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Chiral Monodentate Phosphine Ligand MOP for Transition-Metal-Catalyzed Asymmetric Reactions

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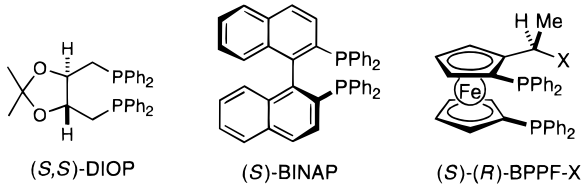
ABSTRACT
Chiral monophosphines, whose chirality is due to biaryl axial chirality, have been prepared from enantiomerically pure 2,2′-dihydroxy-1,1′-binaphthyl and demonstrated to be highly efficient chiral ligands for transition-metal-catalyzed organic transformations, especially for reactions where chelating bisphosphine ligands cannot be used. The high efficiency is observed in palladium-catalyzed asymmetric hydrosilylation of a wide variety of olefins such as alkyl-substituted terminal olefins and in asymmetric reactions via π-allylpalladium intermediates represented by asymmetric reduction of allylic esters with formic acid.

Introduction

Among various types of enantiomerically pure ligands used for catalytic asymmetric reactions, chiral tertiary phosphines have established their positions as the most effective ligands for most homogeneous transition-metal catalysts.[1] The phosphine-metal complexes have found broad application to catalytic reactions, especially for the reactions which involve, in the catalytic cycle, oxidative addition and/or insertion of an organic substrate, and reductive elimination of a product. Tertiary phosphine ligands coordinate to transition-metal complexes throughout the catalytic cycle because of their high affinity, especially with late transition metals, and they can stabilize low-valent metal intermediates to keep the high activity of the catalysts. Owing to these characteristic features, chiral phosphine ligands have often been used for the creation of chiral surroundings around the central metal. Thus, one of the most exciting and challenging subjects in the research of catalytic asymmetric synthesis is the development of a chiral phosphine ligand which will influence the reaction efficiency in terms of catalytic activity and enantioselectivity.

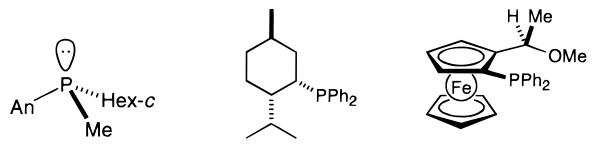
In the first asymmetric reaction by homogeneous transition-metal catalysts reported by Knowles and Horner, methylphenylpropylphosphine was used as a chiral monodentate phosphine ligand with a rhodium catalyst which gave 4−15% ee in asymmetric hydrogenation of prochiral olefins.[2,3] In 1972, Kagan found that a bisphosphine ligand, DIOP, derived from tartaric acid, is much more effective for the rhodium-catalyzed asymmetric hydrogenation, producing amino acids.[4] Since this finding, the development of chiral phosphine ligands has been concentrated into the design and preparation of bisphosphine compounds. They are, in general, anticipated to be more effective than monophosphine ligands in constructing a chiral environment by coordination to a metal. One of the most effective chiral bisphosphine ligands is BINAP,[5] which has exhibited its high enantioselectivity in several asymmetric reactions including rhodium- or ruthenium-catalyzed hydrogenation. We also have prepared ferrocenylbisphosphines BPPF-X[6] as chelating bisphosphine ligands, which have been demonstrated to be effective for palladium-catalyzed allylic substitution reactions, gold- or silver-catalyzed aldol reactions, and so on. On the other hand, only a limited number of monodentate chiral phosphine ligands have been reported, probably because they have been described as being of little practical use.[1] However, there exist transition-metal-catalyzed reactions where the bisphosphine−metal complexes cannot be used because of their low catalytic activity and/or low selectivity toward a desired reaction pathway. Chelating bisphosphine ligands are incompatible with the catalytic reactions where the catalyst can provide only one coordination site for a phosphine ligand during some of the steps in the catalytic cycle. Thus, powerful chiral monodentate phosphine ligands are required for the realization of a high level of enantioselectivity in this type of catalytic asymmetric reactions. Nevertheless, the monodentate phosphine ligands that satisfy the above requirements have not been well developed so far except for 2-methoxyphenyl(cyclohexyl)methylphosphine (CAMP)[7] and neomenthyldiphenylphosphine (NMDPP).[8]

Chiral Bisphosphine Ligands



(*S,S*)-DIOP (*S*)-BINAP (*S*)-(*R*)-BPPF-X

Chiral Monophosphine Ligands



(*S*)-CAMP NMDPP (*S*)-(*R*)-PPF-OMe

We have previously reported a nickel-catalyzed asymmetric cross-coupling forming axially chiral binaphthyls, which was realized for the first time by use of a monophosphine ligand, PPFOMe, containing ferrocene planar chirality,[9] and we have continued our efforts to develop

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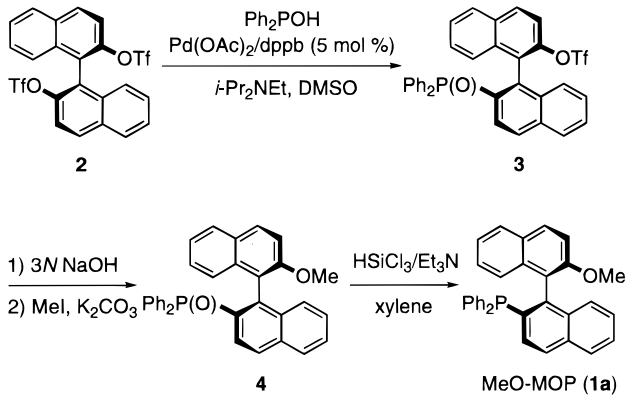
Scheme 1



new enantioselective chiral monodentate phosphine ligands for transition-metal-catalyzed reactions where only a monodentate phosphine ligand can be used. We have prepared a series of monophosphine ligands, whose chirality is due to 1,1′-binaphthyl axial chirality, represented by MeO-MOP (**1a**), which stands for 2-(diphenylphosphino)-2′-methoxy-1,1′-binaphthyl. We found that high enantioselectivity and high catalytic activity can be achieved in some of the transition-metal-catalyzed asymmetric reactions, especially those with palladium catalysts, including hydrosilylation of olefins and reduction of allylic esters with formic acid by use of MeO-MOP and its derivatives, where the methoxy group is replaced by some other groups, or its biphenanthryl analogue (MOP-phen). Here we describe the preparation of the chiral monodentate phosphine ligands (MOP ligands) and their use in the catalytic asymmetric reactions.

