic ketones reached up to 20.10^6 and $1.33.10^6.h^{-1}$. Although lower conversion and TONs are obtained with electron rich aromatic ketones, the catalytic activity **L5**-Ru complex is still higher than other catalysts (TOF 133-$800.10^3.h^{-1}$).

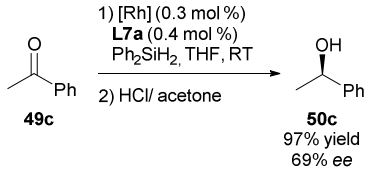


	Substrate	Yield	TON	TOF(h^{-1})
49a	cyclohexanone	100	20.10^6	$1.33.10^6$
49b	syn-2,5-dimethylcyclohexanone	100	20.10^6	$1.33.10^6$
49c	acetophenone	90	18.10^6	$1.20.10^6$
49d	2-acetylpyridine	87	$17.4.10^6$	$1.16.10^6$
49e	benzophenone	77	$15.4.10^6$	$1.03.10^6$
49f	4-bromoacetophenone	67	$13.4.10^6$	$0.89.10^6$
49g	4-methoxyacetophenone	60	12.10^6	$0.80.10^6$

Scheme 38

Chiral phosphole-oxazoline ligands **L7a-b**, reported by Helmchen and co-workers,[78] have been used in asymmetric transfer hydrogenation and hydrosilylation of ketones. Ruthenium complex [$RuCl_2$(**L7a-b)**(PPh_3)] proved to be highly efficient catalysts for the enantioselective transfer hydrogenation of various alkyl phenylketones (acetophenone, propiophenone and 2-methylpropiophenone) as well as cyclohexyl methyl ketone at a substrate/catalyst mole ratio of 1000 :1, in refluxing *i*PrOH.[79] High (up to 94% for phenylketones) to moderate (up to 60% for alkylketone) enantioselectivities were obtained using either preformed or *in situ* catalysts and excellent turnovers (ca 5000 h^{-1}) were recorded for the alkyl phenylketones with the preformed catalyst.

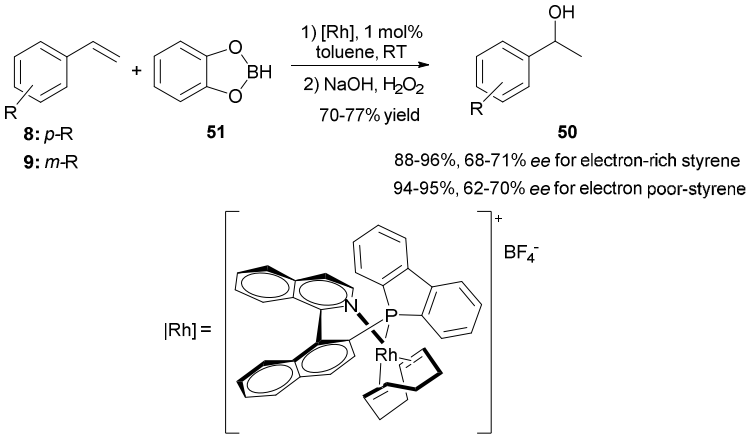
L7a-Rhodium (I) complex, engendered *in-situ* from the reaction of **L7a** with $[Rh(COD)Cl]_2$, was applied in hydrosilylation of acetophenone **49c** with moderate enantioselectivity (69% in favor of *R* configuration, Scheme 39).[80] It is noteworthy that this catalytic performance is comparable to that of the diphenylphosphinoxazoline rhodium system.



49c **50c** 97% yield 69% *ee*

Scheme 39

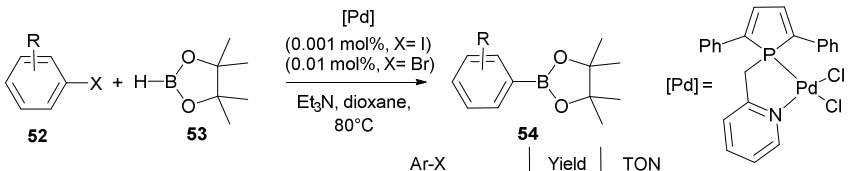
(*R*)-**L8**-Rh(I) complex has been shown to catalyze the asymmetric hydroboration/oxydation of various electron-rich and electron-poor styrenes. Very good regioselectivities (up to 96%) in favor of branched isomer and moderated enantioselectivity (up to 71%) were obtained at room temperature using 1 mol% catalyst (Scheme 40). Electron-releasing or electron-withdrawing substituents on styrene do not impact the regioselectivity and result in a very slight change of enantiomeric excess values which remains lower than the parent Rh-catalyst bearing the (*R*)-1'-(2-P-diphenylphosphino-1-naphthyl)isoquinoline ligand (93-97% *ee*).



Scheme 40

3.1.4. C-C coupling reactions

L5-Pd(II) complex, isolated from the stoechiometric reaction of **L5** with palladium precursor [Pd(COD)Cl_2], has been used in several cross coupling reactions such as the Heck, Suzuki and Miyaura processes.[81] Modest performances were obtained in the Suzuki coupling between bromoacetophenone and phenylboronic acid and in the Heck coupling reaction of bromobenzene with styrene. However, **L5**-Pd(II) complex proved to be very efficient in the Miyaura cross coupling reaction that furnishes arylboronic esters **54** (Scheme 41). Nearly quantitative yield and high TON number (up to 10^5) were obtained in the reaction of pinacolborane with various iodoaromatics at 80°C in 48h using Et_3N as a base.

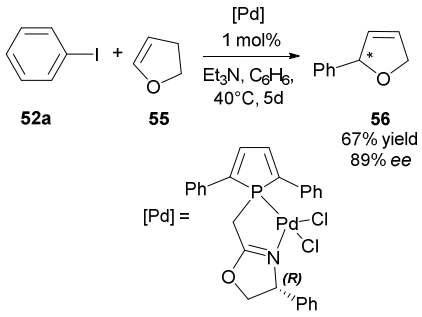


Ar-X	Yield	TON
C_6H_5I	100	100.10^3
p-IC_6H_4OMe	91	91.10^3
o-IC_6H_4OMe	97	97.10^3
o-IC_6H_4Me	99	99.10^3
C_6H_5Br	71	71.10^2
p-BrC_6H_4OMe	61	61.10^2
o-BrC_6H_4OMe	90	90.10^2
o-BrC_6H_4Me	79	79.10^2

Scheme 41

L5-Pd(II) complex proved to be still active with less reactive bromide substrates though lower conversion yields and TON (up to 9.10^3) were obtained under the same experimental conditions using higher catalyst loading.

Chiral **L6**-Pd (II) complex gave moderate results in asymmetric Heck coupling reaction between iodobenzene **52a** and 2,3-dihydrofuran **55** (Scheme 42).[70] The best *ee*'s value of 89 % was obtained at 1 mol % of catalyst loading at 40°C in benzene. Although moderate yield was achieved even after 5 days. Working at higher temperature expectedly results in a significant acceleration of reaction rate but to the detriment of the *ee*. Using coordinating solvent such as N-methylpyrrolidinone gave higher reaction rate but only racemic product probably due to the displacement of P,N coordinated ligand **L6** by the solvent.



Scheme 42

Palladium-catalyzed asymmetric allylic substitution of 1,3-diphenylprop-2-enyl acetate **31** with the anion of dimethyl malonate was also reported (Scheme 19). The chiral phosphole-oxazoline ligand **L7c**[72] provided quite satisfactory catalytic activity and good enantioselectivity (89% *ee*) as well using 1 mol% of $[Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}Cl)]_2$ in THF as solvent. On the other hand, the planar chiral ferrocenylamine phosphole ligands **L9a-c** gave lower enantioselectivities (up to 67%) but higher activities for this model reaction (complete conversions in 30-90 min at room temperature in CH_2Cl_2 using BSA/AcOK as base).[74]

3.2. Bidentate phosphole-PR_3 ligands

Most of the bidentate phosphole-phosphine, -phosphite and -phosphoramidite ligands reported to date are C_1-symmetric chelating ligands based on chiral backbone **L10-L15** except the phosphole-phosphine ligands **L16** (Figure 5).

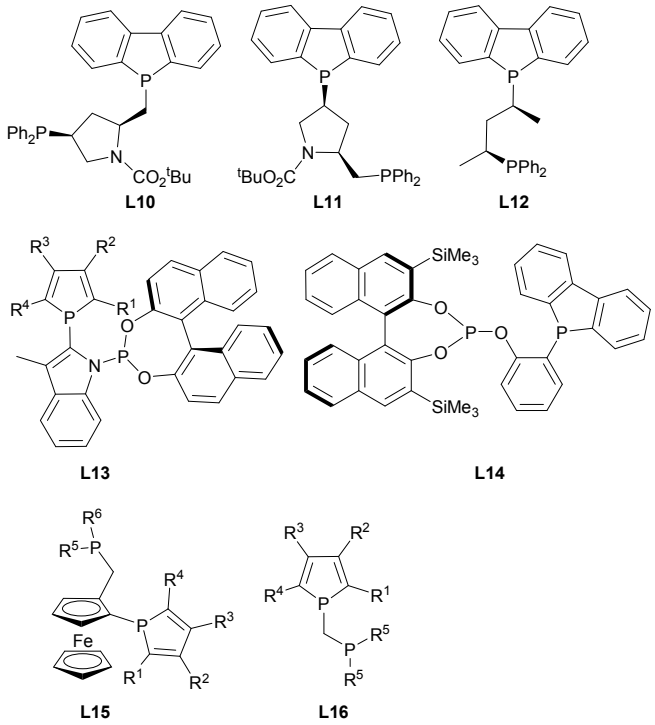
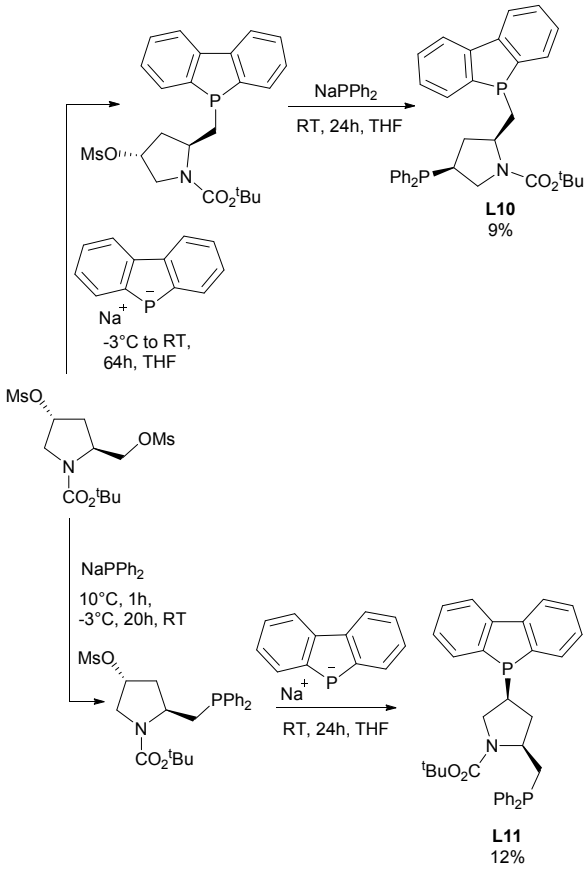


Figure 5: Bidentate phosphole-phosphine, -phosphite and -phosphoramidite ligands

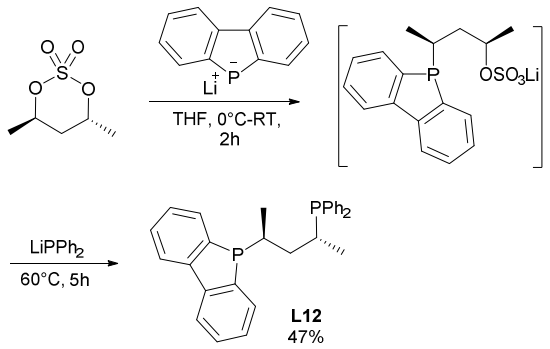
3.2.1. Synthesis

In an early work, Hegedus *et al.* have investigated the preparation of the benzophosphole-phosphine ligands **L10** and **L11** (Scheme 43) via two successive nucleophilic substitutions on a chiral dimesylate pyrrolidine derivative, leading to mixed phosphole-phosphine ligands in poor yields due to non-selective substitutions.[82]



