Palladium-Catalyzed Allylic Substitution with a Monodentate Phosphine Ligand

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CONTENTS

General Introduction 1

Chapter I Catalytic Asymmetric Synthesis of Optically Active Alkenes by Palladium-Catalyzed Asymmetric Reduction of Racemic Allylic Esters with Formic Acid 12

Chapter II Palladium-Catalyzed Asymmetric Reduction of Racemic Allylic Esters with Formic Acid: Effects of Isomerization of π-Allylpalladium Intermediates on Enantioselectivity 24

Chapter III Regio- and Enantio-selective Allylic Alkylation Catalyzed by a Chiral Monophosphine–palladium Complex 48

Chapter IV Retention of Regiochemistry of Allylic Esters in Palladium-Catalyzed Allylic Alkylation in the Presence of a MOP Ligand 59

Chapter V Regiocontrol in Palladium-Catalyzed Allylic Alkylation by Addition of Lithium Salts 80

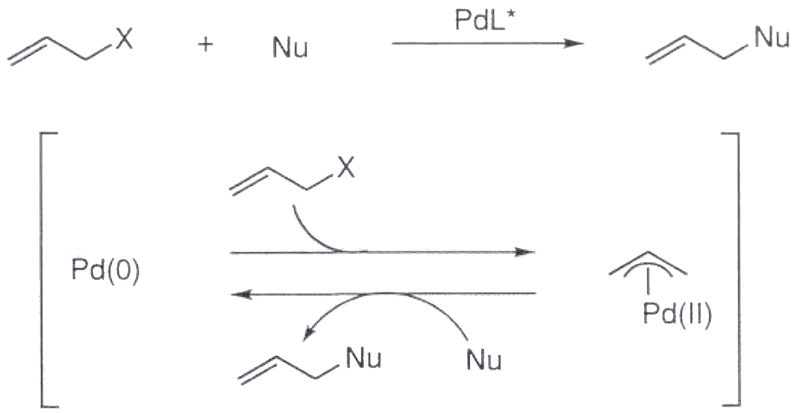
General Introduction

In biological systems, a pair of enantiomers will elicit different responses. One enantiomer may act as a very effective therapeutic drug whereas the other enantiomer is highly toxic. In synthetic organic chemistry, it is a challenging theme to access optically active molecules. Of the various ways to obtain the optically active compounds in chemical reactions,[1] catalytic asymmetric synthesis is an ideal and practical method as far as high enantioselectivity is obtained, because a large amount of chiral product can be produced with only a small investment of chiral material in the catalyst system.[2] Since tertiary phosphines are used as ligands for many reactions catalyzed by homogeneous transition-metal complexes, it only needs, in principle, incorporation of optically active phosphines as ligands to produce optically active products.[3] Of course, it is necessary to design a chiral ligand that will fit in with a given reaction for high asymmetric induction. While a number of chiral phosphine ligand have been designed and prepared, only a few of those are excellent ligands which are fit for use from the viewpoint of the stereoselectivity. BINAP,[4] chiraphos,[5] DIOP,[6] BPPM,[7] PPF–X and BPPF–X[8] are such excellent ones. It has been shown that transition metal complexes coordinated with some tertiary phosphine ligands have high catalytic activity for a variety of catalytic reactions[9] and the catalytic asymmetric synthesis has been realized by incorporation of optically active phosphines on the transition metal catalysts.[10] High enantioselectivity has been reported in several types of asymmetric reactions including rhodium- or ruthenium-catalyzed hydrogenation,[11,12] nickel- or palladium-catalyzed cross-coupling reactions,[13] and palladium-catalyzed allylic substitution reactions.[14,15]

Palladium-Catalyzed Allylic Substitution

As an example of allylic substitution reaction, carbon–carbon bond forming reaction with π-allylpalladium complexes was first reported by Tsuji in 1965.[16] In 1970, Walker and Hata discovered palladium-catalyzed allylic substitution of allylic substrate using various allylic leaving groups.[17] The catalytic cycle of the allylic substitution is generally accepted to involve a π-allylpalladium(II) complex as a key intermediate, which is formed by oxidative addition of an allylic substrate to palladium(0) and undergoes nucleophilic attack to yield a substituted product and to regenerate palladium(0) (Scheme

Scheme 1



1). Development of the palladium-catalyzed allylic substitution owes much to the works by Trost[18] and Tsuji,[19] who heightened this reaction to one of the most useful synthetic methods in organic synthesis using organometallic compounds.

Palladium-catalyzed allylic substitutions have found very wide application. A variety of nucleophiles have been reported to undergo the palladium-catalyzed allylic substitution; hydride[20], organometals such as Grignard[21] and organozinc reagent,[22] nitrogen,[23] oxygen,[24] phosphorous,[25] sulphur,[26] silicon,[27] and tin[28] nucleophiles, as well as soft carbon nucleophiles. Furthermore, a wide range of leaving groups, halogen, OH, OR, OCOOR, OSO_2R, $OP(O)(OR)_2$, $OCONR_2$, OC(=NR)NHR, and so on, can also be used on allylic substrates. As an applied version of the palladium-catalyzed allylic substitution, there have been reported intramolecular allylic substitution reactions forming vinylcyclopropanes, vinylethylene carbonates, and vinyloxazolidones,[29] or [3+2] cycloaddition reactions[30] which proceed via a zwitter-ionic π-allylpalladium intermediate. Such a wide applicability of the palladium-catalyzed allylic substitution will offer a great advantage of the catalytic asymmetric substitution over others.

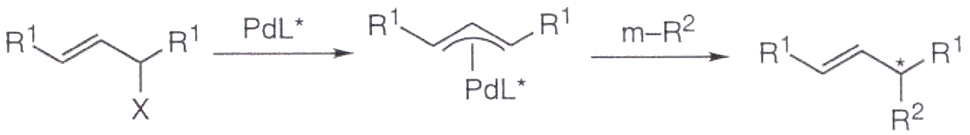
Asymmetric Catalytic Allylic Substitution

It is possible to classify allylic substitution into two types from the viewpoint of asymmetric synthesis (Scheme 2).[31] Type **I** is the reaction where a new chiral carbon center can be created in nucleophiles, and type **II** is the reaction where a new chiral carbon center can be created in allylic substrates. Type **II** is subdivided into three types, type **IIa, IIb,** and **IIc**, according to the substitution pattern of π-allyl group on the π-allylpalladium intermediate. In type **IIa**, the π-allylpalladium intermediate contains a