Design and Preparation of Chiral Monodentate Ligands

As a basic chiral backbone for an enantiomerically pure monodentate phosphine ligand, we chose the axially chiral 1,1′-binaphthyl skeleton because there are many successful examples of the application of chiral binaphthyl derivatives to asymmetric reactions, though they are usually used as chelating chiral ligands.[1] In 1990, Morgans and co-workers reported[10] the selective monophosphinylation of 1,1′-binaphthyl 2,2′-ditriflate (**2**) with diphenylphosphine oxide in the presence of a palladium catalyst, giving a high yield of the monophosphinylation product **3**, which attracted our attention as a versatile starting compound for the preparation of chiral monophosphine ligands. The triflate group on **3** was considered to be a convenient functionality for the introduction of various types of functional groups onto the binaphthyl ring. The conversion of **3** into MeO-MOP (**1a**) was achieved[11,12] in a high yield by the three-step sequence shown in Scheme 1. The overall yield from 2,2′-dihydroxy-1,1′-binaphthyl was about 90%, the procedures being much more convenient than those previously reported from (*S*)-2′-methoxy-1,1′-binaphthyl-2-carboxylic acid.[13]

In the palladium-catalyzed diphenylphosphinylation of ditriflate **2**, only one of the two triflate groups undergoes the substitution, probably because the oxidative addition

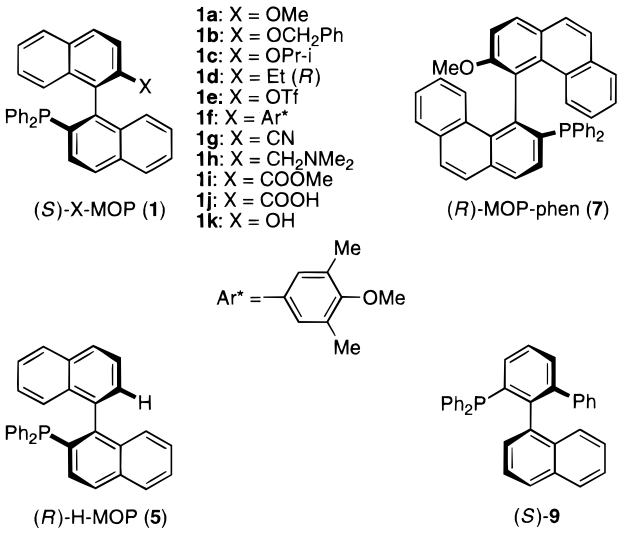
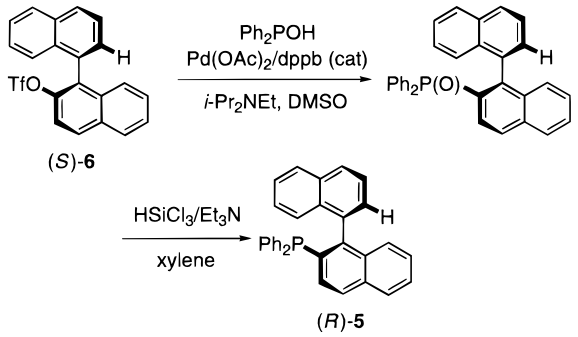


FIGURE 1. MOP ligands prepared and used for catalytic asymmetric reactions.

Scheme 2

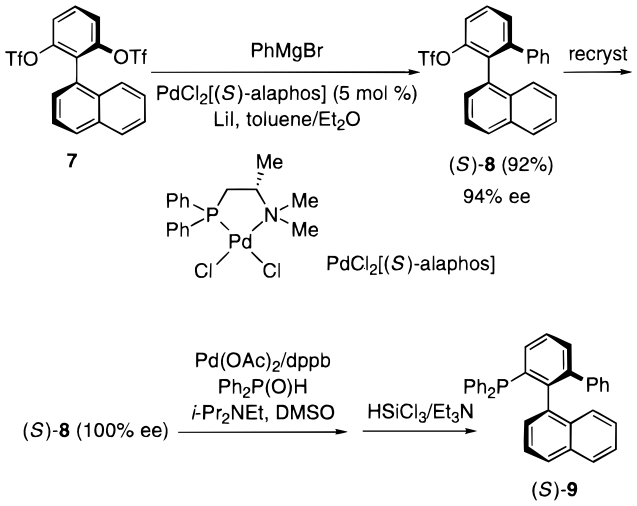


of triflate to a palladium(0) species is sensitive to steric bulkiness, the diphenylphosphinyl group introduced at the 2 position of the 1,1′-binaphthyl skeleton hindering the second triflate from the oxidative addition. The remaining triflate group on the 2′ position of (*S*)-**3** was found to be replaced by carbon nucleophiles by nickel-catalyzed cross-coupling reactions. Thus, (*R*)-Et-MOP (**1d**) and (*S*)-Ar*-MOP (**1f**) (Figure 1) were obtained by the nickel-catalyzed substitution of (*S*)-**3** or TfO-MOP (**1e**) with the corresponding Grignard reagents.[14]

The MOP derivative (*R*)-**5** bearing no substituent at the 2′ position, which is needed to evaluate the steric and/or electronic effects of various functional groups in other MOP derivatives, was prepared starting with (*S*)-monotriflate **6** by the palladium-catalyzed phosphinylation and reduction of the phosphine oxide (Scheme 2).[14] The enantiomerically pure monophosphine containing the biphenanthryl skeleton, MOP-phen (**7**), was also prepared by a sequence of reactions from 3,3′-dihydroxy-4,4′-biphenanthryl which are essentially the same as those for the binaphthyl analogue **1a**.[15]

A catalytic enantioposition-selective substitution reaction opened another route to the chiral monophosphine ligand (Scheme 3).[16] Enantiomerically pure monotriflate (*S*)-**8**, obtained by the asymmetric cross-coupling of achiral biaryl ditriflate **7** with phenylmagnesium bromide

Scheme 3



in the presence of $PdCl_2$[(*S*)-alaphos], was subjected to the palladium-catalyzed diphenylphosphinylation, giving the new axially chiral triarylmonophosphine (*S*)-**9**. Now we are in a position to design and prepare MOP ligands which are functionalized on several types of axially chiral biaryl backbones. Some of the MOP ligands prepared are shown in Figure 1.