Scheme 43

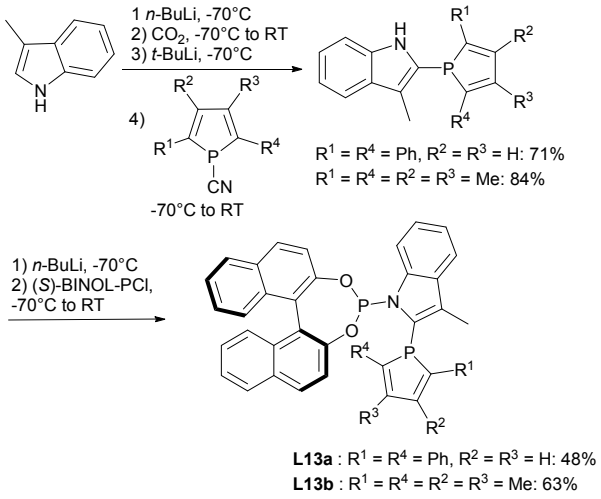
Another chiral dibenzophosphole-phosphine ligand based on 2,4-pentanediol skeleton, ligand **L12**, was prepared by Bakos *et al.* with a more convenient procedure from the cyclic sulfate of (*2R,4R*)-pentanediol (Scheme 44).[83]



Scheme 44

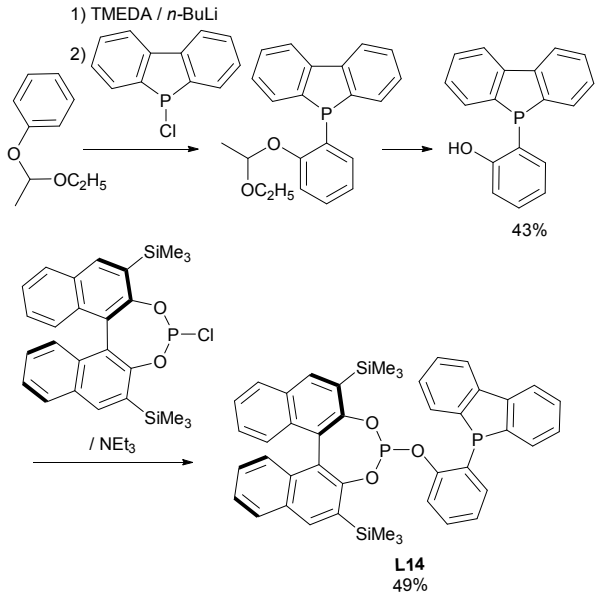
Axial chirality of the BINOL backbone was exploited for the design of chiral hybrid phosphole-phosphoramidite **L13** and phosphole-phosphite **L14** ligands.

L13a and **L13b** ligands, namely INDOLPhospholes, have been prepared by Reek *et al.*, in a two steps synthetic sequence from 3-methylindole, (*S*)-BINOL and the corresponding P-cyanophosphole (Scheme 45).[84]



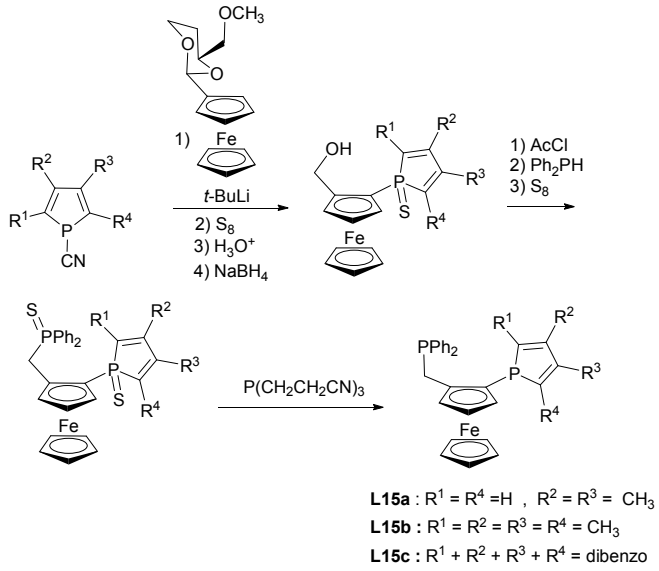
Scheme 45

Then, van Leeuwen synthesized the chiral dibenzophosphole-phosphite ligand **L14** from the condensation of phenol-dibenzophosphole derivative with chiral 3,3'-bis(trimethylsilyl)-2,2'-bisnaphthol phosphorochloridite in the presence of triethylamine (Scheme 46).[85]



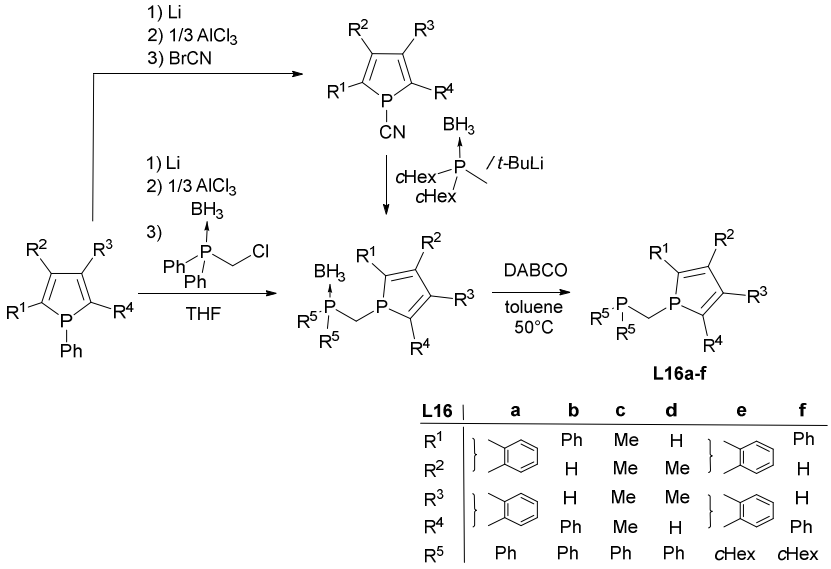
Scheme 46

The planar chirality of ferrocene was also used to prepare chiral phosphole-ferrocenylphosphine ligands **L15**. A family of ligands was synthetized by Gouygou and co-workers[86] via multistep procedures adapted from the synthesis of planar chiral ferrocenylamine phosphole ligands (Scheme 47).



Scheme 47

The same author has developed a small library of hybrid phosphole-methano bridged-phosphine ligands **L16a-f**, *via* P-C bond formation on the methano bridge, using electrophilic or nucleophilic phosphine borane building blocks (Scheme 48).[87] Both synthetic strategies allow access to **L16** combining different phosphole moiety to aryl and alkyl phosphino group, in moderate to good yields (18-67%).



L16	a	b	c	d	e	f
R^1		Ph	Me	H		Ph
R^2		H	Me	Me		H
R^3		H	Me	Me		H
R^4		Ph	Me	H		Ph
R^5	Ph	Ph	Ph	Ph	*c*Hex	*c*Hex

Scheme 48

3.2.2. Hydroformylation

Preformed [$PtCl_2$(**L10**)] and [$PtCl_2$(**L11**)] complexes were evaluated in asymmetric hydroformylation of styrene **6a** in the presence of $SnCl_2$ as co-catalyst.[82] These two catalysts gave higher regioselectivity in favor of the branched aldehyde **10b** than the diphenylphosphino analogue. It is interesting to note that the **L11**/Pt system is more efficient than the **L10**/Pt one in terms of conversion (65% *vs* 22%), regioselectivity (**10b** /**10l** : 1.35 *vs* 1) but less efficient in terms of enantioselectivity (12% *vs* 74%) under standard reaction conditions (1:1 H_2/CO, 165.4 bar, toluene, 60°C, 4h, substrate/Pt= 400). The observed enantiomeric excesses are not indicative of the intrinsic enantioselectivity of catalyst since racemization of the branched aldehyde **10b** can occur under catalytic conditions. Indeed in presence of triethyl orthoformate (2-4 equiv/equiv of styrene) to trap the aldehyde as acetal upon formation, excellent *ee*'s values (> 96%) were reached for both ligands without modification of the b/l ratios. Although the reactions were considerably slower and required longer reaction times (26% conversion in 114h with **L11**, 90% conversion in 115h with **L10**).

The exchange of a diphenylphosphino group for a dibenzophospholyl group has also had a favorable effect on the catalytic performance of ligand **L12** in the asymmetric hydroformylation of styrene.[83] Platinum catalyst, generated *in situ* by mixing [$PtCl_2(PhCN)_2$], 1.1 equiv. of (*2S*,*4S*)-**L12** and 1 equiv. of $SnCl_2$, showed higher catalytic performances in particular in terms of regio- and enantioselectivities (**9b**/**9l** : 56/44 vs 36/74, *ee*: 43% vs 26%) under standard conditions (H_2/CO (1:1), 70 bar, toluene, 70°C, 8h, substrate/Pt= 2000). A

remarkable increase in chemo-, regio- and enantioselectivities have been obtained at room temperature depending on the pressure and ratio of H_2/CO. The best catalytic performance was found under 195 bar of H_2:CO (2:1) (70% conversion in 45h, 94% aldehyde, **9b**/**9n** : 85/15, 89% *ee*). The rhodium-catalyzed hydroformylation of styrene, (*2S*,*4S*)-**L12** gave excellent chemo- and regioselectivities (100% aldehyde, 92/8 for **9b**/**9n** ratio) with slightly lower enantioselectivity than the diphenylphosphino analogous ligand (47% *vs* 54% *ee*).

The chiral dibenzophosphole-phosphite ligand **L14**[85] was also evaluated in asymmetric rhodium-catalyzed hydroformylation of styrene and vinyl acetate derivatives using [Rh(acac)$(CO)_2$]. Under standard conditions (H_2:CO (1:1), 20 bar, toluene, 60 °C, substrate/Rh = 1000, [L]/[Rh] = 5), total conversion was obtained with excellent regioselectivity in favor of branched isomer (>94%) but poor enantioselectivities (15-20% *ee* for styrene derivatives and 3% *ee* for the vinyl acetate derivatives). However, these selectivities (regio- and enantio-) are quite comparable to those obtained by other isostructural arylphosphine-phosphite ligands.

3.2.3. C-C coupling reactions

Palladium-catalyzed asymmetric allylic substitutions were studied with two different types of chiral ligands: phosphole-ferrocenyphosphine **L15** and INDOLPhosphole **L13**.

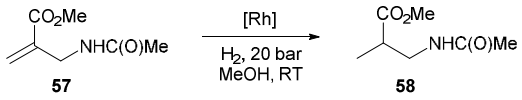
Planar chiral phosphole-ferrocenyphosphine ligands, **L15a-b**, showed high activities but moderate enantioselectivities (respectively 38% *ee* and 61% *ee*) in the palladium-catalyzed asymmetric allylic substitution of 1,3-diphenylprop-2-enyl acetate **31** with dimethyl malonate (Scheme 19) under standard conditions (1 mol% of $[Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}Cl)]_2$ as palladium precursor, BSA/AcOK as base, RT, CH_2Cl_2, 1h).[86]

INDOLPhosphole ligands **L13**, evaluated in the same conditions, also gave full conversion of the substrate in 1 hr with moderate enantioselectivities (respectively 32 and 56%), lower than INDOLPhos ligands bearing diaryl or dialkylphosphino groups. These ligands achieved poor to fair results with other substrates (1,3-dimethylprop-3enyl acetate, acetoxycyclohexene, cinnamyl acetate).