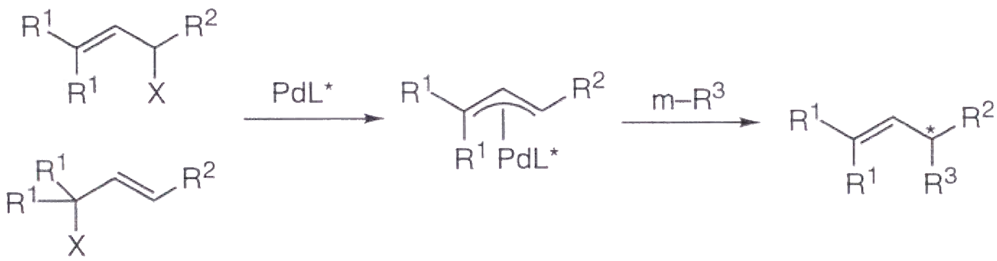
Scheme 2

Type **I**

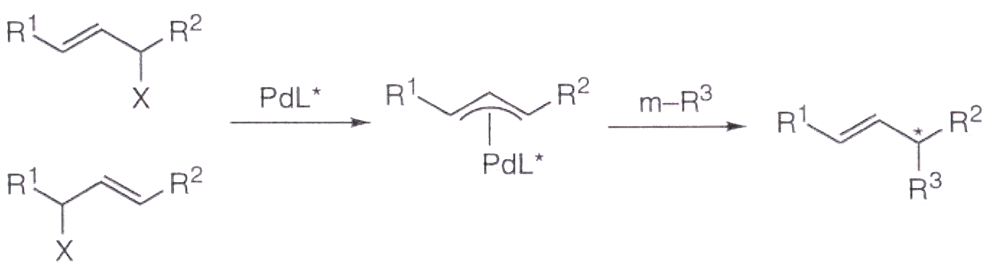
Type **IIa**



Type **IIb**



Type **IIc**



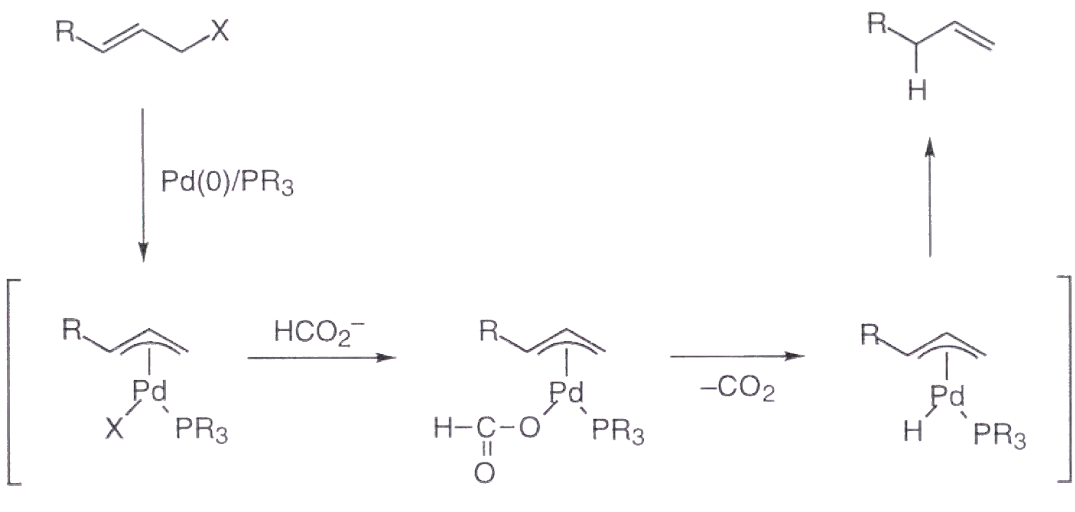
meso type π-allyl group which has identical substituents at 1 and 3 positions. In type **IIb**, the π-allyl group is chiral, but the π-allylpalladium intermediate can epimerize by π-σ-π isomerization mechanism[14] since the π-allyl group has the same substituents on one allylic terminal. In type **IIc,** the π-allyl group is chiral, which has the different substituents at 1 and 3 positions, and the π-allylpalladium intermediate can not epimerize by the π-σ-π mechanism.

First example of catalytic asymmetric allylic substitution has been reported by Trost in 1977, who obtained 24% and 46% optical yields in the allylic alkylation of type **IIa** and **IIc**, respectively.[32] Type **I** allylic substitution has been reported by Kagan in 1978, in which the optical yields of the substituted products were less than 10%.[33] During the past twenty years, several attempts have been made to improved the enantioselectivity by devising chiral ligands, allylic substrates, nucleophiles, and other reaction conditions. There have been reported type **I** reactions[34] by Hayashi and Genet, type **IIa** reactions[35,34b] by Fiaud, Trost, Hiyama, Bosnich, and Consiglio, and type **IIb** reactions[33c,d,36] by Yamamoto, Hiyama, Bosnich, Consiglio, and Hiroi, though the optical yields were not necessarily satisfactory except in a few notable examples. One excellent example is type **IIb** allylic substitution (up to 86% ee) using chiraphos as a ligand reported by Bosnich and co-workers.[24b–d] They have made detailed investigation on the mechanism of asymmetric induction connected with the enantioface selection. Other outstanding examples are palladium-catalyzed asymmetric allylic substitution of type **IIa**, where many chiral bisphosphine or aminophosphine ligands can exhibit high enantioselectivity (up to >99% ee),[37] and type **I** allylic substitution (up to 82% ee) using optically active ferrocenylphosphines reported by Hayashi.[22b] The limited number of the successful examples results mainly from the unsuitable chiral environment around π-allylpalladium intermediate and nucleophile. It is essential to design a chiral ligand which will fit in with a given reaction by creating effective environment to bring about high stereoselectivity. It is also important to clarify the stereochemistry of the reaction pathway because information on the mechanism of the reaction, which can be drawn on the basis of stereochemical results, helps the design of an effective chiral ligand.

Monodentate Phosphine Ligand

As a ligand for palladium–catalyzed asymmetric allylic substitution, chiral bisphosphine ligands were predominantly used.[14] On the other hand, there have been reported only a limited number of monodentate chiral phosphine ligands,[38] probably because with the exception of some they have been exhorted as being of little practical use as a bisphosphine ligand. However, there exist transition metal-catalyzed reactions where the bisphosphine-metal complexes can not be used because of their low activity and/or low selectivity toward a desired reaction pathway and therefore chiral monodentate phosphine ligands are required for the catalytic asymmetric synthesis to be viable. Hayashi has reported that the optically active monodentate phosphine, 2-(diphenylphosphino)-2'-methoxy-1,1'-binaphthyl (MeO-MOP)[39] is effective ligand for palladium–catalyzed asymmetric hydrosilylation of alkenes[37a,40] and palladium–catalyzed asymmetric hydroboration of 1,3-enynes.[41] Furthermore, MeO-MOP and its biphenanthryl analog (MOP-phen)[42] are very effective for the asymmetric reduction of allylic esters with formic acid.[40,43] Mechanistic studies[44] 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 the decarboxylation of the palladium formate complex and that the use of monodentate phosphine ligand is essential for the high regioselectivity (Scheme 3). In this manner, the MOP ligands form a neutral monophosphine π-allylpalladium complexes as a reaction intermediate. The MOP ligands are also expected to find utility in other types of catalytic asymmetric reactions where the use of monodentate phosphine ligands are essential or favorable for steric and/or electronic reasons.

Scheme 3



Survey of Thesis

From these viewpoints, the author has focused his effort on developing the palladium–catalyzed allylic substitution with monodentate phosphine ligand. This thesis deals with the asymmetric reduction of racemic allylic esters with formic acid catalyzed by palladium–MOP complexes and regio- and enantio-selective allylic alkylation of allylic esters catalysed by monophosphine–palladium complexes.

The first two chapters are concerned with the asymmetric reduction of racemic allylic esters with formic acid catalyzed by palladium–MOP complexes.

Chapter I deals with asymmetric reduction of tertiary allylic esters catalyzed by palladium–MOP complexes. The high enantioselectivity is attained with some racemic tertiary allylic esters where one of the alkyl groups at the 1 position is bulky enough to bring about high *syn* selectivity at the oxidative addition step. The allylic ester, obtained from tetralone, gave reduction product of up to 93% enantiomeric purity.

Chapter II deals with improvement of the enantioselectivity in asymmetric reduction of tertiary allylic esters catalyzed by palladium–MOP complexes and ligand effect for *syn-anti* isomerization of π-allylpalladium intermediate with new MOP analogs. Slow addition of formic acid and a new MOP analog, (*R*)-2-(bis(3-trifluoromethylphenyl)phosphinyl)-2'-methoxy-1,1'-binaphthyl, improved the enantioselectivity of reduction product in up to 90% ee. Furthermore, the rate constants for the isomerization in π-allylpalladium intermediate which were measured by the magnetization saturation transfer technique[45] in ^{1}H NMR has revealed the new MOP analog accelerate the *syn–anti* isomerization in π-allylpalladium intermediate.