The crystal structure of *trans*-[$PdCl_2${(*R*)-MeO-MOP}$_2$] is shown in Figure 2.[17] The complex has a square-planar geometry with two phosphorus atoms and two chlorine atoms, where the MeO-MOP ligand coordinates to palladium with the phosphorus atom as a monodentate ligand. The methoxy group is located far from the palladium atom, the distance between palladium and methoxy oxygen being 6.33 Å. Thus, the methoxy group is not coordinating to palladium. It should be noted that the naphthyl ring having a methoxy group plays an important role in the construction of the chiral environment of the palladium. Thus, the naphthyl ring A (A′) points toward the vicinity of palladium, while the methoxy group is located in the side opposite palladium. These structural features are very different from those commonly observed in complexes coordinated with chiral bidentate bisphosphine ligands such as BINAP. In another palladium−MOP complex which has a π-allyl ligand,[18] the MeO-MOP ligand adopts a conformation similar to that in the bis(MeO-MOP)palladium complex. Thus, the A ring is located close to palladium, and the methoxy group is well removed. The high enantioselectivity of the MOP ligands in the catalytic asymmetric reactions is mainly ascribed to the chiral environment created by the A ring of the naphthyl group which is located close to the central metal.

Palladium-Catalyzed Asymmetric Hydrosilylation of Olefins

Catalytic asymmetric functionalization of olefins is an important goal in synthetic organic chemistry. Catalytic asymmetric hydrosilylation could be a useful method for the asymmetric synthesis of optically active alcohols because the carbon−silicon bond in some organosilicon

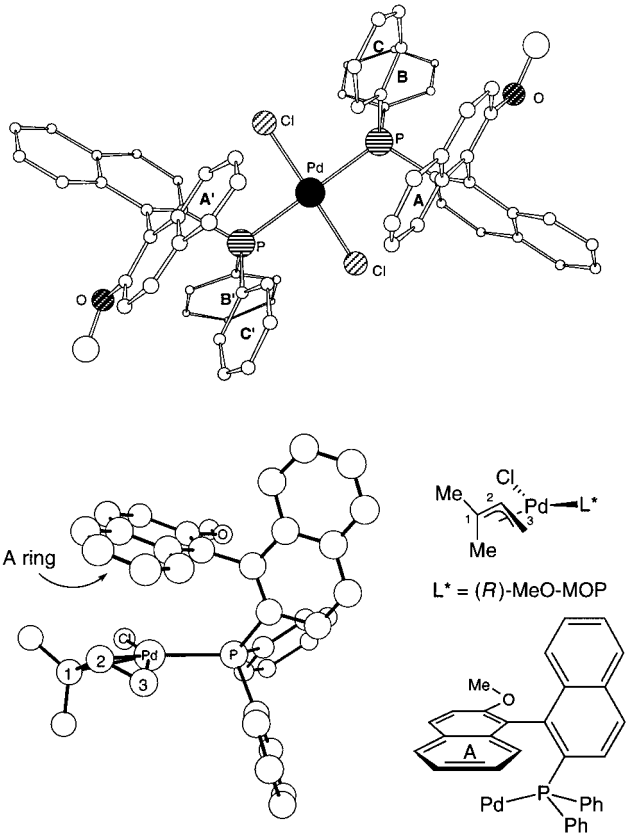
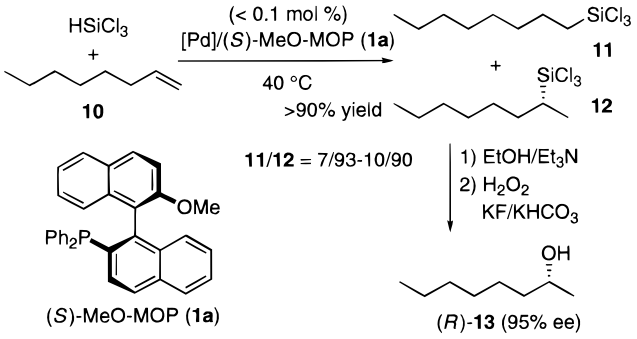


FIGURE 2. Molecular structures of *trans*-$PdCl_2${(*R*)-MeO-MOP}$_2$·Et_2O and $PdCl(\eta^3$-1,1-dimethylallyl)((*R*)-MeO-MOP). The ether molecule is omitted for simplicity.

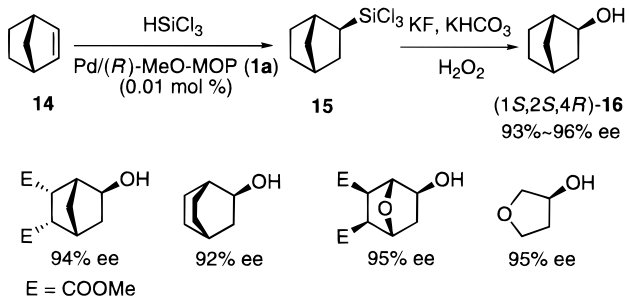
compounds is readily oxidized into a carbon−oxygen bond with retention of configuration at the stereogenic carbon center.[19] However, the asymmetric hydrosilylation has typically been one of low enantioselectivity with platinum, rhodium, or nickel catalysts.[1] Its regioselectivity is another problem to solve in the catalytic hydrosilylation.