3.2.4. Hydrogenation/Hydroboration

Ligands **L16a** and **L16b** were applied to the Rh-catalyzed hydrogenation and hydroboration reactions.[87b] Rhodium complexes, preformed or prepared *in situ* by mixing $[Rh(\eta^4\text{-}COD)_2][BF_4]$ and **L16a** or **L16b**, catalyzed the hydrogenation of methyl 2-(acetamidomethyl)acrylate **57** at room temperature under 20 bar of H_2 (Scheme 49). **L16b**

formed the most robust catalyst which enables work at low catalyst loading of 0.25 mol% without significant decrease of the catalytic activity (91% yield).



Scheme 49

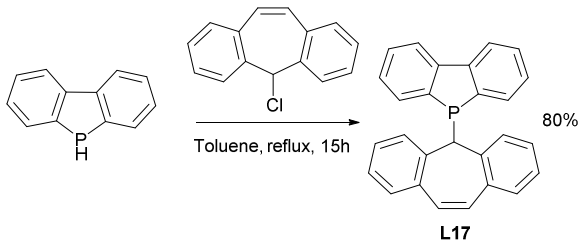
L16a-b-Rh complexes, prepared *in situ* with $[Rh(\eta^4\text{-}COD)_2][BF_4]$ and the ligand**,** also provided high activities in the hydroboration reactions of styrene **6a** with catecholborane (Scheme 40) but with low regioselectivity (54%) in favor of branched isomer compared to dppm (77%).

3.3. Bidendate phosphole based ligands bearing other coordinating groups

3.3.1. Phosphole/Olefin ligands

Le Floch and co-workers have developed mixed bidentate ligands combining phosphole and olefinic binding sites.

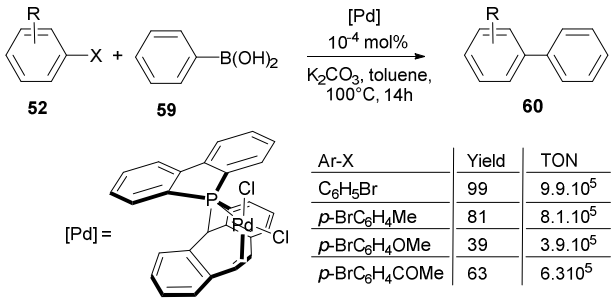
The synthesis of dibenzo[a,d]cycloheptenyl dibenzophosphole ligand **L17** was achieved through the reaction of secondary dibenzophosphole with chlorodibenzotropilydene (Scheme 50). [88]



Scheme 50

L17 has a rigid concave shaped binding site which coordinates palladium (II) through the phosphorus and the olefinic part in cis fashion giving stable neutral or cationic palladium (II) complexes combining a good σ-donor ability to favor the oxidative addition with a good π-accepting capacity to favor reductive elimination for Pd-catalyzed C-C coupling processes.

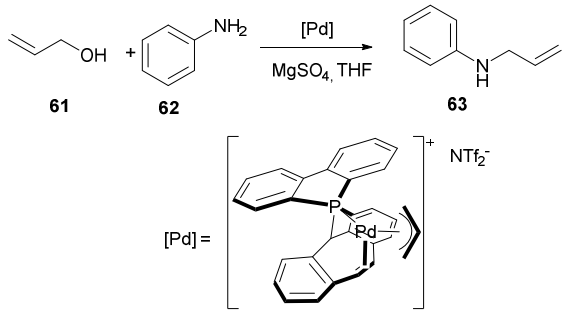
Indeed Suzuki cross-coupling reactions of bromoarenes **52** with phenyl boronic acid **59** in toluene at 100°C with K_2CO_3 as base and **L17**-Pd(II) provided a very impressive activity at very low loading of catalyst (10^{-4} mol%) with TON value up to $9.9.10^5$ (Scheme 51).[88] Cross-coupling reaction of chlorobenzene with phenyl boronic acid is more challenging and thus required higher catalyst loading (2 mol% of **L17**-Pd(II)) yielding only 32% of desired product.



Ar-X	Yield	TON
C_6H_5Br	99	$9.9.10^5$
p-BrC_6H_4Me	81	$8.1.10^5$
p-BrC_6H_4OMe	39	$3.9.10^5$
p-BrC_6H_4COMe	63	6.310^5

Scheme 51

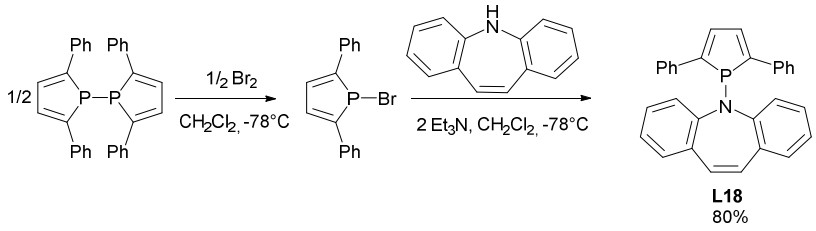
In another coupling reaction governed by the π-accepting capacity of ligand, **L17** allylpalladium(II) cationic complex with the Tf_2N^- counter-ion gave complete conversion of the allylic alcohol **61** (98%) in 24 h using 1 mol% of catalyst at room temperature with $MgSO_4$ as a water scavenger (Scheme 52).[16] Under the same reaction conditions, the triflate complex gave only a 20% conversion which is indicative of a strong counter–ion effect.



Scheme 52

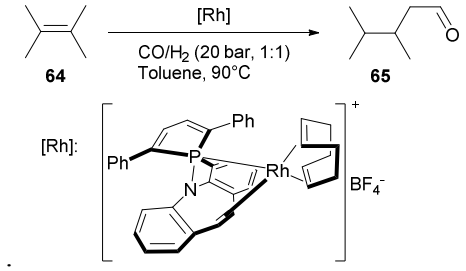
In 2006, the same group reported the synthesis of an analogous ligand bearing diphenylphosphole tethered to a dibenzoazepine moiety.[89] Ligand **L18** was prepared in a one

pot approach from 1,1'-bis(2,5-diphenyl phosphole) involving the cleavage of P-P bond with bromine, following by the addition of 10,11-dihydro-5H-dibenzo[b,f]azepine in presence of triethylamine (Scheme 53).



Scheme 53

L18 also behaves as a chelate by coordinating the phosphorus atom and the olefinic moiety to the rhodium center. The preformed **L18-**Rh(I) complex was found moderately active in the hydroformylation of olefins (styrene, cyclohexene, cyclooctene). In the more challenging isomerization/hydroformylation of tetramethylethylene **64** into 3,4-dimethylpentanal **65** (Scheme 54), **L18-**Rh complex catalyzed the transformation in mild conditions (at 90°C under 20 bar of CO/H_2) with a modest TOF.

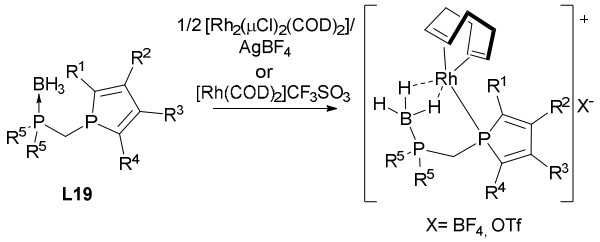


Scheme 54

3.3.2. Phosphole/BH_3 ligands

The hybrid phosphole-phosphine borane ligands **L19**, precursors of ligands **L16**, acts as a chelating P-(η^2-BH_3) ligand to afford an air stable cationic **L19-**Rh(I) complexes (Scheme 55), which provided active catalysts for hydrogenation and hydroboration reactions. These rhodium complexes, preformed or formed *in situ*, are catalytically active in hydrogenation of methyl 2-(acetamidomethyl)acrylate[87b] (Scheme 49). However, they required higher catalyst loading in comparison with the BH_3 free **L16-**Rh(I) counterparts suggesting the P-(η^2-BH_3)-

Rh bonding feature is maintained during catalytic cycle, as later supported by ^{31}P NMR spectroscopy for the reaction solution after catalysis.



Scheme 55

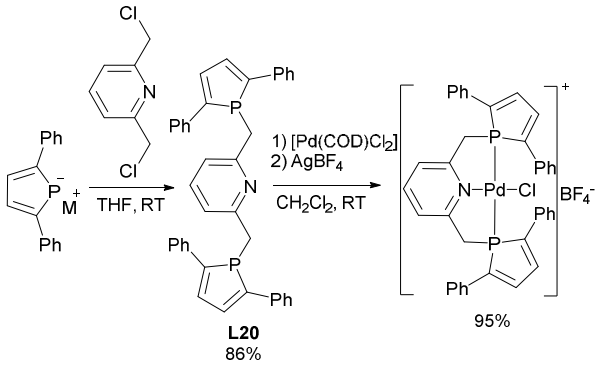
In the hydroboration of styrene **6a** (Scheme 40), **L19-**Rh(I) complexes are less active but seem to be more regio-selective.[87b] It is noteworthy that the nature of substituent on the phosphine-borane moiety has impact on the catalytic performance. For example, use of **L19f** ligand decreases the activity (57%) while the selectivity for branched isomer increases up to 65/35 ratio.

3.4. Multidentate phosphole-based ligands

The development of multidentate ligands incorporating phospholes has gained attention of several research groups.

3.4.1. Tridentate phosphole-based ligands

Le Floch prepared a tridentate P,N,P ligand, **L20,** based on a central pyridine unit connected by a methylene group to 2,5-diphenylphosphole rings. This rigid pincer ligand was very attractive for the elaboration of robust catalysts due to its low sensitivity towards oxidation and its high thermal stability. It was prepared according to a classical nucleophilic substitution reaction between the 2,5-diphenylphospholide anion and the 2,6-bis(chloromethyl)pyridine (Scheme 56).[90]

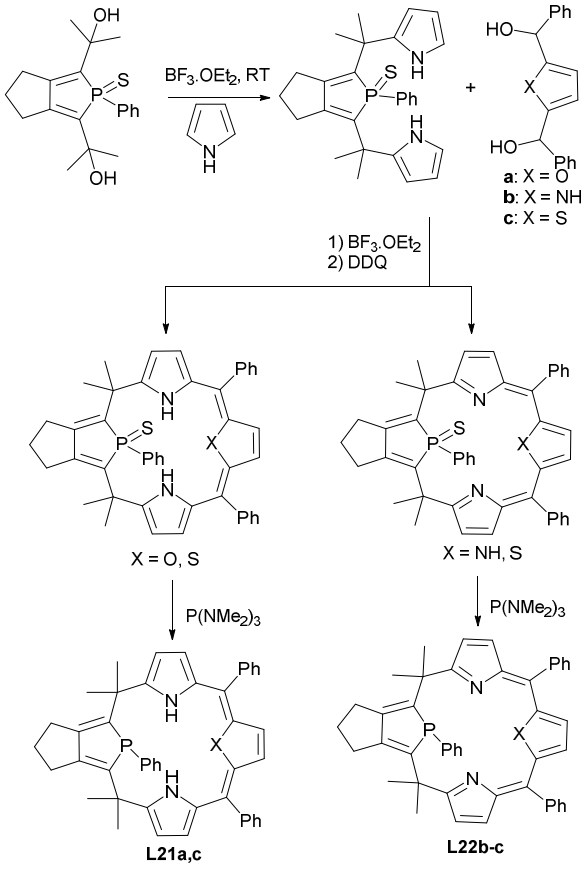


Scheme 56

The corresponding cationic palladium (II) complex, engendered from the reaction of **L20** with $[Pd(COD)Cl_2]$ precursor in presence of chloride abstractor $AgBF_4$ was evaluated in Miyaura cross-coupling reactions between haloarenes and pinacolborane (Scheme 41). Iodoarenes were easily converted at 80°C in dioxane using 0.001 mol% catalyst loading and triethylamine as base (TON up to 100.10^3), while bromoarenes required higher catalyst concentration (0.01 mol%) in order to give satisfactory conversions (55-86%) and TON (55-89.10^2). The high TONs obtained with **L20**-Pd complex as catalyst are comparable to those of obtained with **L5**-Pd complex in this Miyaura cross-coupling process.