The next three chapters are concerned with allylic alkylation catalyzed by a monophosphine–palladium complex.

Chapter III deals with regio- and enantio-selective allylic alkylation catalyzed by a chiral monophosphine–palladium complex. 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 branch isomer. The use of (*R*)-MeO-MOP, which is a sterically bulky chiral monophosphine ligand, for the palladium catalyzed allylic alkylation of 1-aryl-2-propenyl acetates reversed the regiochemistry to give branch isomers with high selectivity (90%) and up to 87% ee in this new allylic alkylation system.

Chapter IV deals with retention of regiochemistry of allylic esters in palladium–catalyzed allylic alkylation in the presence of a MOP ligand. In the palladium-catalyzed allylic alkylation which proceeds through 1,3-unsymmetrically substituted π-allylpalladium intermediates, selective substitution at the position originally substituted with leaving group was observed by use of a sterically bulky monodentate phosphine ligand, MeO-MOP. Studies of the structure of π-allylpalladium complexes generated by mixing $[PdCl(\pi\text{-cyclohexenyl})]_2$ with MeO-MOP revealed that cationic bisphosphine complex is not formed but neutral monophosphine complex PdCl(MeO-MOP)(π-cyclohexenyl) is formed and that the exchange of the coordination site of Cl and MeO-MOP in this complex (*cis-trans* isomerization) is much slower than that in triphenylphosphine complex $PdCl(PPh_3)$(π-cyclohexenyl). The slow exchange can rationalize the retention of regiochemistry in the allylic alkylation catalyzed by palladium/MeO-MOP complex.

Chapter V deals with regiocontrol in palladium-catalyzed allylic alkylation by addition of lithium iodide. In palladium-catalyzed allylic alkylation of allylic esters that proceeds through unsymmetrically substituted π-allylpalladium intermediate, usually produces two regioisomers, the ratio being dependent on the substituents, nucleophiles, and reaction conditions. But the regioselectivity in palladium-catalyzed allylic alkylation of 1-aryl-2-propenyl acetates or (*E*)-3-phenyl-2-propenyl acetate with sodium enolates of soft carbon nucleophiles was controlled by addition of a catalytic amount of lithium iodide to give linear products exclusively. In this reaction condition, their branch isomers were not detected at all.

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Chapter I

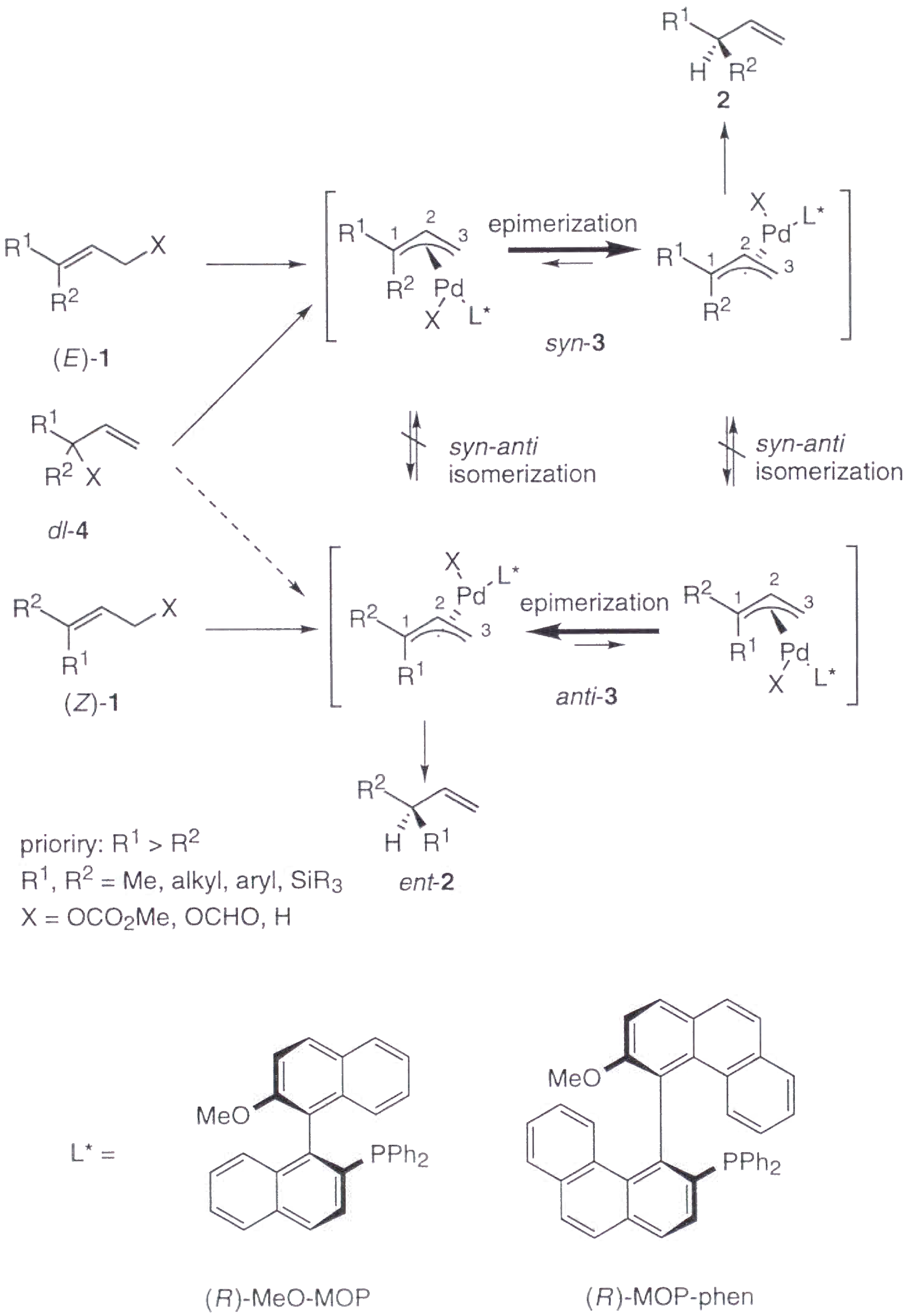
Catalytic Asymmetric Synthesis of Optically Active Alkenes by Palladium-Catalyzed Asymmetric Reduction of Racemic Allylic Esters with Formic Acid

Summary: Asymmetric reduction of racemic allyl esters, *e.g.* methyl 1-vinyl-1,2,3,4-tetrahydronaphth-1-yl carbonate, which contain two different alkyl groups at the α-position, with formic acid in the presence of 1 mol % of palladium catalyst coordinated with (*R*)-3-diphenylphosphino-3'-methoxy-4,4'-biphenanthryl [(*R*)-MOP-phen] ligand gives optically active terminal alkenes in up to 93% ee.