It is well documented[20] that hydrosilylation of alkyl-substituted terminal olefins is catalyzed by platinum, rhodium, or nickel complexes and proceeds with anti-Markovnikov selectivity to 1-silylalkanes which do not contain a stereogenic carbon center. To develop a new catalyst system which possesses high regioselectivity in giving 2-silylalkanes and high catalytic activity at the same time, we examined several types of phosphine−palladium catalysts, to which little attention has been paid. It was found that palladium complexes coordinated with a chelating bisphosphine ligand such as BINAP did not catalyze the hydrosilylation of 1-hexene with trichlorosilane even upon elevation of the reaction temperature to 80 °C. On the other hand, the reaction took place at 40 °C with monodentate phosphine ligands, though the chemical yields of hexylsilanes were low. For example, the reaction in the presence of 0.1 mol % palladium−triphenylphosphine catalyst at 40 °C gave a 12% yield of the hydrosilylation products consisting of 2-hexylsilane and its 1-isomer in a ratio of 9:91, the hydrosilylation being accompanied by isomerization of 1-hexene into internal olefins. The regioselectivity for forming 2-silylhexane was

Scheme 4



Scheme 5



increased to some extent by use of a sterically more bulky monophosphine ligand. It is reasonable to expect that a monodentate phosphine ligand generates a palladium catalyst that is more active for the hydrosilylation than a chelating bisphosphine ligand. The former can form a square-planar 16-electron palladium(II) intermediate, $PdH(SiCl_3)L(CH_2{=}CHR)$ (L = monophosphine), that offers a coordination site for the activation of the olefin, while the latter cannot. Further studies revealed that MeO-MOP (**1a**) is a unique ligand for the hydrosilylation, its palladium complex exhibiting both high catalytic activity and unusually high regioselectivity in forming 2-alkylsilanes, and, moreover, high enantioselectivity.[11,17] The predominant formation of 2-alkylsilanes from aliphatic 1-olefins has never before been observed with any transition-metal catalysts.

The asymmetric hydrosilylation of 1-octene (**10**) with trichlorosilane in the presence of 0.1 mol % palladium catalyst generated from $[PdCl(\pi\text{-}C_3H_5)]_2$ and (*S*)-MeO-MOP (**1a**) at 40 °C for 24 h gave a 90% yield of the hydrosilylation products consisting of 1-octylsilane **11** and 2-octylsilane **12** in a ratio of 7:93 (Scheme 4). The hydrosilylation product **12** was readily converted into optically active 2-octanol (**13**), which is an *R* isomer of 95% ee, by treatment of **12** with $EtOH/Et_3N$ followed by oxidation of the resulting (triethoxy)silane with hydrogen peroxide in the presence of a fluoride anion.[19] The hydrosilylation of 1-octene (**10**) with a palladium catalyst coordinated with Et-MOP (**1d**), where the methoxy group in MeO-MOP is replaced by an ethyl group, proceeded with almost the same regioselectivity and enantioselectivity, indicating that the oxygen functionality in MeO-MOP is not essential for the high and rather unusual selectivities. This observation is consistent with the structure of the palladium complexes of the MeO-MOP ligand shown in Figure 2, where the substituent at the 2′ position of the binaphthyl moiety is far from the palladium center. The terminal olefins 1-hexene, 1-dodecene, 4-phenyl-1-butene, and vinylcyclohexane were also transformed efficiently into the corresponding 2-alkanols with enantioselectivities ranging between 94% and 97% ee by the catalytic hydrosilylation−oxidation procedure, the selectivity being highest for the enantioface selection of simple terminal olefins. The regioselectivity in forming 2-(silyl)alkanes is surprisingly high for the terminal olefins substituted with a primary alkyl group.

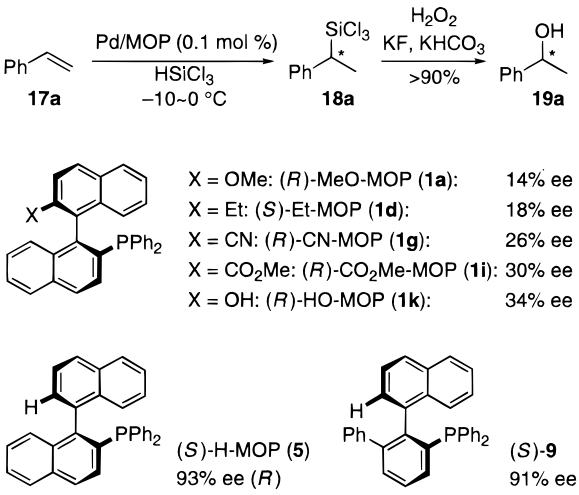
Asymmetric synthesis through a selective monofunctionalization of enantiotopic positions is one of the most attractive strategies for one-step construction of multiple chiral carbon centers. We have applied the MOP/palladium-catalyzed hydrosilylation to the catalytic asymmetric functionalization of a meso bicyclo[2.2.1] system,[21] because the optically active bicyclo[2.2.1]heptane derivatives represented by norbornanol are indispensable as versatile chiral building blocks for the synthesis of a variety of important compounds.

The hydrosilylation of norbornene (**14**) with trichlorosilane took place smoothly below 0 °C in the presence of 0.01 mol % MeO-MOP/palladium catalyst to give a quantitative yield of *exo*-2-(trichlorosilyl)norbornane (**15**) as a single product (Scheme 5). Direct oxidation of **15** with hydrogen peroxide in the presence of a large excess of potassium fluoride and potassium bicarbonate gave *exo*-norbornanol (**16**) of 93−96% ee in yields greater than 90%. Bicyclo[2.2.2]octene and 2,5-dihydrofuran derivatives[22] were also successfully subjected to the asymmetric hydrosilylation−oxidation to give the corresponding optically active alcohols, with the enantioselectivity being in excess of 92%. The hydrosilylation of norbornadiene gave monohydrosilylation product (95% ee) or bishydrosilylation product (>99% ee) according to the amount of trichlorosilane employed.