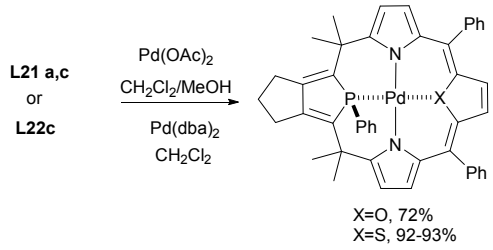
3.4.2. Tetradentate phosphole-based ligands

Matano *et al.* were interested in the synthesis of macrocyclic phosphole-containing hybrid calixphyrins combining P,N_2,X-mixed donor ligands (X= O, S, N) as hemilabile and redox-active ligands.[91] The 5,10-porphodimethene type 14π-$P,(NH)_2,X$- **L21** and 16π-P,N_2,X-hybrid calixphyrins **L22** (X = O, S, NH) are prepared in poor to moderate yields (5-30%) *via* Lewis acid-promoted dehydrative condensation between a σ^4-phosphotripyrane and the corresponding 2,5-bis[hydroxyl(phenyl)methylheteroles, followed by oxidation with 2,3-dichloro-5,6-dicyanobenzoquinone and desulfuration with $P(NMe_2)_3$ (Scheme 57).



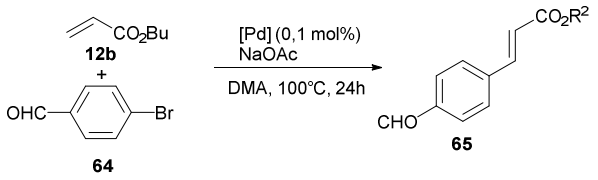
Scheme 57

Square planar calixphyrin-Pd(II) complexes have been obtained either by complexation of **L21a,c** with $[Pd(OAc)_2]$ or **L22c** with $[Pd(dba)_2]$, which is indicative of electron transfer between the π-conjugated N-S-N unit and the palladium center (Scheme 58),. These palladium complexes exhibit the hemilabile nature of phosphole-containing hybrid calixphyrin plateform since the dissociation of the furan/thiophene and pyrrole rings take place to generate vacant coordination sites at the metal center accompanied by the reduction of the palladium from +2 to 0 valent state and the oxidation of N-X-N unit from 16 π to 14 π electrons.



Scheme 58

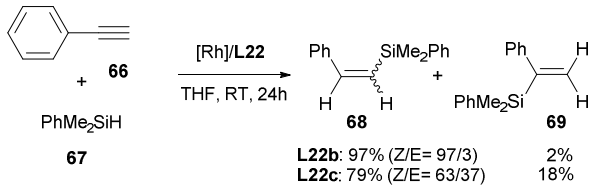
They were used in Pd-catalyzed Mirozoki-Heck reaction. Both **L21a**-Pd(II) and **L21b**-Pd(II) complexes catalyzed coupling reaction of *p*-bromobenzaldehyde **64** with n-butyl acrylate **12b** (Scheme 59) in DMA at 100°C to give the desired product **65** in 68 and 98% yields respectively (TON= 680-980 after 24h).



Scheme 59

The **L22**-Rh complexes, generated *in situ* with $[RhCl(CO)_2]_2$, were tested in the hydrosilylation of acetophenone and phenylacetylene. The hydrosilylation of acetophenone **49c** (Scheme 39) with Ph_2SiH_2 in presence of **L22b**/$[Rh(Cl(CO)_2]_2$ (0.5/0.25 mol%) in THF for 6h at room temperature gives 91% of the 1-phenylethanol **50c** after hydrolysis. When **L22c** was used in place of **L22b**, the rate of hydrosilylation was dramatically accelerated (87% yield after 0.5h).

The high catalytic activity of **L22**/$[Rh(Cl(CO)_2]_2$ system was also reached in the hydrosilylation of phenylacetylene **66** with $PhMe_2SiH$ **67** which resulted in the formation of a mixture of styrylsilanes **68** and **69** (Scheme 60). A high Z/E selectivity (97/2) as well as a high β/α selectivity were achieved in the reaction with **L22b** implying that the catalyst operates as a totally neutral Rh complex. Lower selectivities observed for the reaction using **L22c** suggest that the rhodium center in the catalyst possess a cationic character (to some extent).



Scheme 60

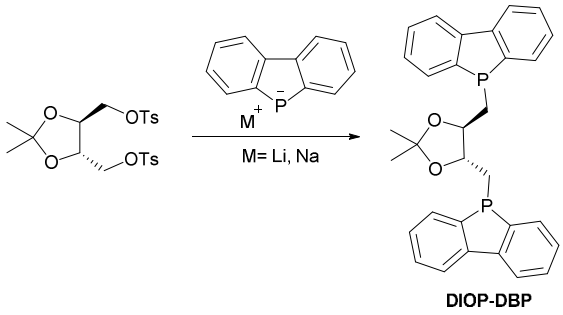
4. Diphosphole-based ligands

Diphosphines play a dominant role as P,P ligands in homogeneous transition metal catalysis, especially chiral diphosphines which proved to be one of the most successful and widely used ligands for transition metal catalyzed asymmetric synthesis. As phospholes have proven to be efficient ligands in homogeneous catalysis, they have been used for the design and synthesis of new diphosphine ligands based on chiral or achiral backbone.

4.1. Diphospholes with chiral backbones

4.1.1. Synthesis

The first chiral diphosphole ligand **DIOP-DBP** was developed independently by Kagan[92] and Tanaka[93] in 1975 by replacing the DIOP's diphenylphosphino groups with dibenzophosphole residues. The synthetic approach involves the addition of a phospholyl anion on the ditosylate derivative (scheme 61).



Scheme 61

This synthetic pathway was then generalized to become the method of choice for preparing different chiral diphospholes. By varying the nature of the chiral ditosylate (dimesylate) derivative, the **cyb-DBP** and **cyb-DBP** [94], **Bco-DBP**[95], **Skewphos-DBP**[96,97] and **BPPM-DBP**[82] were synthesized (Figure 6). Changing the phospholyl anion provided access to ligands **DIOP-TPP**[98] and **BPPM-TPP**.[99] In addition, immobilization of **DIOP-DBP** and **BPPM-TPP** *via* covalent bonding onto polymer and carbon nanotubes respectively has been performed (Figure 6).

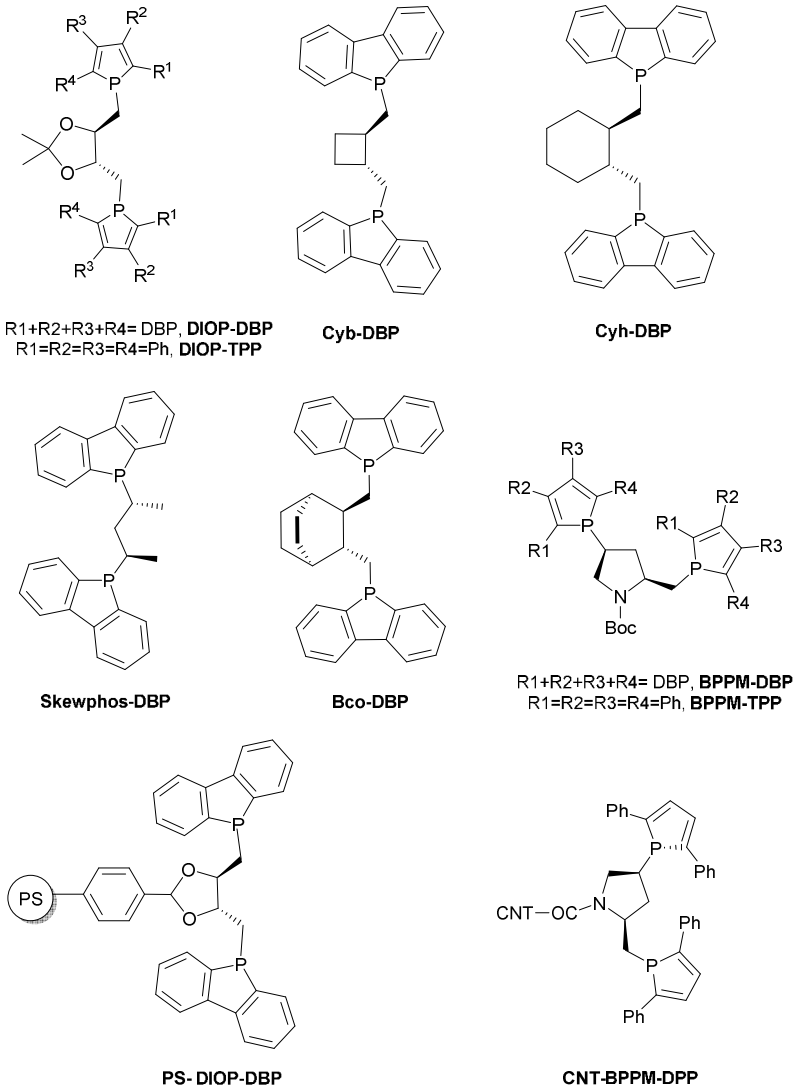
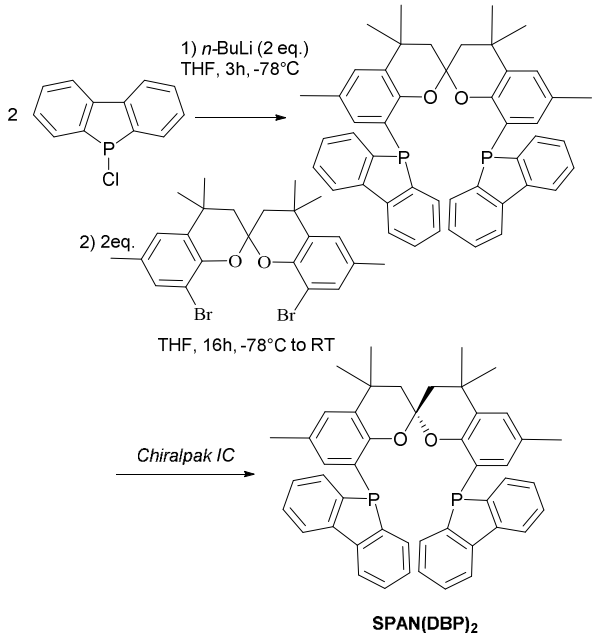


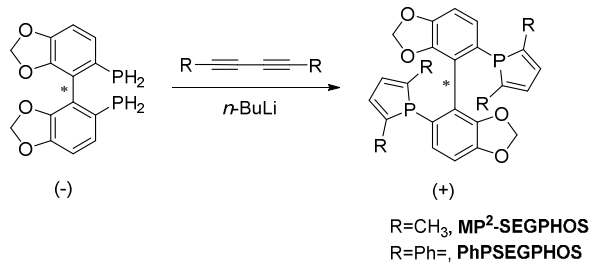
Figure 6 : Chiral diphosphole ligands

Two other types of chiral diphospholes have been prepared by different procedures. The enantiopure SPANphos ligand bearing dibenzophosphole moiety, **SPAN(DBP)$_2$**, has been synthetized by reaction of the chlorodibenzophosphole with a dilithio compound and a subsequent separation of the enantiomers by semipreparative chiral HPLC (Scheme 62). [100]



Scheme 62

Chiral phosphole ligands, analogous to the SEGPHOS chiral phosphine, namely **MP^2-SEGPHOS** and **Ph-SEGPHOS**, have been obtained by a double condensation of diyne with the enantiopure ((-)-4,4'-bi-1,3-benzodioxole)5,5'-diylbisphosphine in a presence of *n*-butyllithium (Scheme 63).[101]



Scheme 63

4.1.2. Hydrogenation

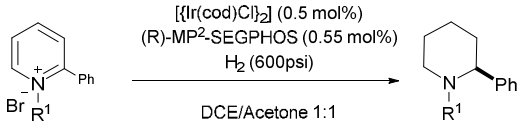
The preliminary asymmetric hydrogenation was performed with **DIOP-DBP** rhodium systems. However, the enantioselectivities obtained for hydrogenation of various dehydroamino acids in standard conditions were lower than those of the DIOP ligand.[92,93]

Diphospholes **Cyb-DBP** and **Cyh-DBP** have been applied in the asymmetric hydrogenation of (Z)-α-acetamidocinnamic acid **4** (Scheme 9) with enantiomeric excess lower than the phosphine analogues but similar to those observed with **DIOP-DBP**.[102] Better results in terms

of enantioselectivity were obtained with **DIOP-TPP-**Rh catalyst, isolated or preformed *in situ* from both $[Rh(cod)_2]BF_4$ or $[Rh(cod)(acac)]BF_4$. These systems are able to hydrogenate **4** under 3 bar of H_2 at room temperature with 70% *ee*.[103] It is interesting to note that (*R,R*)-**DIOP-TPP** leads to the (*S*) enantiomer of N-acetylphenylalanine **5** whereas the (*R,R*)-DIOP analogue leads to the (*R*) enantiomer.