Introduction

It has been reported that the palladium-catalyzed reduction of allylic carbonates **1** with formic acid[1] in the presence of a palladium catalyst coordinated with axially chiral monodentate phosphine ligand, (*R*)-2-diphenylphosphino-2'-methoxy-1,1'-binaphthyl ((*R*)-MeO-MOP),[2] or its biphenanthryl analog, (*R*)-MOP-phen,[3] gives optically active olefins **2** of up to 91% ee (Scheme 1).[4,5,6] The reduction proceeds by way of Pd(II)X(π-allyl)(L*) intermediates **3** which undergo epimerization but do not undergo the *syn-anti* isomerization, and the stereochemical outcome is determined by the thermodynamic stability of the epimeric π-allylpalladium intermediates.[3,4,5] The esters of 3,3-disubstituted-2-propenols hitherto used for the asymmetric reduction are limited to those with a geometrically pure *E*- or *Z*- double bond for the high enantioselectivity because opposite enantiomers are produced from the *E*- and *Z*- esters. The palladium-catalyzed reduction of racemic 1,1-disubstituted-2-propenyl ester **4**, which is a regioisomeric ester of **1**, should proceed through the same π-allylpalladium intermediate **3**. If the oxidative addition of ester **4** to palladium(0) takes place with high selectivity in forming either the *syn* or *anti* π-allylpalladium intermediate, the reduction product **2** is expected to have high enantioisomeric purity, as high as that from the regioisomer (*E*)-**1** or (*Z*)-**1**. We found that the high enantioselectivity is attained with some racemic tertiary allylic esters **4** where one of the alkyl groups at the 1 position is bulky enough to bring about high *syn* selectivity at the oxidative addition step. This asymmetric transformation provides a practically useful method for the synthesis of optically active olefins because the starting racemic 1,1-disubstituted-2-propenyl ester **4** is readily available by the reaction of ketone

Scheme 1



epimerization
syn-3
syn-anti isomerization
syn-anti isomerization
epimerization
anti-3
(E)-1
dl-4
(Z)-1
2
ent-2
prioriry: R1 > R2
R1, R2 = Me, alkyl, aryl, SiR3
X = OCO2Me, OCHO, H
L* =
(R)-MeO-MOP
(R)-MOP-phen

with the vinyl Grignard reagent followed by esterification.

Rsults and discussion

The results obtained for the asymmetric reduction of racemic esters **4** are summarized in Table 1, which also contains data for the reaction of (*E*)-**1** for comparison. The reduction of methyl 1-vinyl-1,2,3,4-tetrahydronaphth-1-yl carbonate (**4a**) with formic acid (2.2 equiv.) in the presence of 1,8-bis(dimethylamino)naphthalene (proton sponge) (1.2 equiv.) and 1.0 mol % of palladium catalyst, generated in situ by mixing $Pd_2(dba)_3 \cdot CHCl_3$ and (*R*)-MOP-phen (Pd/P = 1/2), proceeded at –20 °C in THF-dioxane to give optically active (*R*)-1-vinyl-1,2,3,4-teterahydronaphthalene (**2a**) in 87% yield ($[\alpha]_D^{20}$ –84.0 (*c* 0.9, chloroform)) (entry 1 in Table 1) (Scheme 2). The absolute configuration was assigned by correlation with known (*S*)-(–)-1,2,3,4-tetrahydro-1-naphthoic acid[7] ($[\alpha]_D^{20}$ –56.7 (*c* 0.5, benzene)), and the enantiomeric purity was determined to be 93% ee by capillary GLC analysis with chiral stationary phase column, CP Cyclodex β–236M. At higher reaction temperature, the enantioselectivity was a little lower, the % ee of **2a** being 91% and 84% at 0 °C and 20 °C, respectively (entries 2 and 3). Benzoate ester *dl*-**4a'** and pivalate ester *dl*-**4a''** also underwent the asymmetric reduction to give (*R*)-**2a** in 93% ee and 92% ee, respectively (entries 5 and 6). The reduction of *dl*-**4a'** stopped at a low conversion (45%) gave (*R*)-**2a** with essentially the same enantiomeric purity (91% ee) as that obtained at complete conversion, and the recovered ester was racemic (entry 7). These results indicate that the present asymmetric reduction does not involve a kinetic resolution process of the starting racemic ester. The asymmetric reduction of *dl*-**4b**, which is a racemic ester derived from 1-indanone, also proceeded with high enantioselectivity giving the corresponding terminal olefin (*R*)-**2b**[8] of 86% ee (entry 10).

Interestingly, the asymmetric reduction of *dl*-**4a** is much faster than that of its regioisomeric ester, 3,3-disubstituted-2-propenyl carbonate (*E*)-**1a**. The reduction of (*E*)-**1a** did not take place at the reaction temperature of 0 °C or lower (entry 8). At 20 °C it gave (*R*)-**2a** in 83% ee (entry 9), the stereoselectivity being essentially the same as that for *dl*-**4a** at 20 °C (entry 3). The lower reactivity of (*E*)-**1a** is ascribed to the two alkyl substituents at the 3 position of (*E*)-**1a**. The steric hindrance retards the oxidative addition step in the catalytic cycle which takes place in an S_N' manner.[6,9]

The stereochemical results in the reduction of *dl*-**4a** and (*E*)-**1a** is illustrated in Scheme 3. The π-allylpalladium intermediate resulting from (*E*)-**1a** should be *syn*-**5**, which contains the aromatic ring at *syn* position with respect to the hydrogen at 2 position