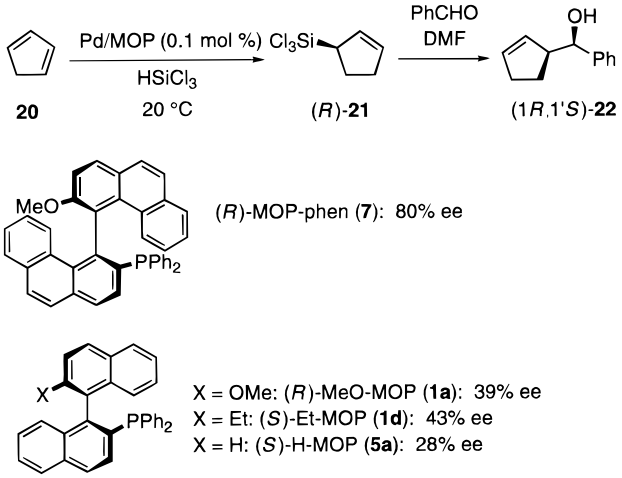
Palladium-catalyzed hydrosilylation of styrene derivatives with trichlorosilane is known to proceed with perfect regioselectivity in giving benzylic silanes due to the contribution of a π-benzylpalladium intermediate. It seems much easier to realize the asymmetric hydrosilylation of styrenes than that of simple terminal olefins because the reaction produces chiral products exclusively, but high enantioselectivity has not been reported despite considerable research on this subject.[1] The MeO-MOP/palladium catalyst, which has been efficiently applied to the hydrosilylation of simple terminal olefins and cyclic olefins, was not so effective for styrene derivatives. Thus, the palladium-catalyzed hydrosilylation of styrene (**17a**) with trichlorosilane in the presence of MeO-MOP (**1a**) ligand under standard conditions (without solvent) followed by oxidation gave 1-phenylethanol (**18a**) of only 14% ee.

We have examined MOP ligands where the methoxy group at the 2′ position in MeO-MOP is replaced by several groups for their enantioselectivity in the palladium-catalyzed asymmetric hydrosilylation of styrene

Scheme 6



Scheme 7



(**17a**). The enantiomeric purities and absolute configuration of alcohol **18a** obtained with some 2′-substituted MOP ligands are shown in Scheme 6. These results suggest that the electronic nature of the substituent is not a decisive factor in the enantioselection, since all of the MOPs substituted with methoxy, hydroxy, methoxycarbonyl, cyano, and ethyl groups show low enantioselectivity irrespective of their electron-withdrawing or electron-donating character. It turned out that (*S*)-H-MOP (**5**), which has the same 1,1′-binaphthyl skeleton as MeO-MOP but lacks the methoxy group, is particularly effective for the palladium-catalyzed hydrosilylation of styrene.[23] Thus, hydrosilylation of styrene (**17a**) in the presence of 0.1 mol % H-MOP/palladium catalyst at 0 °C gave a quantitative yield of 1-phenyl-1-trichlorosilylethane (**18a**) as a single regioisomer, whose enantiomeric purity was determined to be 93% ee (*R*) by oxidation to **19a**. The monophosphine (*S*)-**9** was as effective as (*S*)-H-MOP (**5**) for the hydrosilylation of styrene, giving (*R*)-**18a** of 91% ee.[16] Neither of the ligands (*S*)-**5** or (*S*)-**9** has any substituent at the 2′ position. It follows that the small size of the hydrogen at the 2′ position in H-MOP (**5**) is important for high enantioselectivity. The dihedral angle between the two naphthyl rings in the binaphthyl skeleton, which is controlled by the steric bulkiness of the 2′-substituent, is presumably related to the enantioselectivity.

Palladium-catalyzed hydrosilylation of 1,3-dienes is one of the important synthetic methods for allylic silanes, and considerable attention has been paid to their asymmetric synthesis by this catalytic method.[1] Unfortunately, the binaphthyl monophosphine, MeO-MOP (**1a**) or H-MOP (**5**), is not as effective as a chiral ligand for the asymmetric hydrosilylation of 1,3-dienes as for that of other types of prochiral olefins shown above, where over 90% enantioselectivity is usually observed. We found that MOP-phen (**7**), which is the 4,4′-biphenanthryl analogue of MeO-MOP, shows higher enantioselectivity than others in the hydrosilylation of cyclic 1,3-dienes giving optically active allylic silanes.[24] The reaction of cyclopentadiene (**20**) with trichlorosilane in the presence of MOP-phen/palladium catalyst proceeded in a 1,4-fashion to give a quantitative yield of (*R*)-3-silylcyclopentene (**21**). The enantiomeric purity of homoallylic alcohol **22** was 80% ee, obtained in a high yield by treatment of the allylsilane **21** with benzaldehyde in DMF (Scheme 7).

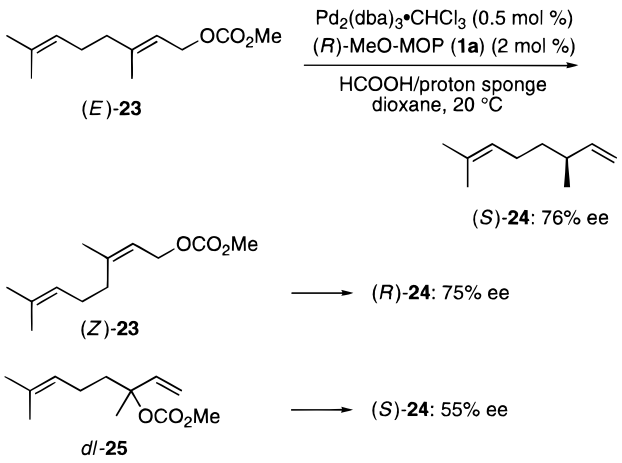
Catalytic Asymmetric Reactions via π-Allylpalladium Intermediates