Recently, the chiral **BPPM-DPP-**rhodium complex covalently anchored to the surface of carbon nanotube has demonstrated its ability to hydrogenate **4** (5.5 atm of H_2, at RT in MeOH using 0.5 mol% of catalyst) with moderate enantioselectivity (54%).[99] Recycling this catalyst has not yet been reported.

MP^2-SEGPHOS was also reported in Rh-catalyzed asymmetric hydrogenation of **4**, with moderate enantioselectivity (60% *ee*).[101] It is only very recently that highly efficient selective catalysts for asymmetric hydrogenation have been reported with diphosphole ligands. Indeed **MP^2-SEGPHOS** and **PhP-SEGPHOS** iridium systems have successfully catalyzed the hydrogenation of 2-substituted pyridinium salts (Scheme 64).[104] **MP^2-SEGPHOS** proved to be highly efficient and more selective than **PhP-SEGPHOS** and the others classical SEGPHOS ligands for the reduction of a wide range of pyridinium substrates in good to excellent yields and enantioselectivities using 0.5 mol% of iridium precursor and 0.55 mol% of ligand. N-substituents could be declined using benzyl, paramethoxybenzyl, ethyl or isopropyl. The corresponding 1,2-substituted piperidines could be obtained in excellent yields (57-97%) and with enantiomeric excess over 95% *ee* (Scheme 64). The reaction was shown, also, to tolerate different groups in the 2-position. Aryl groups with electron withdrawing or donating substituents led to excellent yields and enantiomeric excess (yields above 88% and excess above 90% *ee*). Some limits appeared when 2-alkyl substituted pyridinium salts were reduced (24% yield and 69% *ee* with isopropyl group in position 2).



R^1	Yield (%)	*ee* (%)
a : Bn	97	96
b : PMB	92	95
c : Me	57	86
d : iPr	82	96

Scheme 64

These exceptional catalytic activities and chiral inductions, probably due to the ability of phospholes to bring both unusual electronic properties and rigidity to provide a well defined chiral pocket and really active catalyst, is the unique example of chiral-phosphole-based ligand for highly efficient asymmetric hydrogenation.

4.1.3. Hydroformylation

Most of the DBP based diphospholes have been applied in asymmetric hydroformylation of alkenes.

In an early work, Tanaka *et al.* showed the superiority of the **DIOP-DBP** in terms of regioselectivity and enantioselectivity compare to the DIOP for Rh-catalyzed hydroformylation reactions of styrene, 1-butene and *cis* 2-butene.[93] However, the enantioselectivities remained low (37% *ee* for styrene). The efficiency of the **Cyb-DBP** or **Cyh-DBP** ligands was also examined in the same reactions without improved enantioselectivities.[64,102] However it should be noted that replacement of PPh_2 by phospholyl moiety induced in all cases an inversion of configuration of the branched aldehyde.

DIOP-DBP-Rh systems have been explored in asymmetric hydroformylation of various substrates such as N-vinylimides[105], N-acyl-2-pyrrolidines,[105] vinylacetate[106] and vinyl propionate.[102] Enantioselectivities still slightly higher than the DIOP were observed but the asymmetric induction has never been higher than about 50% *ee*, the highest enantiomeric excess being achieved in the hydroformylation of vinyl acetate.

The efficiency of DBP based-diphospholes was examined in parallel in Pt-catalyzed hydroformylation of styrene and a few other olefins. If the [$PtCl_2$(**DIOP-DBP**)] complex has not been very effective in the hydroformylation reactions of styrene and butene derivatives (*ee* up to 22%),[107] more interesting results were obtained in presence of $SnCl_2$ and H_2O additives. Good enantioselectivity (73%) and regioselectivity (82%) in favor of the branched aldehyde were obtained using [$PtCl_2$(**DIOP-DBP**)]/$SnCl_2$ system at 40-60°C, under 220.5 bar of H_2/CO (2.4/1).[108] Under same conditions, [$PtCl_2$(**BCO-DBP**)]/$SnCl_2$ system exhibited improved enantioselectivity (86% *ee*) for styrene and moderate enantioselectivity (67% *ee*) for 1-butene.[95,109]

For other styrene derivatives bearing electron donating groups, **Skewphos-DBP** provides higher branched aldehyde selectivity but lower enantioselectivity than the phosphine analogue (b/l =8.2 *vs* 0.42, *ee*= 26% *vs* 75%) in Pt-Sn catalyzed hydroformylation conducted with 0.1 mol% of catalyst in toluene at 20°C under 70 bar of CO/H_2.[97]

The non C_2-symmetric ligand **BPPM-DBP** has been applied in Pt-Sn catalyzed hydroformylation of various vinyl aromatic compounds.[82] Hydroformylation of styrene with [$PtCl_2$(**BPPM-DBP**)]/$SnCl_2$ system led to excellent enantioselectivities (> 96%) under standard conditions (1:1 H_2/CO, 165.4 bar, 60°C, toluene) in the presence of 4 equiv. of triethyl orthoformate. This catalytic system gave higher regioselectivity in favor of the branched aldehyde than the mixed ligand DBP-PPh_2 and the PPh_2 analogue. In the same catalytic conditions, precursors of 2-arylpropionic acids such as ketoprofen, fenoprofen, naproxen, tiaprofenic and indoprofen were efficiently hydroformylated with excellent chemoselectivities for aldehyde (> 90%) and enantiomeric excess (> 96%) (Figure 7), the b/l ratios depending strongly on the aromatic substituents.

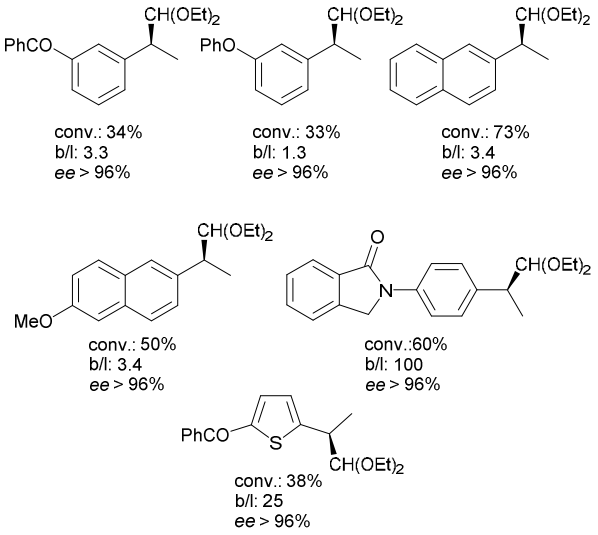
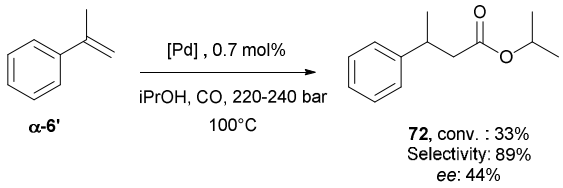


Figure 7

Finally, we can mention the work done by Still and co-workers in asymmetric hydroformylation using **DIOP-DBP** grafted on styrene polymers and styrene-divinylbenzene copolymers. The copolymer-supported Rh system catalyzed the hydroformylation of styrene in 12h under 96.5 bar (1:1 H_2/CO) at 80°C affording complete selectivity to aldehyde, high isomer b/l ratio (b/l: 17), but poor asymmetric induction (6% *ee*).[110] Better results were obtained in Pt-catalyzed hydroformylation of styrene and vinyl acetate using the supported **DIOP-DBP** catalysts.[111] Indeed, the Pt-Sn immobilized systems showed comparable rates and gave nearly the enantioselectivities as the homogeneous analogue (around 56-65% *ee*). In addition, the soluble polymer-supported catalyst could be recovered by precipitation with diethyl ether and filtration, and reused without any loss in terms of both rate and selectivity.

In the same way, recycling of the cross-linked copolymer was achieved by simple filtration with slight loss in rate but no loss in selectivity.

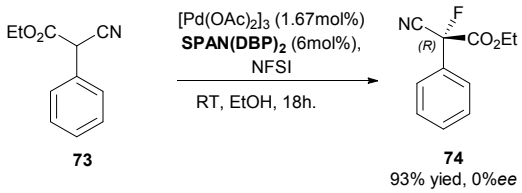
The complementary palladium catalyzed-alkoxycarbonylation have been explored with **Cyb-DBP**, **Cyh-DBP** and **DIOP-DBP** /[$PdCl_2(PhCN]_2$ systems. Among the systems tested, DIOP/Pd system gave the best results for the methylstyrene alkoxycarbonylation (89% selectivity, 44% *ee*), and showed a slight superiority over similar phosphine systems (Scheme 65). [94,112]



Scheme 65

4.1.4. Fluorination

The enantiopure **SPAN(DBP)$_2$** recently reported by van Leeuwen and coworkers was applied in palladium-catalyzed fluorination of ethyl 2-cyano-2-phenylacetate **73** (Scheme 66).[100] In presence of $[Pd(OAc)_2]_3$/**SPAN(DBP)$_2$** catalytic system, and NFSI as fluorine donor, complete conversion and high yield (93%) were obtained in EtOH at RT in 18h but the reaction was not enantioselective since only racemic mixture **74** was produced. For comparison, the diphenylphosphine analogue also gave a total conversion, high yield (97%) and high enantioselectivity (78% *ee*) under the same conditions.



Scheme 66

4.2. Diphospholes with achiral backbones

The diphospholes with achiral backbones reported to date can be divided into two categories; diphospholes based on various C_n-backbones and the diphospholes based on a xanthyl backbone (Figure 8).