Scheme 2

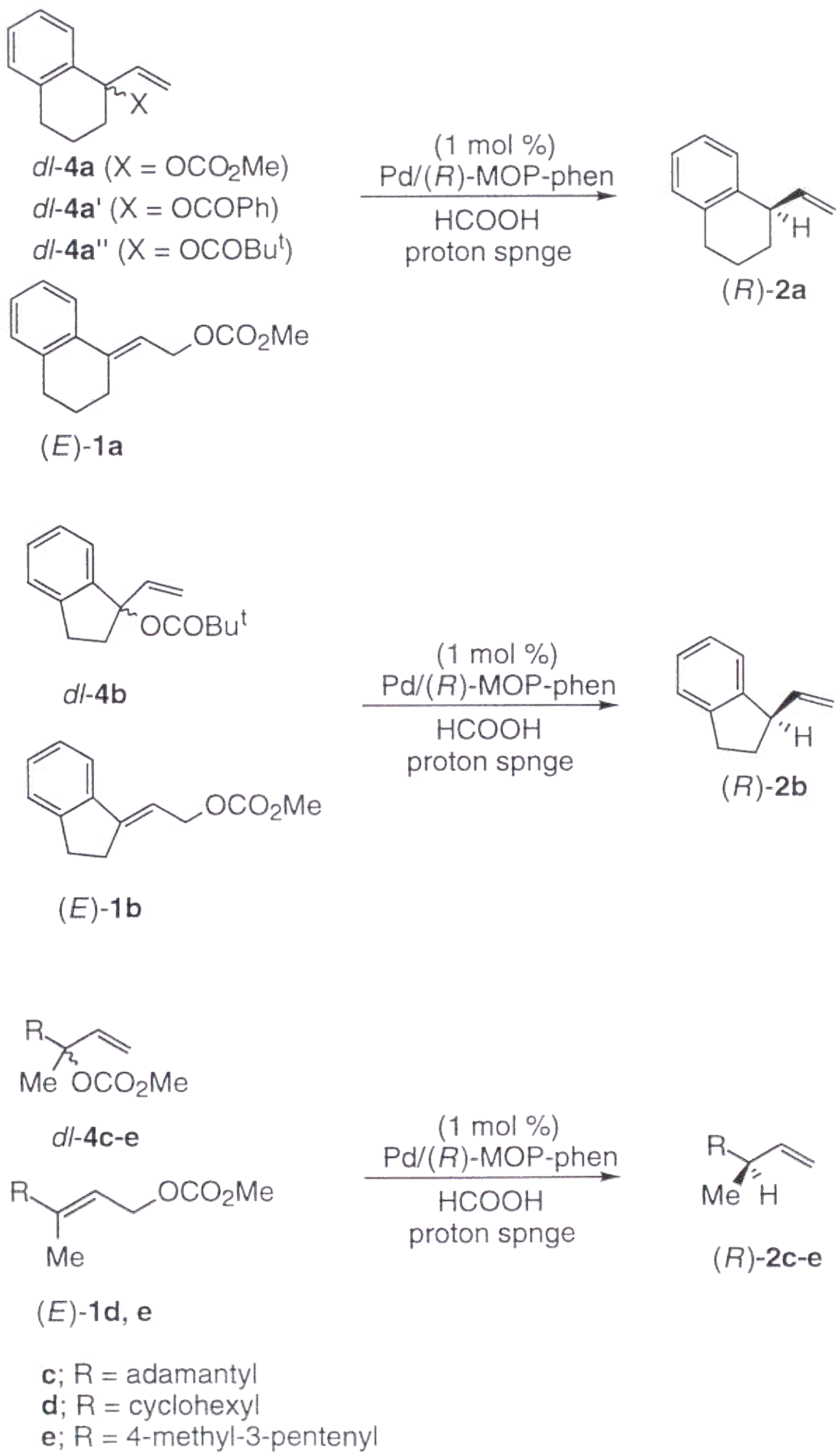

dl-4a (X = OCO2Me)
dl-4a' (X = OCOPh)
dl-4a'' (X = OCOBut)
OCO2Me
(E)-1a
(1 mol %)
Pd/(R)-MOP-phen
HCOOH
proton spnge
(R)-2a
OCOBut
dl-4b
OCO2Me
(E)-1b
(1 mol %)
Pd/(R)-MOP-phen
HCOOH
proton spnge
(R)-2b
Me OCO2Me
dl-4c-e
OCO2Me
Me
(E)-1d, e
(1 mol %)
Pd/(R)-MOP-phen
HCOOH
proton spnge
Me H
(R)-2c-e
c; R = adamantyl
d; R = cyclohexyl
e; R = 4-methyl-3-pentenyl

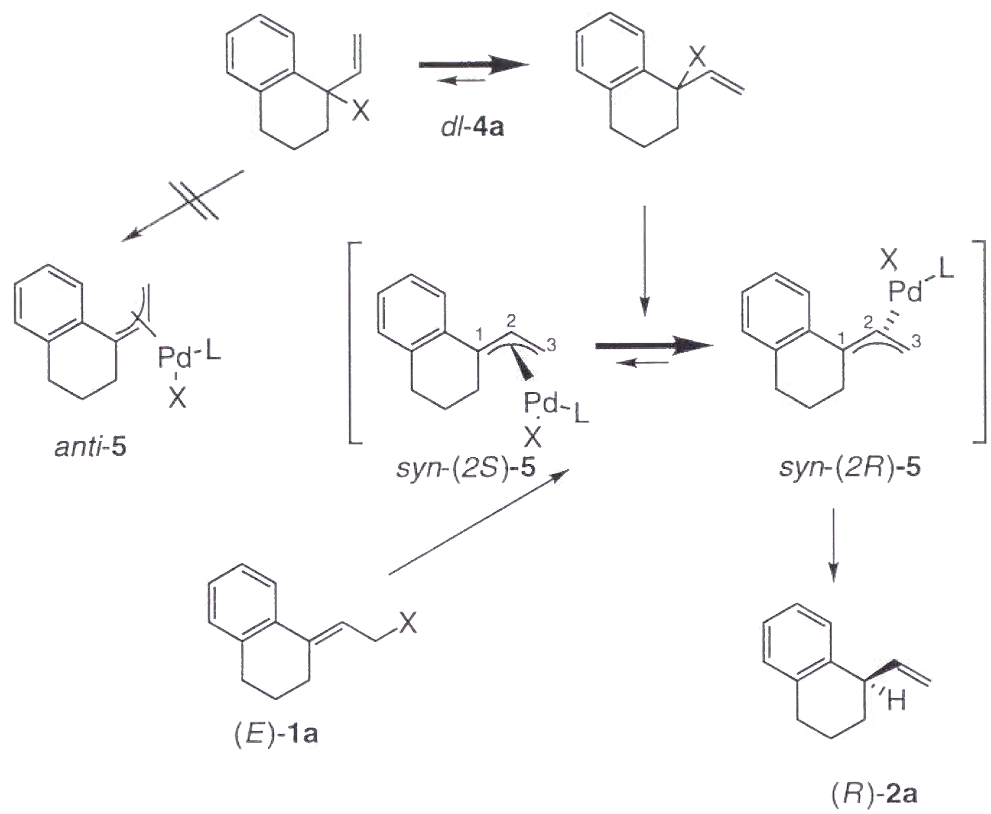
Table 1. Asymmetric Reduction of Allylic Esters with Formic Acid Catalyzed by Palladium/MOP-phen[a]

entry	allyl ester	conditions temp (°C)	time (h)	yield (%)[b] of **2**	% ee of **2** (config)
1	*dl*-**4a**	–20	48	85 (**2a**)	93[c] (*R*)[d]
2	*dl*-**4a**	0	24	91 (**2a**)	91[c] (*R*)
3	*dl*-**4a**	20	5	87 (**2a**)	84[c] (*R*)
4[e]	*dl*-**4a**	20	12	89 (**2a**)	78[c] (*R*)
5	*dl*-**4a'**	–20	48	87 (**2a**)	93[c] (*R*)
6	*dl*-**4a''**	–20	96	90 (**2a**)	92[c] (*R*)
7	*dl*-**4a''**	–20	48	45 (**2a**)[f]	91[c] (*R*)
8	(*E*)-**1a**	0	120	0 (**2a**)	—
9	(*E*)-**1a**	20	12	91 (**2a**)	83[c] (*R*)
10	*dl*-**4b**	0	24	81 (**2b**)	86[c] (*R*)[d]
11	(*E*)-**1b**	20	11	88 (**2b**)	78[c] (*R*)
12	*dl*-**4c**	0	36	96 (**2c**)	75[d,g]
13	*dl*-**4d**	20	3	92 (**2d**)	13[g] (*R*)
14	(*E*)-**1d**	20	22	96 (**2d**)	85[g] (*R*)
15	*dl*-**4e**	20	12	>99 (**2e**)	8[h] (*S*)
16	(*E*)-**1e**	20	17	>99 (**2e**)	85[h] (*S*)

[a] The reaction was carried out with 2.2 equiv. of formic acid in THF-dioxane (1:1) in the presence of 1.2 equiv. of proton sponge and 1.0 mol % of catalyst prepared in situ by mixing $Pd_2(dba)_3 \cdot CHCl_3$ and (*R*)-MOP-phen (P/Pd = 2/1). [b] Isolated yield by silica gel column chromatography. [c] Determined by GLC analysis with chiral stationary phase column, CP Cyclodex β236M. [d] Specific rotation of of **2a** (entry 1) and **2b** (entry 10) are $[\alpha]_D^{20}$ –84.0 (*c* 0.9, chloroform) and $[\alpha]_D^{20}$ –74.6 (*c* 1.0, chloroform), respectively. [e] Reaction with (*R*)-MeO-MOP. [f] The recovered (48%) ester **7** was racemic, which was determined by the GLC analysis (CP Cyclodex β236M) of 1-vinyl-1,2,3,4-teterahydro-1-naphthol. [g] Determined by HPLC analysis of anilide of carboxylic acid, obtained by the oxidation ($NaIO_4$–$KMnO_4$) of **2c** or **2d**, with Sumichiral OA-2000 (hexane/dichloroethane/ethanol = 250/20/1). [h] Determined by HPLC analysis of dianilide of 2-methylpentene-dioic acid, obtained by the oxidation ($NaIO_4$–$KMnO_4$) of **2e**, with Sumichiral OA-4100 (hexane/dichloroethane/ethanol = 50/15/1).

of π-allyl. The same stereochemical outcome in the reaction of (*E*)-**1a** and *dl*-**4a** indicates that the π-allylpalladium intermediate formed from *dl*-**4a** is also *syn*-**5**, and the configuration *R* of the product **2a** indicates that the configuration of the predominant π-allylpalladium intermediate is *syn*-(2*R*)-**5**[10] in both cases. In the reaction of racemic 1,1-

Scheme 3



disubstituted-2-propenyl ester *dl*-**4** where one of the substituents on the 1 position is much bigger than the other, the allyl ester undergoes the oxidative addition with the conformation forming a π-allylpalladium intermediate with the bigger alkyl group substituted at the *syn* position. After the epimerization between *syn*-(2*R*)-**5** and *syn*-(2*S*)-**5** the product (*R*)-**2a** is formed from thermodynamically more stable *syn*-(2*R*)-**5** (Scheme 3).