Palladium-catalyzed reduction of allylic esters with formic acid, a reaction which was developed by Tsuji and coworkers,[25] provides a convenient method for regioselective synthesis of less-substituted olefins. Mechanistic studies on the catalytic reduction have revealed that the olefin is produced by reductive elimination from the key intermediate, Pd(II)(π-allyl)(hydrido)(L), which is generated by decarboxylation of the palladium formate complex. An important point is that the use of a monodentate phosphine ligand is essential for the high catalytic activity and regioselectivity in forming less-substituted olefins. We found that the chiral monodentate phosphine ligands, (*R*)-MeO-MOP (**1a**) and its biphenanthryl analogue (*R*)-MOP-phen (**7**), can be successfully applied to the catalytic asymmetric reduction, forming optically active olefins.[15,18]

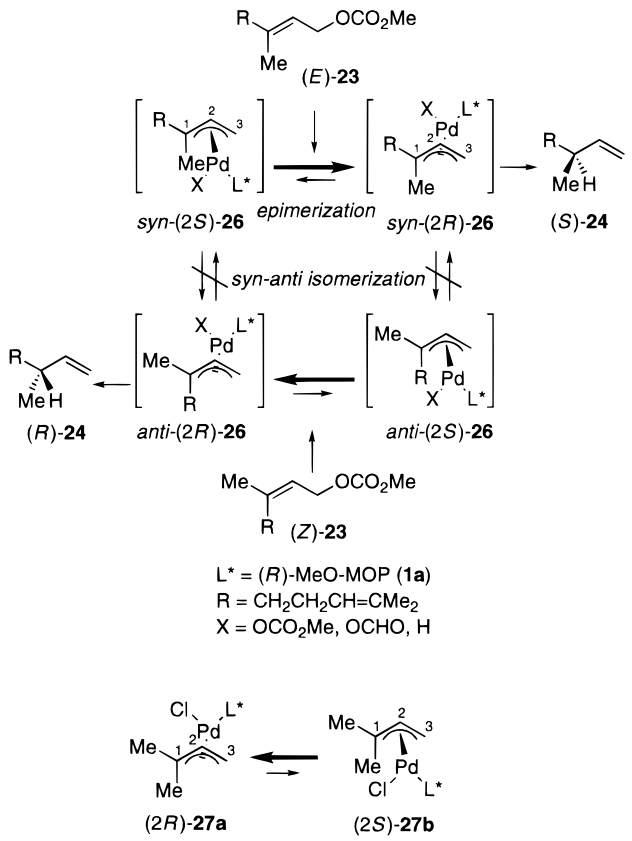
Reaction of geranyl methyl carbonate ((*E*)-**23**) with formic acid and 1,8-bis(dimethylamino)naphthalene in the presence of 1 mol % palladium catalyst generated from $Pd_2(dba)_3{\cdot}CHCl_3$ and (*R*)-MeO-MOP (P:Pd = 2:1) proceeded regioselectively to give a quantitative yield of (*S*)-3,7-dimethyl-1,6-octadiene (**24**) in 76% ee (Scheme 8). The reduction of (*Z*)-carbonate, neryl methyl carbonate ((*Z*)-**23**), under the same reaction conditions gave the olefin (*R*)-**24** which has essentially the same enantiomeric purity (75% ee) but the opposite absolute configuration. Similarly, the reduction of racemic linalyl carbonate **25** gave an 82% yield of (*S*)-**24** in 55% ee. In contrast to the high catalytic activity and high regioselectivity observed with the MOP/palladium catalyst, the reduction is very slow and not regioselective with chelating bisphosphine ligands such as (*R*)-BINAP.

The reduction of **23** must proceed via a π-{1-(4-methyl-3-pentenyl)-1-methylallyl}palladium(II) intermediate, **26**, which possibly undergoes syn−anti isomerization (*syn*-

Scheme 8



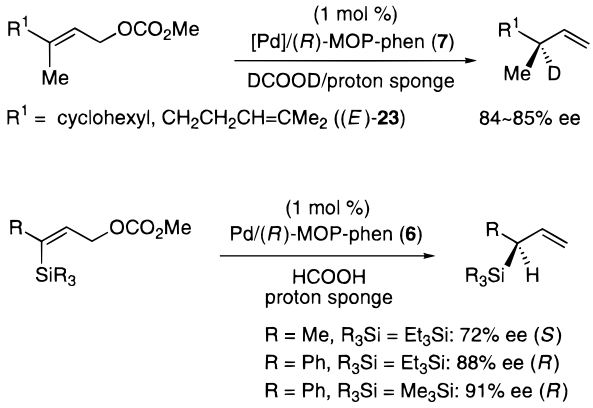
Scheme 9



26 ↔ *anti*-**26**) and epimerization ((2*R*)-**26** ↔ (2*S*)-**26**) by the $\sigma-\pi-\sigma$ mechanism (Scheme 9).[25] The reversal of configuration of **24** observed for the asymmetric reduction of (*E*)-**23** and (*Z*)-**23** demonstrates that the rate of syn−anti isomerization is much slower than the rate of reduction in forming **24**. The epimerization is taking place because the racemic carbonate **25** gave nonracemic product.

^{1}H and ^{31}P NMR studies of PdCl(η^3-1,1-dimethylallyl)-((*R*)-MeO-MOP) (**27**) revealed that the π-allylpalladium **27** exists as a mixture of two isomers, **27a** and **27b**, which are in equilibrium between −60 and +20 °C, the ratio of the major isomer to the minor isomer being 4.5:1 and 6.5:1

Scheme 10

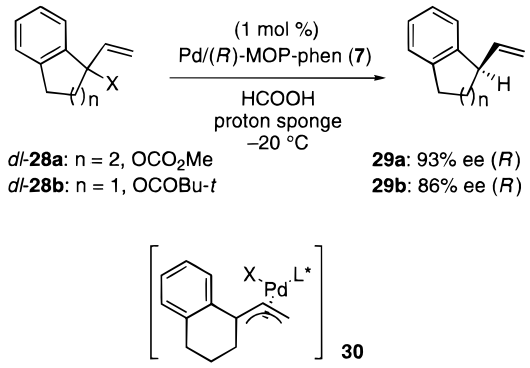


at +20 and −60 °C, respectively, and that the structure of the major isomer in solution is quite similar to that in the X-ray crystal structure (Figure 2). The stereochemical outcome in forming (*S*)-**24** observed in the catalytic asymmetric reduction of (*E*)-**23** is accounted for by the reductive elimination of the hydrido and π-allyl from the intermediate *syn*-(2*R*)-**26** (X = H) after equilibration between *syn*-(2*R*)-**26** and *syn*-(2*S*)-**26**, the former possessing the same configuration for the π-allyl moiety as **27a**. Similarly, in the reaction of (*Z*)-**23**, (*R*)-**24** is formed from *anti*-(2*R*)-**26** after the equilibration with *anti*-(2*S*)-**26**.