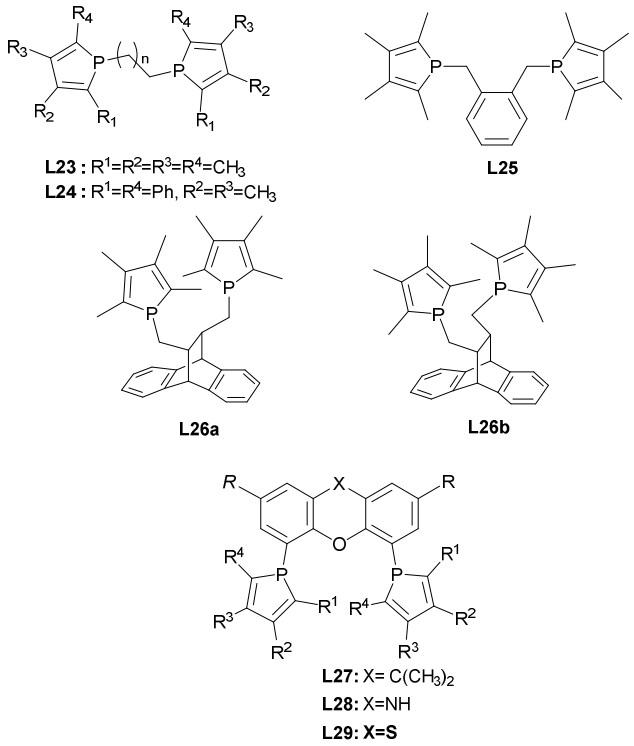
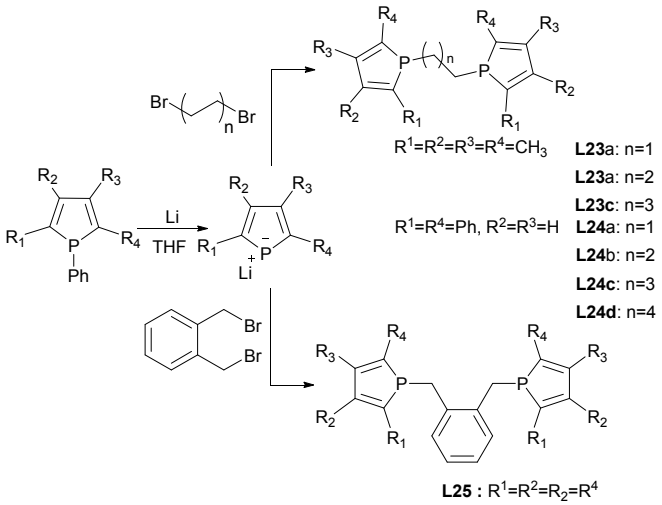


Figure 8: diphospholes with achiral backbone

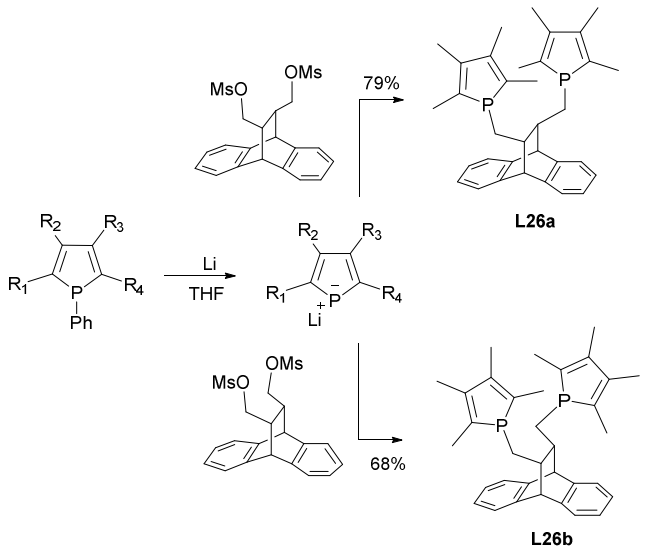
4.2.1. Diphospholes based on C_n-backbones

4.2.1.a. Synthesis

Several C_n-bridged di(phospholes) ligands **L25-27** have been prepared according to the procedure outlined in Schemes **67** and **68**. Ligands **L23**[113], **L24**[114] and **L25**[113] were synthetized by quenching a THF solution of phospholyl lithium with the corresponding 1,n-dibromoalkanes (Scheme 67) while the anthracene-bridged diphosphole ligands **L26a-b**[113] were prepared by reacting the corresponding dimesylate with 2,3,4,5-tetramethylphospholyl lithium (Scheme 68).



Scheme 67



Scheme 68

4.2.1.b. Pd-catalyzed copolymerization

L23, **L25** and **L26** have been investigated in the Pd-catalyzed copolymerization of ethylene and carbon monoxide (Scheme 37).[113] Under 20 bar of CO/ C_2H_4 at 90°C in MeOH in presence of $MeSO_3H$, **L23b**, **L25** and **L26a-b/** Pd(II) complexes, preformed or prepared *in situ* with $[Pd_3(OAc)_6]$, have been found to be active. However, catalytic system based on **L23a** and **L23c** are inactive probably due to the inability of these ligands to form stable chelates at Pd (II). From this series of ligands, **L25** provided a highly productive catalytic system and was more active than the dppp, its PPh_2 analogue, (46.3 *vs* 33.1 kg of polyketone/mol of cat/h). It generated high molecular weight polymers (M_w=14400,

M_n=8530) with narrow molecular weight distributions (M_w/M_n=1.7). It is also interesting to note the marked influence of the nature of the four carbon-tether on the productivity and the degree of polymerization. **L26b** gives less active catalyst than those obtained with **L26a** (20.6 *vs* 9.5 kg of polyketone/mol of cat/h and n=80 *vs* 50).

On the other hand, Fagan showed that **L23a** cationic palladium complex, [Pd(**L23a**)Me]SbF_6, provides an acid free catalytic system for the copolymerization ethylene and carbon monoxide.[115] This system is able to produce 28 kg of polyketone per mole of catalyst per hour (M_w=236000, M_w/M_n=5) under 45 bar at 100°C over 18h.

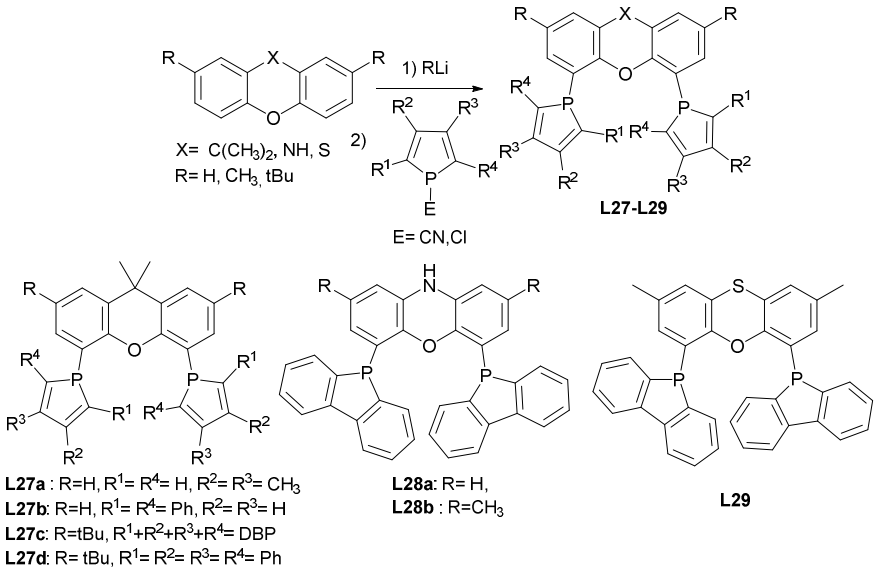
4.2.1.c. Pd-catalyzed allylation of primary amines

Among the ligands **L24**, **L24a** and **L24b** were the only ones to be studied in the Pd-catalyzed allylation of aniline described previously (Scheme 19). Under the same conditions as those used with the **TPP** ligand, the **L24b**-Pd-allyl complex showed a moderate activity (73% conversion in 24h), lower than those of **TPP**-Pd allyl complex, while the **L24a**-Pd-allyl complex was inactive.[16]

4.2.2. Diphospholes with Xanthyl backbone

4.2.2.a. Synthesis

In order to design new diphosphines with wide natural bite angles for application in hydroformylation reactions, van Leeuwen *et al.* have developed diphospholes by introduction of a dibenzophosphole moiety on the xanthene backbone[116,117] Le Floch *et al.* further synthesized other Xantphos-phosphole derivatives by the variation of the phospholyl groups.[118] The syntheses of these ligands were performed *via* the conventional method by reaction of the 4,5-dilithium salt of xanthenes derivatives with the corresponding P-chloro phosphole or P-cyanophosphole (Scheme 69).

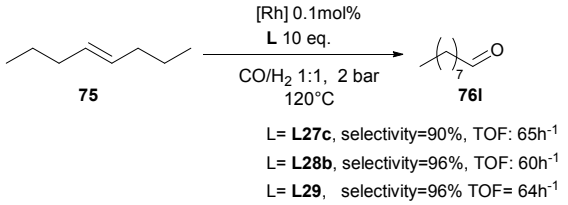


Scheme 69

The phosphole-based Xantphos ligands **L27-L29** combine the wide bite angle offered by the xanthene heterocycle (wide natural bite angles of 111.8, 121.4, 124,3 and 128.9° for **L29**, **L27c**, **L27d** and **L28b** respectively) with the rigidity and unusual electronic properties of the phosphole ring.

4.2.2.b. Hydroformylation

The specificity of the dibenzophospholyl-substituted Xantphos ligands is to form $[Rh(CO)_2(P\text{-}P)]_2$ dimer complexes, which are catalytically inactive under hydroformylation conditions but in equilibrium with $[RhH(CO)_2(P\text{-}P)]$ active complexes under syn gas atmosphere. Xantphos-derived diphospholes **L27c**, **L28b** and **L29**, have mainly found applications in the rhodium-catalyzed hydroformylation of octenes. Moderate activities but high selectivities have been recorded for the hydroformylation of 1-octene **1d** into linear aldehyde **3dl** (Scheme 8) at 80 °C and 20 bar of CO/H2 (1:1) using a 0.1 mol% of rhodium catalyst prepared from $[Rh(acac)(CO)_2]$ and 5 equiv. of ligand. These moderate activities, resulting from the preferred formation of the rhodium-dimer resting state, are similar or higher than those of the diphenylphosphino-substituted parent ligand**.** However, **L27c**, **L28b** and **L29** (10 eq.) combined with 0.1 mol% of $[Rh(PPh_3)_3H(CO)]$ exhibit unprecedented high selectivity in the isomerisation-hydroformylation process of *trans* 4-octene **75** into *linear* nonanal **76l** with acceptable activities (Scheme 70) at 120 °C under 2 bar of 1:1 CO/H_2.[117]

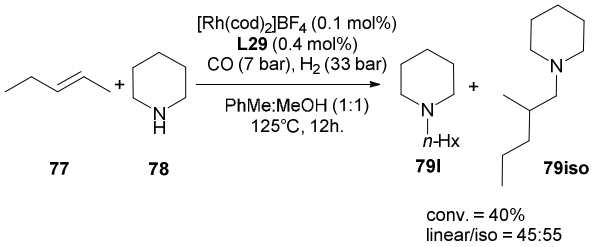


Scheme 70

The high selectivity of **L27c** is also pronounced in the hydroformylation of *trans* 2-octene into linear nonanal (90% of linear aldehyde). These excellent performances in the hydroformylation of internal octenes have been attributed by both the low phosphine basicity, leading to the required high isomerization, and the wide natural bite angles of the ligands inducing the high selectivity for linear aldehyde formation.

4.2.2.c. Hydroaminomethylation

Beller and coworkers have also used phosphole based Xantphos ligand **L29** in the hydroaminomethylation of pent-2-ene **78** and piperidine **79** (Scheme 71).[119] **L29-**rhodium catalytic system showed high selectivities in amine **80** (96%, l:b = 45:55) and no enamine formation indicating that the catalyst is particularly active in the hydrogenation step. However the rather low conversion reported for **L29** (20% in 12h) relative to the other phenoxaphosphino-modified Xantphos-type ligands was attributed to slow catalyst pre-formation and demonstrates the importance of the nature of the phosphorus substituents as well as the ligand backbone.