The asymmetric reduction of acyclic allylic ester *dl*-**4c** that contains sterically bulky 1-adamanthyl group at 1-position also proceeded with high enantioselectivity to give **2c** of 75% ee (entry 12). Much lower enantioselectivity (around 10% ee) was observed in the reaction of sterically less bulky esters *dl*-**4d** and *dl*-**4e** (entries 13 and 15). Comparing the low selectivity in the reaction of *dl*-**4d** and *dl*-**4e** with the high selectivity in the reaction of their regioisomers (*E*)-**1d** and (*E*)-**1e** which gave the corresponding olefines[11] of 85% ee[4] (entries 14 and 16), it follows that the selectivity forming *syn*-isomer of the π-allylpalladium intermediates is low with these sterically less bulky 1,1-disubstituted-2-propenyl esters.

To summarize, high enantioselectivity was obtained in the palladium-catalyzed asymmetric reduction of racemic 1,1-disubstituted 2-propenyl esters *dl*-**4** that contain a sterically bulky group at 1 position. The higher reactivity of *dl*-**4** towards palladium(0) than their regioisomeric allylic esters (*E*)-**1** made it possible to carry out the asymmetric reduction at lower temperature to result in high enantioselectivity.

Experimental Section

General. All manipulations were carried out under a nitrogen atmosphere. Nitrogen gas was dried by passage through P_2O_5 (Merck, SICAPENT). NMR spectra were recorded on a JEOL JNM-EX270 spectrometer (270 MHz for ^1H and 109 MHz for ^{31}P), JEOL JNM-AL400 spectrometer (400 MHz for ^1H NMR), or JEOL JNM LA500 spectrometer (500 MHz for ^1H, 125 MHz for ^{13}C and 202 MHz for ^{31}P). Chemical shifts are reported in δ ppm referenced to an internal $SiMe_4$ standard for ^1H NMR, and to an external 85% H_3PO_4 standard for ^{31}P NMR. Residual chloroform (δ 77.0 for ^{13}C) was used as internal reference for ^{13}C NMR. ^1H, ^{13}C and ^{31}P NMR spectra were recorded in $CDCl_3$ at 25 °C unless otherwise noted. HPLC analysis was performed on a Shimazu LC-6A liquid chromatograph system and a JASCO PU-980 liquid chromatograph system with chiral stationary phase column Sumitomo Chemical Co. Ltd., Sumipax OA series. GLC analysis was performed on a HEWLETT PACKARD HP 6890 series with a chiral stationary phase column, CP Cyclodex β-236M (50 m). Optical rotation were measured on a JASCO DIP-370 polarimeter.

Materials. THF was dried over sodium benzophenone ketyl and distilled prior to use. $Pd_2(dba)_3{\cdot}CHCl_3$,[12] (*R*)-MeO-MOP,[2] (*R*)-MOP-phen,[3] (*E*)-3-cyclohexyl-2-butenol[13] and geranyl methyl carbonate[14] ((*E*)-**1e**) were prepared according to the reported procedures.

Preparation of 3,3-Disubstituted Propenyl Esters ((*E*)-1a,b and d): Methyl (*E*)-2-(1,2,3,4-tetrahydronaphthylidenyl)ethyl carbonate ((***E***)**-1a**) and methyl (*E*)-2-(2,3-dihydroindenylidenyl)ethyl carbonate ((***E***)**-1b**) were obtained by the 1,3-rearrangement of carbomethoxy group during the silica gel column chromatography of methyl 1-vinyl-1,2,3,4-tetrahydronaphtyl carbonate (*dl*-**4a**) and methyl 1-vinyl-2,3-dihydroindenyl carbonate, respectively. **Methyl (*E*)-2-(1,2,3,4-Tetrahydronaphthylidenyl)ethylcarbonate ((*E*)-1a):** ^1H NMR ($CDCl_3$) δ 1.81–1.92 (m, 2H), 2.57–2.65 (m, 2H), 2.78–2.82 (m, 2H), 3.80 (s, 3H), 4.86 (d, J = 7.2 Hz, 2H), 6.17 (t, J = 7.2 Hz, 1H), 7.12–7.23 (m, 3H), 7.58–7.62 (m, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 22.9, 26.6, 30.2, 54.7, 64.6, 116.3, 124.1, 126.0, 127.6, 128.9, 134.7, 138.0, 140.0, 155.8. Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C,72.19; H, 7.01. **Methyl (*E*)-2-(2,3-Dihydroindenylidenyl)ethyl-carbonate ((*E*)-1b):** ^{1}H NMR ($CDCl_3$) δ 2.79–2.84 (m, 2H), 2.95–3.07 (m, 2H), 3.78 (s, 3H), 4.75 (d, J = 7.4 Hz, 2H), 6.03 (t, J = 7.4 Hz, 1H), 7.16–7.50 (m, 4H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 27.8, 35.0, 54.4, 62.4, 79.8, 112.4, 120.6, 126.5, 128.5, 146.7, 147.4, 153.5, 178.6. Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.28; H, 6.55. Methyl (*E*)-3-cyclohexyl-2-butenyl carbonate ((*E*)-**1d**) was obtained by treatment of (*E*)-3-cyclohexyl-2-butenol with methyl chloroformate and pyridine. Experimental procedures: To a solution of (*E*)-3-cyclohexyl-2-butenol and pyridine (522 mg, 6.6 mmol) in benzene (10 mL) was added methyl chloroformate (467 mg, 4.9 mmol) dropwise at 0 °C and the mixture was stirred for 1.5 h. The reaction was quenched with brine and extracted with ether. The organic layer was washed with saturated sodium bicarbonate solution, dried over anhydrous sodium sulfate and evaporated. The crude product was purified by silica gel column chromatography (hexane/ EtOAc = 10/1) to give 657 mg (94%) of methyl (*E*)-3-cyclohexyl-2-butenyl carbonate ((*E*)-**1d**): ^{1}H NMR ($CDCl_3$) δ 1.15–1.92 (m, 11H), 1.70 (s, 3H), 3.79 (s, 3H), 4.66 (d, J = 7.0 Hz, 2H), 5.36 (t, J = 7.0 Hz, 1H). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.49. Found: C, 67.78; H, 9.47.