The monodentate biphenanthryl phosphine (*R*)-MOP-phen (**7**) was found to be a more enantioselective ligand than the binaphthyl ligand MeO-MOP (**1a**) for the asymmetric reduction of allylic esters. Thus, the use of **7** for the reduction of (*E*)-**24** and (*Z*)-**24** increased the enantioselectivity to 85% ee and 82% ee, respectively. Asymmetric syntheses of optically active olefins which all bear a deuterium atom at the stereogenic center in the allylic position were also successful with the use of formic acid-d_2 (DCOOD) (Scheme 10).[15] No deuterium scrambling was observed in the reduction products. The higher enantioselectivity of MOP-phen (**7**) than MeO-MOP (**1a**) is ascribed to the higher ratio of two diastereoisomers which was observed in NMR studies of PdCl(η^3-1,1-dimethylallyl)((*R*)-MOP-phen)). The catalytic asymmetric reduction was applied to the synthesis of optically active allylic silanes that have a stereogenic carbon center at the α-position and thus would be considered as useful chiral reagents in organic synthesis.[26]

The allylic esters used for the asymmetric reduction have been limited to those with a geometrically pure *E* or *Z* double bond for high enantioselectivity, because the *E* and *Z* isomers produce the enantiomeric olefins. The reversal of configuration is exemplified by the reaction of geranyl and neryl esters (see Scheme 8). However, it was found that racemic tertiary allylic esters can also be used for asymmetric reduction if one of the alkyl groups at the α position is a sterically bulky group (Scheme 11).[27] Since the racemic tertiary allylic esters are readily obtained from a ketone and the vinyl Grignard reagent, Scheme 11 provides a practical method for the synthesis of optically active olefins. For example, the asymmetric reduction of racemic ester *dl*-**28a**, obtained from tetralone, gave (*R*)-

Scheme 11



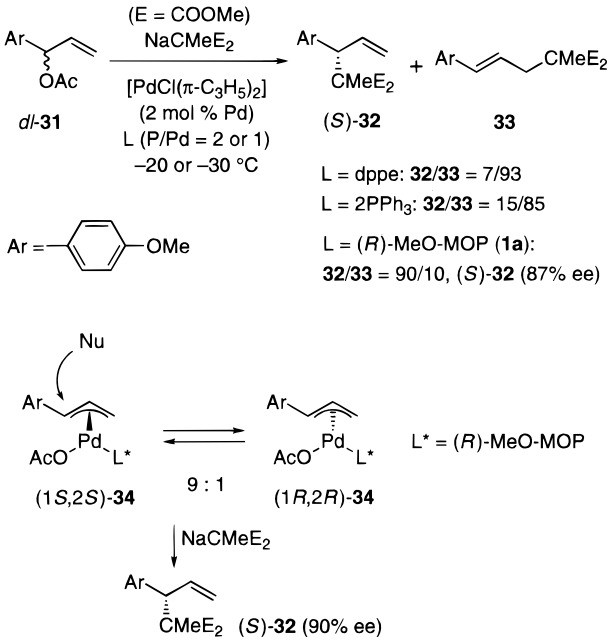
29a of 93% enantiomeric purity. The high enantioselectivity can be accounted for by the selective formation of the π-allylpalladium **30** that contains the more bulky group at the syn position. In the asymmetric reduction of racemic 2-(1-naphthyl)-3-buten-2-yl benzoate, the enantioselectivity was dependent on the substituent on the diphenylphosphino group of the MeO-MOP ligand. Introduction of an electron-withdrawing group increased the enantiomeric purity of the reduction product. The MeO-MOP ligand substituted with a bis(3-trifluoromethylphenyl)phosphino group exhibited the highest (86% ee) enantioselectivity.[28] The higher selectivity is ascribed to fast syn−anti isomerization of π-allylpalladium intermediates formed by oxidative addition of the allylic ester to a palladium(0) species.

One of the major problems in developing catalytic asymmetric allylic alkylation is undesirable regiochemistry, which limits the substitution patterns of allylic substrates. As a typical example, the substitution with soft carbon nucleophiles that proceeds through π-allylpalladium intermediates containing one substituent at the C-1 position produces the linear isomer rather than the branched isomer.[1] It follows that the reaction cannot be extended to asymmetric synthesis because the linear isomer lacks the chiral carbon center.

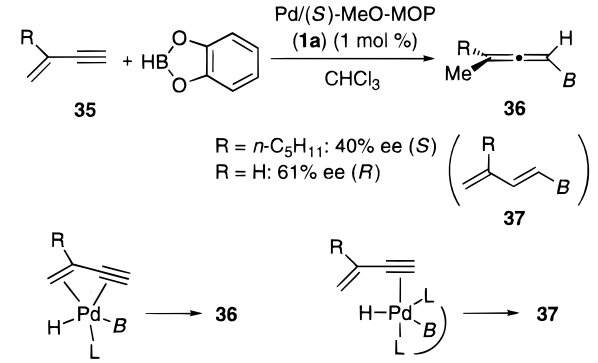
We found that the use of MeO-MOP (**1a**) for the allylic alkylation of 1-aryl-2-propenyl acetates reversed the regiochemistry to give branched isomers with high selectivity, and asymmetric synthesis was realized in this type of allylic alkylation system (Scheme 12).[29] For example, the reaction of *dl*-**31** with the sodium salt of dimethyl methylmalonate in the presence of MeO-MOP/palladium catalyst gave the branched isomer **32** (87% ee) with 90% regioselectivity. The stoichiometric reaction of an isolated π-allylpalladium complex, **34**, which exists as a mixture of isomers in a ratio of 9:1, with the sodium enolate of dimethyl methylmalonate gave (*S*)-**32** of 90% ee with 88% regioselectivity, which is in good agreement with the catalytic reactions in terms of both regio- and enantioselectivity.