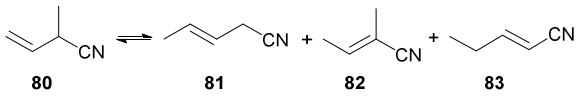


Scheme 71

4.2.2.d. Isomerization

L27c has been evaluated in Ni(0)-catalyzed isomerization of 2-methyl-3-butenenitrile **80** (Scheme 72).[120] **L27c**-Ni complex, prepared *in situ* using [Ni(COD)$_2$] as precursor, showed moderate activity in toluene at 90 °C (30% of conversion in 1 h) and moderate selectivity of

the desired 3-pentenenitrile **81** (32.5%) in comparison to tBuXantphos (97 % conversion, 65% of **81**) probably due to a too high ligand rigidity. In fact, **L27c** yielded a high proportion of the thermodynamic product **83** due to the irreversible formation of stable alkylnickel complexes with this internal alkene which causes the catalyst deactivation and explains the low conversion obtained.

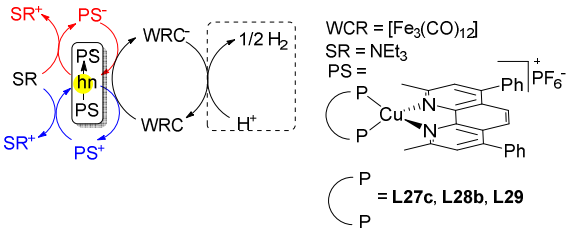


		Selectivity (%)		
Ligand	Conv. (%)	**81**	**82**	**83**
L27c	30	32.5	7.9	59.6
tBu-Xantphos	97	64	7.9	27.6

Scheme 72

4.2.2.c. Photocatalytic reduction

Dibenzophosphole-based Xantphos ligands have recently found another catalytic application as active copper-based photosensitizers in the photocatalytic hydrogen generation from water under basic conditions (Scheme 73). Cationic copper(I) complexes combining **L27c**, **L28b** and **L29** with a bathocuproine as N,N ligand promoted proton reduction under Xenon light irradiation at pH=11.5 and room temperature using $[Fe_3(CO)_{12}]$ as water reduction catalyst, and triethylamine as sacrificial reductant.[121] Whereas **L28b** and **L28b** based-copper complexes showed low to moderate activities with turnover numbers (TON) of 150-397 (equiv. of H/equiv. of Cu), the electron enriched **L29** provided a higher active photosensitizer copper complex that is able to produce up to 34 mL of H_2 in 18h (TON= 797). Actually, this system performs better than the previously described noble metal based photosensiters.



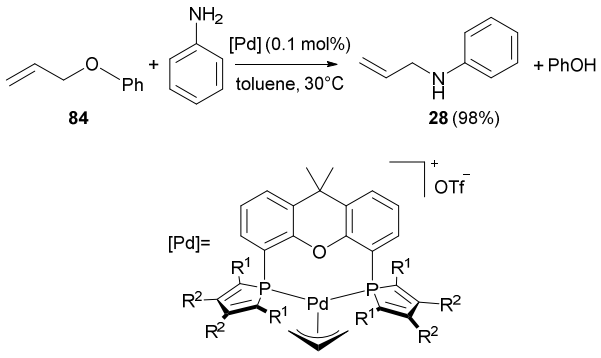
Scheme 73

4.2.2.f. Miscellaneous reactions

Other Xanthphos derived diphospholes, **L27a and L27b** have shown good performances in nickel-, palladium-, platinum- and gold-catalyzed reactions.

Ni(II)-complex obtained only with Xanthphos-phosphole ligand **L27a** demonstrates high activity and selectivity in ethylene dimerization (Scheme 37). Reactions conducted in toluene at 20°C in the presence of methylaluminoxane as co-catalyst (300 equiv.) under an ethylene pressure of 30 bar afforded 97% of C_4 in 30 min with 90% selectivity in 1-C_4.[122] This catalytic system is more selective (90% of 1-C_4 *vs* 80%) than the Ni complex with 1-(2-pyridyl)phosphole **L4** but less active (TOF of 43 000 *vs* 56 150.mol(C_2H_4).mol^{-1}[Ni].h^{-1}).

L27a-b-Pd cationic complexes, in particular the one containing the ligand **L27b**, exhibit high catalytic activities in the allylation of aniline with allyl alcohol in mild conditions (100% conversion in 1h using 1 mol% of catalyst in toluene at room temperature) without additives (Scheme 17).[118] The catalyst performance of **L27b** could be later extended to Pd-catalyzed-deallylation of various alkyl allylethers.[123] The deallylation of allylether **84** (Scheme 74) occurs in 98% yield with 0.1 mol% of catalyst loading at room temperature within 40 min whereas longer reaction times (1-4h), heating (50°C) and higher loading of catalyst (1 mol%) were needed to reach completion with other alkyl derivatives.

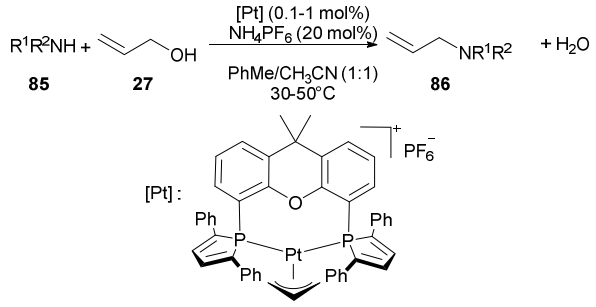


Scheme 74

This catalytic activity has been attributed to a perfect combination between a large P-Pd-P bite angle which enhances the reactivity of the allyl ligand, and an exceptional π accepting properties offered by the phosphole moiety which allows the easy formation of 14 electrons Pd-active species involved in the catalytic cycle. [123]

When using **L27b**-Pt(II) allyl complex, the scope of amine could be extended to a broad variety of alkyl amines and aryl amines (Scheme 75).[124] This system performs well even at

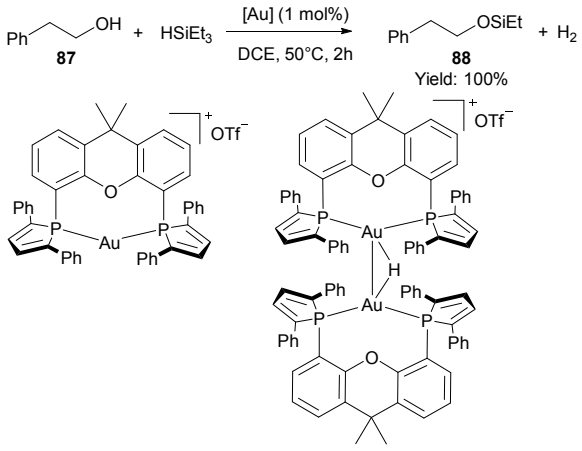
0.1-1 mol% of catalyst loading, at low temperatures (30–50°C), in presence of catalytic amount of NH_4PF_6 as protons source and with high selectivity for the desired mono-allylamine product (Scheme 75).



Scheme 75

Theoretical studies showed that the Pt-catalyzed allylation of amine occurs by a catalytic cycle different from that of Pd. It also emphasized the importance of a large bite angle of the ligands to prevent formation of cationic platinum hydride complexes on protonation which could eventually lead to deactivation of the catalyst.

Mononuclear cationic complexes [Au(**L27b**)][X] (X= BF_4, PF_6, OTf and NTf_2) and a dinuclear cationic gold hydride complex [Au_2-(**L27b**)$_2$(H)]OTf, formally resulting from the stabilization of the gold hydride complex by the [Au(**L27b**)],[125] proved to be highly active in the dehydrogenative silylation of 2-phenylethanol **87** at 50°C in 1,2-dichloroethane within 2h (Scheme 76).[126]



Scheme 76

These results validated the hypothesis of "Au_2H^+" species as an intermediate during the catalytic cycle.

5. 2,2'-Biphosphole-based ligands

2,2'-Biphospholes belong to the *tropos*[127] class of phosphorus ligands. Although recently applied to molecular materials,[128] they were originally designed as ligands for metal-catalyzed reactions. The promising performances of the chiral stereochemically dynamic 2,2'-biphosphole ligand (BIPHOS) in asymmetric catalysis encouraged the development of new derivatives of 2,2'-biphosphole ligands: diphosphines **L30** and diphosphinites **L31** (Figure 10). Alternatively, the 2,2'-biphosphole moiety was used for the synthesis of macrocycles of variable ring sizes. Among them, a ten-membered tetraphosphole macrocycle **L32** (Figure 10) showed interesting catalytic performances.

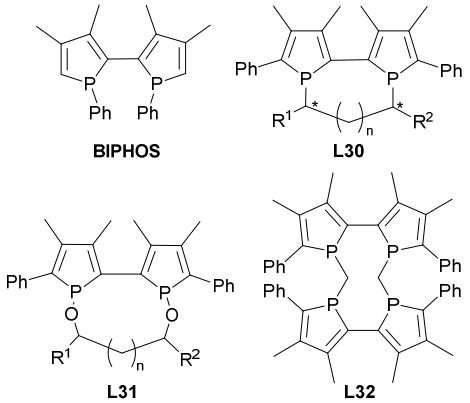
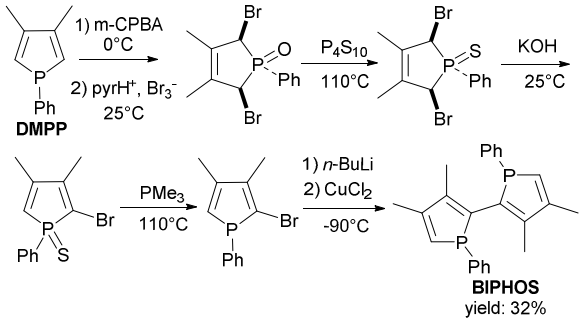


Figure 10 : 2,2'-biphosphole based ligands used in catalysis

5.1. 2,2'-biphosphole (BIPHOS)

The first example of 2,2'-biphosphole type-ligands, the 1,1'-diphenyl-3,3',4,4'-tetramethyl-2,2'-biphosphole named BIPHOS, was originally synthesized by Mathey and coworkers[129] starting from the simple 3,4-dimethylphosphole **DMPP**. The most convenient method is based on the oxidative coupling reaction of 2-lithiophosphole obtain from 2-bromophosphole as described in Scheme 77.[130] As phospholes are not aromatic compounds, the α-functionalisation of the phosphole ring imply a sequence of oxidation at phosphorus and bromination of dienic system, oxygen-sulfur exchange at the phosphorus, dehydrohalogenation of the dienic system and then reduction to obtain the 2-bromophosphole.