Preparation of Racemic 1,1-Disubstituted Propenyl Esters (*dl*-4a-e). A typical procedure is given for 1-vinyl-1,2,3,4-tetrahydronaphthyl benzoate (*dl*-**4a'**). To a solution of vinylmagnesium bromide (25 mL of 0.9 M, 22.5 mmol) in diethyl ether at 0 °C was added dropwise a solution of α-tetralone (3.0 g, 20.5 mmol) in diethyl ether (15 mL) in THF (30 mL). The mixture was stirred at room temperature for 5 h. It was quenched with 0.5% sulfuric acid solution and extracted with ether. The ether extracts were dried over anhydrous sodium sulfate. Evaporation of the solvent gave a crude product. To a solution of this crude product in THF/MeOH (20 mL/10 mL) added a $NaBH_4$ (150 mg, 4 mmol) to reduce an unreacted α-tetralone and stirred at room temperature for 12 h. Evaporation of the solvent and the crude product was purified by silica gel column chromatography (hexane/EtOAc = 10/1) to give 2.0 g (56%) of allyl alcohol: ^{1}H NMR ($CDCl_3$) δ 1.8–2.0 (m, 5H), 2,7–2.9 (m, 2H), 5,21 (d, J = 10.7 Hz, 1H), 5.32 (d, J = 18.3 Hz, 1H), 5.32 (dd, J = 10.7, 18.3 Hz, 1H), 7.13–7.40 (m, 4H). To a solution of this allyl alcohol (671 mg, 3.85 mmol) and 1,10-phenanthroline (ca. 5 mg) in THF (10 mL) was added 1.5 M *n*-butyllithium in hexane (2.8 mL, 4.2 mmol) at –78 °C and stirred for 1 h. To this reaction mixture was added benzoyl chloride (605 mg, 4.3 mmol). The mixture was allowed to warm to room temperature and stirred for 30 min. The reaction was quenched with saturated sodium bicarbonate solution and extracted with EtOAc. The organic layer was washed with saturated sodium bicarbonate solution and brine, dried over anhydrous sodium sulfate and evaporated. The crude product was purified by alumina column chromatography (hexane/Et_3N = 20/1) to give 738 mg (69%) of *dl*-1-vinyl-1,2,3,4-tetrahydronaphthyl benzoate (*dl*-**4a'**): ^1H NMR ($CDCl_3$) δ 1.7–2.1 (m, 2H), 2,3–2.4 (m, 1H), 2.6–3.0 (m, 3H), 4.97 (d, J = 17.2 Hz, 1H), 5.22 (d, J = 9.8 Hz, 1H), 6.42 (dd, J = 9.8, 17.2 Hz, 1H), 7.1–8.0 (m, 9H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 20.3, 29.3, 33.1, 84.2, 115.8, 125.1, 125.9, 127.4, 127.8, 128.2, 128.3, 128.7, 129.6, 131.6, 132.7, 136.9, 137.7, 141.9, 164.9. Anal. Calcd for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52. Found: C, 82.25; H, 6.67. ***dl*-Methyl 2-Adamantyl-3-buten-2-yl Carbonate** (*dl*-**4a**): ^1H NMR ($CDCl_3$) δ 1.59 (s, 3H), 1.60–1.80 (m, 15H), 1.95–2.05 (m, 3H), 3.72 (s, 3H), 5.01 (d, J = 16.5 Hz, 1H), 5.26 (d, J = 9.5 Hz, 1H), 5.92 (dd, J = 9.5, 16.5 Hz, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 28.4, 35.8, 36.9, 39.5, 53.9, 89.2, 115.0, 138.7, 154.2. Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C,72.60; H, 9.30. ***dl*-Methyl 2-Cyclohexyl-3-buten-2-yl Carbonate** (*dl*-**4d**): ^1H NMR ($CDCl_3$) δ 0.90–1.76 (m, 11H), 1.50 (s, 3H), 3.66 (s, 3H), 5.10 (d, J = 16.5 Hz, 1H), 5.17 (d, J = 9.5 Hz,1H), 5.90 (dd, J = 9.5, 16.5 Hz, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 19.1, 26.3, 26.9, 27.1, 46.6, 53.9, 87.2, 114.8, 139.8, 153.9. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.90; H, 9.50. Found: C, 67.55; H, 9.66. ***dl*-Methyl Linalyl Carbonate** (*dl*-**4e**): ^1H NMR ($CDCl_3$) δ 1.64 (s, 3H), 1.66 (s, 3H), 1.70 (s, 3H), 0.92 (t, J = 7.0 Hz, 3H), 1.90–2.00 (m, 2H), 2.10–2.20 (m, 3H), 3.80 (s, 3H), 5.17–5.22 (m, 1H), 5.24 (d, J = 9.5 Hz, 1H), 5.34 (d, J = 16.2 Hz, 1H), 5.79 (dd, J = 9.5 and 16.2 Hz, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 17.5, 22.0, 22.8, 25.2, 39.2, 53.5, 83.9, 113.6, 123.3, 131.4, 140.8, 153.5. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.49. Found: C, 68.16; H, 9.78. ***dl*-Methyl 1-Vinyl-1,2,3,4-tetrahydronaphthyl Carbonate** (*dl*-**4a**): ^1H NMR ($CDCl_3$) δ 1.77–1.81 (m, 1H), 1.93–1.97 (m, 1H), 2.19–2.23 (m, 1H), 2.58–2.63 (m, 1H), 2.72–2.77 m, 1H), 2.87–2.93 (m, 1H), 4.86 (d, J = 17.1 Hz, 1H), 5.21 (d, J = 10.7 Hz, 1H), 6.26 (dd, J = 10.7 and 17.1 Hz, 1H), 7.08–7.34 (m, 4H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 20.1, 29.2, 32.7, 54.1, 85.1, 116.2, 125.9, 127.6, 127.7, 128.6, 136.2, 137.9, 141.3, 153.5. Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.00; H, 6.90. ***dl*-1-Vinyl-1,2,3,4-tetrahydronaphtyl Pivalate** (*dl*-**4a''**): ^1H NMR ($CDCl_3$) δ 1.20 (s, 9H), 1.68–2.00 (m, 2H), 2.18–2.27 (m, 1H), 2.46–2.58 (m, 1H), 2.70–2.99 (m, 2H), 4.90 (d, J = 17.2 Hz, 1H), 5.16 (d, J = 9.8 Hz, 1H), 6.27 (dd, J = 9.8, 17.2 Hz, 1H), 7.08–7.28 (m, 4H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 20.2, 27.0, 29.2, 32.7, 39.3, 46.2, 82.7, 114.8, 125.7, 127.1, 128.5, 137.1, 137.4, 142.0, 176.6. Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C,79.00; H, 8.79. ***dl*-1-**

Pivaloyloxy-1-vinylindan (*dl*-**4b**): ^{1}H NMR ($CDCl_3$) δ 1.20 (s, 9H), 2.40–3.08 (m, 4H), 2.6–3.0 (m, 3H), 5.06 (d, *J* = 17.8 Hz, 1H), 5.14 (d, *J* = 10.4 Hz, 1H), 6.29 (dd, *J* = 10.4, 17.8 Hz, 1H), 7.20–7.32 (m, 4H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 27.0, 30.0, 38.9, 90.6, 113.5, 119.4, 124.6, 124.9, 126.4, 128.5, 139.2, 143.1, 143.3, 177.1. Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.65; H, 8.00.