An interesting memory effect has been observed in the palladium-catalyzed allylic alkylation with the MeO-MOP (**1a**) ligand. Thus, in the reaction of (*E*)-3-substituted 2-propenyl acetates, 1-substituted 2-propenyl acetates, and 1- or 3-deuterio-2-cyclohexenyl acetate, which proceed through 1,3-unsymmetrically substituted π-allylpalladium intermediates, selective substitution at the position originally substituted with acetate took place by use of the sterically bulky monodentate phosphine ligand MeO-MOP (**1a**).[30]

Scheme 12



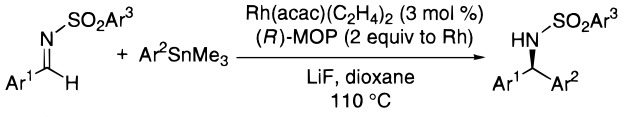
Scheme 13



Palladium-Catalyzed Asymmetric 1,4-Hydroboration of 1,3-Enynes

We have previously found that the addition of catecholborane to 1-buten-3-ynes is catalyzed by phosphine−palladium complexes to give allenylboranes and/or 1,3-dienylboranes and that the selectivity in forming allenylborane is influenced by the molar ratio of phosphine ligand to palladium as well as the structure of the phosphine ligand.[31] The use of a monodentate phosphine ligand is essential for the formation of allenylborane, while the reaction in the presence of bidentate bisphosphine ligands produces 1,3-dienylboranes exclusively. The selectivity is rationalized by the coordination number available for 1-buten-3-ynes in the monophosphine− and bisphosphine−palladium intermediates (Scheme 13). We have applied the monodentate phosphine ligand MeO-

Scheme 14



Ar^1 = 4-$CF_3C_6H_4$
Ar^2 = Ph, 4-$MeOC_6H_4$
Ar^3 = 4-$NO_2C_6H_4$

(*R*)-MeO-MOP (**1a**): 92% ee
(*R*)-Ar*-MOP (**1f**): 96% ee

MOP (**1a**) to the palladium-catalyzed asymmetric hydroboration of 1,3-enynes **35**.[32] Although the enantioselectivity was not high enough, the reaction provides the first example of the catalytic asymmetric synthesis of allenylboranes, which were used for mechanistic studies of the S_E' reaction with an aldehyde.

Other Catalytic Asymmetric Reactions with MOP Ligands

Since we reported the high efficiency of the MOP ligands, MeO-MOP (**1a**) has been applied to some other transition-metal-catalyzed asymmetric reactions, especially to those in which metal complexes of multidentate phosphine ligands cannot be used due to their low catalytic activity. The representatives are the π-allylpalladium-mediated reactions where the reductive elimination of π-allyl and some carbon ligands from π-allylpalladium intermediates is the critical bond-forming step in the catalytic cycle. In the palladium-catalyzed asymmetric reactions, allylic cyanation,[33] allylic alkoxycarbonylaton,[34] metallo−ene reaction,[35] and 1,2-addition of acylzirconocene chloride to enone,[36] the MeO-MOP ligand exhibited higher enantioselectivity than other chiral ligands, though the ee values of the products are not always satisfactory.

High enantioselectivity has been observed in the nickel-catalyzed hydrovinylation of a styrene derivative with ethylene, forming 3-(6-methoxy-2-naphthyl)-1-butene.[37] Interestingly, the catalytic activity and enantioselectivity are strongly dependent on the substituent at the 2′ position of the MOP ligands (**1b**, 80% ee; **1d**, 3% ee). It is proposed that the alkoxy functionality at the 2′ position works as a hemilabile coordinating group, effecting the asymmetric hydrovinylation. MeO-MOP has also been used for nickel-catalyzed [2 + 2 + 2] cycloaddition, giving isoindoline derivatives[38] and a [6]helicene[39] with moderate enantioselectivities.

Recently, MOP ligands have found application in rhodium-catalyzed asymmetric addition reactions, organoboronic acids to aldehydes[40] and organostannanes to imines.[41] In the latter case, the aryl-substituted MOP ligand **1f** is more enantioselective than MeO-MOP to give sulfonamides of diarylmethylamines with 96% ee (Scheme 14).

Conclusion

Chiral monophosphines, whose chirality is due to biaryl axial chirality, have been prepared from enantiomerically pure 2,2′-dihydroxy-1,1′-binaphthyl and demonstrated to be highly efficient chiral ligands for transition-metal-catalyzed organic transformations, especially for reactions where chelating bisphosphine ligands cannot be used because of their low catalytic activity or low selectivity for the desired reaction pathway. The high efficiency is highlighted by palladium-catalyzed asymmetric hydrosilylation of alkyl-substituted terminal olefins, which proceeds with unprecedented regioselectivity, and enantioselectivity giving 2-alkylsilanes of over 95% ee by use of the MeO-MOP ligand. With bisphosphine ligands such as BINAP, the hydrosilylation does not take place. High enantioselectivity has also been observed in the hydrosilylation of other types of alkenes, cyclic olefins, styrene derivatives, and so on. Asymmetric reduction of allylic esters with formic acid is another example of the palladium-catalyzed reactions where the use of MOP ligands is essential for the high catalytic activity and enantioselectivity. The MOP ligands have an advantage over others in that their fine-tuning is readily made by the introduction of a desired group at the 2′ position of the 1,1′-binaphthyl skeleton according to the reaction type and thus enhances the utility of the MOP ligands. Hopefully, asymmetric catalysis with MOP ligands will find wide application in transition-metal-catalyzed asymmetric reactions even in industrial-scale synthesis.

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