Scheme 77

In early studies, BIPHOS was coordinated to various transition metals,[131] such as Rh and Pd, generating catalytic systems for standard reactions. Rhodium complex, [Rh(**BIPHOS**)(COD)]BF_4, showed moderate activity for the hydrogenation of α-acetoamidocinnamic acid **4** (Scheme 9) but was really efficient for hydroformylation of styrene with high conversion and excellent regioselectivity towards the branched aldehyde (up to 98%).[132] The BIPHOS/Pd catalyst proved to be as effective as the best reported catalytic systems in the catalytic allylic substitution of the model substrate **29** (Scheme 18)[133] but showed disappointing results in methoxycarbonylartion of styrene.[134]

Metal free **BIPHOS** exhibits *tropos* nature due to isomerization by phosphorus inversion inducing *atropos* inversion.[135] In 2001, Gouygou and coll. succeeded in applying *tropos*-**BIPHOS** to an catalytic asymmetric reaction for the first time by a process involving crystallization-induced spontaneous resolution and kinetic stabilization by coordination to a metal center.[136] Figure 11 shows the transformation of the *tropos*-**BIPHOS** into an enantiopure *atropos* (S,R_P,R_P)-palladium complex through complete control of chirality without racemization of the complex in solution at room temperature or below.[137]

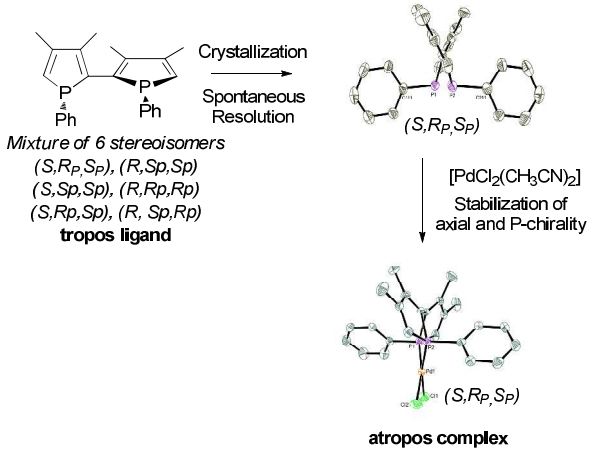
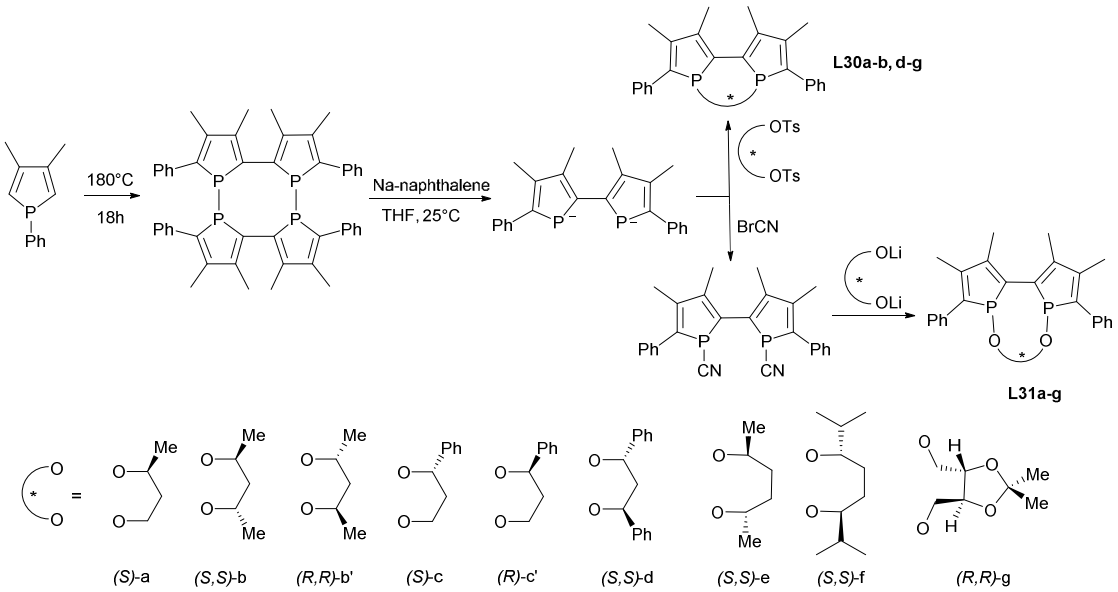


Figure 11 : Transformation of *tropos* BIPHOS into enantiopure *atropos* palladium complex

The (S,R_P,R_P)-(+)-Pd-complex was applied in the asymmetric allylic substitution of acetate **29** (scheme 18) in THF at 25°C using 1 mol% of catalyst, using NaH as base. Under these conditions, the allylic acetate was smoothly converted after 24 hrs into the desired (*S*)-product in 93% yield and with 80% *ee*. Switching to (R,S_P,S_P)-(-)-Pd-complex gave the opposite enantiomer of the product with the same yield and enantioselectivity which confirms the enantiomeric purity of the BIPHOS palladium complex.

5.2. *Tropos* diphosphines and diphosphinites derived from 2,2'-biphosphole

New diphosphines and diphosphinites with the *tropos* structure of 2,2'-biphosphole were then designed to avoid the delicate and random stage of resolution and extend catalytic applications. The synthetic strategy is based on the introduction of a chiral linker between the two phosphorus atoms of the 2,2'-biphosphole to both partially control the axial and the central chiralities and to maintain some degree of freedom to accomplish a metal dynamic resolution. Starting from **DMPP**, **L30** were obtained by asymmetric alkylation of the dianion, resulting from the cleavage of the two phosphorus-phosphorus bonds of the tetraphosphole, using various enantiomerically pure diol ditosylates (or dimesylates),[138] whereas **L31** were prepared by nucleophilic substitution of the dicycano intermediate using enantiomerically pure diols, as described in Scheme 78.[139]

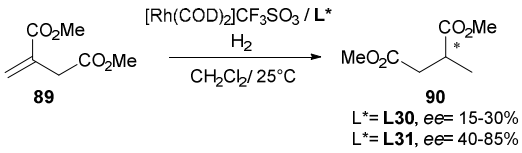


Scheme 78

These *tropos* diphosphines and diphosphinites, **L30** and **L31**, are able to provide diastereo- and enantiopure complexes of palladium, platinum and rhodium by a kinetic dynamic

resolution upon coordination on a metal center. Their potential was demonstrated in particular for Pd-catalyzed allylic substitution and Rh-catalyzed hydrogenation reactions. Notable features are the direct use of **L30** and **L31** to convey enantioselectivity in metal catalyzed reactions through an *in situ* dual chirality control of axial and central chiralities of 2,2'-biphosphole. For example Pd-catalysts, generated *in situ* from 1 mol% of the diphosphine and 0.5 mol% of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$, gave enantioselectivities up to 66% with the diphosphine **L30d** for the asymmetric allylic substitution of acetate **29** (Scheme 18). Under the same conditions, diphosphinite ligands are underperforming giving enantioselectivities up to 35% with the **L31b'**.[140]

In asymmetric hydrogenation of dimethylitaconate (Scheme 79), Rh-catalysts prepared *in situ* by adding ligand **L30** or **L31** to $[Rh(COD)_2]CF_3SO_3$, are active and selective producing enantiomeric excess in the range of 31 to 85%. Diphosphines **L30** gave more active catalytic systems than diphosphinites **L31** since complete conversion was achieved in 3 h at room temperature under a hydrogen pressure of 20 bar with **L30** whereas **L31** require a hydrogen pressure of 40 bar during 6 h. However, the best results in terms of enantioselectivities were obtained with **L31c,c'** and **d** (82-85% of *ee*). It is interesting to note that the absolute configuration of the ligand determined the configuration of the product: the *(R)* enantiomer of the methylsuccinate being obtained with ligands derived from the *(S)* or *(S,S)* diols whereas the *(S)* enantiomer is obtained with the ligand derived from the *(R)* or *(R,R)* diols.



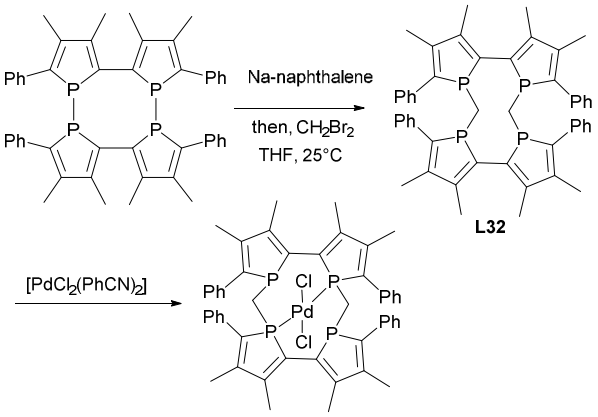
Scheme 79

Pt-catalyzed hydroformylation of styrene **6a** was also performed, using $[PtCl_2(L_2*)]/SnCl_2$ catalytic systems, with modest results both with diphosphines **L30** and diphosphinites **L31** (conversion up to 64%, b/l up to 91%, *ee* up to 18%).[141]

The modular construction of these *tropos* ligands by combination of 2,2'-biphosphole framework and chiral linker offers immense scope for structural variations and catalysts tuning that have not yet been fully exploited.

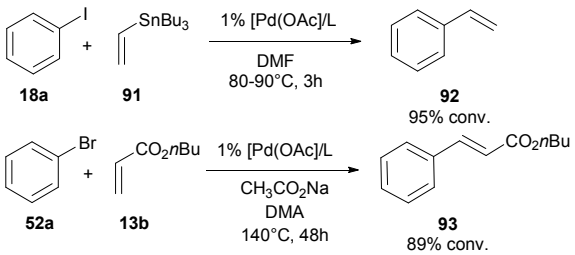
5.3. Macrocyclic tetraphosphole ligand

2,2'-biphosphole units have been incorporated in macrocycles of variable ring sizes which can adjust their conformation to the stereochemical requirements of the metal complexes thanks to the flexibility of the 2,2'-biphosphole units.[142] A ten-membered tetraphosphole macrocycle **L32** has been used to synthetize a very stable palladium complex (Scheme 80) in which the macrocycle adopts a cradle-like conformation to chelate the palladium center between two diagonally related phosphorus atoms.[143]



Scheme 80

The structural characteristics of the **L32**-Pd complex have suggested that some stabilization of a [Pd^0X] intermediate could be achieved due to the conformation of the macrocycle in the complex with possible spatial interactions of the non-complexed phosphorus lone pairs of **L32** with the 14-electron palladium center. This hypothesis was confirmed by the results obtained in Pd-catalyzed reactions. Indeed, **L32** gave stable and recyclable palladium catalysts with very long half-lives for the Stille cross-coupling reaction of iodobenzene **18a** with tributylvinyltin **91** and for the Heck coupling reaction of bromobenzene **52a** with n-butyl acrylate **13b** (Scheme 81).



Scheme 81

In addition, the Pd-catalyst generated *in situ* from **L32** and [$Pd(dba)_3$] also proved to be efficient in the allylic substitution of acetate **29** (Scheme 18) leading to a high conversion (95%) of the substrate in 3h using 0.5 mol% of catalyst.

Despite the promising performance of ligand **L32**, the development of macrocyclic tetraphosphole-based ligands for catalysis has not been achieved so far.

6. Concluding remarks

This review has highlighted the design and the updated applications of the phosphole ligand families in catalysis. Although the first report of the homogeneous catalysis dates from the 1970s, the applications have continued to grow from covering various metal catalysis to extending into organocatalysis as shown by recent publications.

The monophospholes, originally known as efficient ligands for catalytic hydrogenation and hydroformylation reactions, have recently gained importance in C-C coupling reactions especially in Au- and Pt-catalyzed reactions. Furthermore in this family of ligands, the dibenzophosphole compounds offer specific properties that can be exploited as organocatalysts in Appel and Staudinger reactions.

Chemistry of phospholes have also opened a gateway to novel phosphole-based ligands (bi-tri-, tetra-dentate P-P, P-N and P-X ligands) having significant potential in a large number of metal-catalyzed reactions: hydrogenation, hydroformylation, polymerization, isomerization, C-C coupling reactions and more. In addition, some successful results in asymmetric reactions have been achieved with chiral phosphole ligands based on a chiral backbone (P-P and P-N ligands) or on *tropos* 2,2'-biphosphole structure (P-P ligands).

However, the potential in catalysis of the phosphole ligand families has not been fully explored to date, and we anticipate that more new reactions will be developed in the future. Due to the steric and electronic modularity of the phosphole ring, new phosphole-based ligands will provide further opportunity for the development of various reactions (asymmetric reactions included).

Acknowledgments

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Phosphole-based ligands in catalysis

Kévin Fourmy, Duc Hahn Nguyen, Odile Dechy-Cabaret
and Maryse Gouygou

This review provides an overview of phosphole-based ligand families (monophospholes, multidentate hybrid phosphole ligands, diphosphole and 2,2'-biphosphole-based ligands) and their potential in metal- and organo-catalyzed reactions (asymmetric reactions included).