Catalytic Asymmetric Reduction of Allylic Esters ((*E*)-1 and *dl*-4). A typical procedure is given for the reaction of 1-vinyl-1,2,3,4-tetrahydronaphthyl benzoate (***dl*-4a'**). Under nitrogen, a solution of (*R*)-MOP-phen (5.8 mg, 0.011 mmol) and $Pd_2(dba)_3{\cdot}CHCl_3$ (2.6 mg, 0.0024 mmol) in 1,4-dioxane/THF (0.5 mL/0.5 mL) was stirred at room temperature. In about 30 min, the dark-red solution turned orange. The solution was cooled to 0 °C, and 1,8-bis(dimethylamino)naphthalene (128.0 mg, 0.60 mmol) and formic acid (52.8 mg, 1.14 mmol) were added. The solution was cooled to –20 °C, and 1-vinyl-1,2,3,4-tetrahydronaphtyl benzoate ***dl*-4a'** (143.1 mg, 0.51 mmol) was added. The mixture was stirred for 2 days. The completion of the reduction was confirmed by TLC. Pentane and water were added to the reaction mixture, the organic phase was separated, and passed through short silica gel column to give 70.2 mg (87%) of (*R*)-1-vinyl-1,2,3,4-tetrahydronaphthalene ((***R***)-**2a**) as a colorless oil: (*R*)-(–)-93% ee; $[\alpha]_D^{20}$ –84.0 (*c* 0.9, chloroform). The absolute configuration was assigned by correlation with known (*S*)-(–)-1,2,3,4-tetrahydronaphthoic acid {$[\alpha]_D^{20}$ –56.7 (*c* 0.5, benzene), *lit*[7]. $[\alpha]_D^{20}$ –63.8 (benzene)} and the enantiomeric purity was determined to be 93% ee by capillary GLC analysis with a chiral stationary phase column, CP Cyclodex β-236M. **(*R*)-1-Vinyl-1,2,3,4-tetrahydronaphthalene ((*R*)-2a)**[7] (93% ee): $[\alpha]_D^{20}$ –84.0 (*c* 0.9, chloroform) ^{1}H NMR ($CDCl_3$) δ 1.64–2.01 (m, 4H), 2.72–2.81 (m, 2H), 3.40–3.50 (m, 1H), 5.05 (d, *J* = 18.0 Hz, 1H), 5.15 (d, *J* = 9.5 Hz, 1H), 5.56 (ddd, *J* = 8.5, 10.5 and 18.0 Hz, 1H), 7.14–7.25 (m, 4H). **(*R*)-1-Vinylindan ((*R*)-2b)**[15] (86% ee): $[\alpha]_D^{20}$ –74.6 (*c* 1.0, chloroform) ^{1}H NMR ($CDCl_3$) δ 1.78–1.92 (m, 1H), 2.27–2.40 (m, 1H), 2.80–3.01 (m, 2H), 3.75 (dd, *J* = 8.2 and 16.4 Hz, 1H), 5.09 (d, *J* = 10.2 Hz, 1H), 5.16 (d, *J* = 18.2 Hz,1H), 5.84 (ddd, *J* = 8.2 10.2 and 18.2 Hz, 1H), 7.14–7.25 (m, 4H). **3-Adamantyl-1-butene**[16] (**2c**) (75% ee): $[\alpha]_D^{20}$ +3.5 (*c* 1.0, chloroform) ^{1}H NMR ($CDCl_3$) δ 0.90 (d, *J* = 7.3 Hz, 3H), 1.20–2.00 (m, 16H), 1.95–2.05 (m, 3H), 4.87–4.96 (m, 2H), 5.26 (d, *J* = 10.5 Hz, 1H), 5.38 (d, *J* = 17.5 Hz, 1H), 5.92 (dd, *J* = 10.5 and 17.5 Hz, 1H). **(*R*)-3-Cyclohexyl-1-butene ((*R*)-2d)** (85% ee): ^{1}H NMR ($CDCl_3$) δ 0.98 (d, *J* = 6.9 Hz, 3H), 0.92–1.78 (m, 11H), 1.91–2.04 (m, 1H), 4.88–4.94 (m, 2H), 5.68 (m, 1H). $[\alpha]_D^{24}$ +4.2 (c 0.62, chloroform). *lit.*[11b] (*R*)-(+): $[\alpha]_D^{24}$ +4.1 (c 0.67, chloroform). **(*S*)-3,7-Dimethyl-**

1,6-octadiene ((*S*)-**2e**) (85% ee): ^{1}H NMR ($CDCl_3$) δ 0.98 (d, J = 7.0 Hz, 3H), 1.27–1.36 (m, 2H), 1.60 (s, 3H), 1.67 (s, 3H), 1.96 (q, J = 7.0 Hz, 2H), 2.12 (heptet, J = 7.0 Hz, 1H), 4.90 (d, J = 10.1 Hz, 1H), 4.92 (d, J = 17.1 Hz, 1H), 5.05–5.15 (m, 1H), 5.70 (ddd, J = 17.1, 10.1 and 7.0 Hz, 1H). $[\alpha]_D^{20}$ +8.1 (c 1.60, chloroform). *lit.*[11a] (*R*)-(–): $[\alpha]_D$ –9.82 (c 6.18, chloroform).

Determination of Absolute Configuration and Enantiomeric Purities: Olefins **2a** and **2b** were converted into the 1,2,3,4-tetrahydronaphthoic acid and 1-carboxyindan, respectively, by oxidation with $NaIO_4/KMnO_4$. The absolute configuration of **2a** and **2b** were determined by correlation with known (*S*)-(–)-1,2,3,4-tetrahydronaphthoic acid and (*S*)-(–)-1-carboxyindan, respectively. Olefins **2c**, **2d** and **2e** were converted into *N*-phenyl-2-adamantylpropanamide, *N,N'*-diphenyl-2-methylpentane-1,5-dicarboxamide[17] and *N*-phenyl-2-cyclohexylpropanamide,[18] respectively, by oxidation with $NaIO_4/KMnO_4$ followed by treatment of the resulting carboxylic acids with aniline and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (WSC). The conditions for the determination of the enantiomeric purities of anilides with chiral stationary phase columns are as follows: *N*-Phenyl-2-adamantylpropanamide: Sumichiral OA-2500I; hexane/1,2-dichloroethane/EtOH = 1000/20/1; (+) isomer eluted faster than (–) isomer. *N, N'*-Diphenyl-2-methylpentane-1,5-dicarboxamide: Sumichiral OA-4100; hexane/1,2-dichloroethane/EtOH = 50/15/1; *R* isomer eluted faster than *S* isomer. *N*-Phenyl-2-cyclohexylpropanamide: Sumichiral OA-2000; hexane/1,2-dichloroethane/EtOH = 250/20/1; *S* isomers eluted faster than *R* isomers. A typical procedure for the conversion is given for the reaction of **2e**. To a solution of (*S*)-**2e** (61 mg, 0.44 mmol) in *t*-BuOH (10 mL) and water (20 mL), were added $KMnO_4$ (185 mg, 1.17 mmol), $NaIO_4$ (1.46 g, 6.86 mmol) and K_2CO_3 (366 mg, 2.64 mmol), and the mixture was adjusted to pH 8 with 3 N aq NaOH. After stirring at room temperature for 2 h, the mixture was acidified with conc. hydrochloric acid to pH 1 and sodium hydrogen sulfite was added to reduce MnO_2. The mixture was extracted with ether and the ether layer was extracted with 3 N aq NaOH. The aqueous solution was acidified with conc. hydrochloric acid and extracted with ether. The ether extracts were dried ($MgSO_4$) and evaporation of the solvent gave 2-methylpentanedioic acid (38 mg). To a solution of the carboxylic acid (10 mg) obtained above in THF (0.5 mL), were added aniline (15 mg, 0.16 mmol) and WSC (30 μL), and the mixture was stirred at 40 °C for 1 h. Conc. hydrochloric acid was added and the mixture was extracted with EtOAc. Evaporation of the solvent followed by silica gel column chromatography (hexane/EtOAc = 1/1) gave *N,N'*-diphenyl-2-methylpentane-1,5-dicarboxamide (11 mg).

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Chapter II

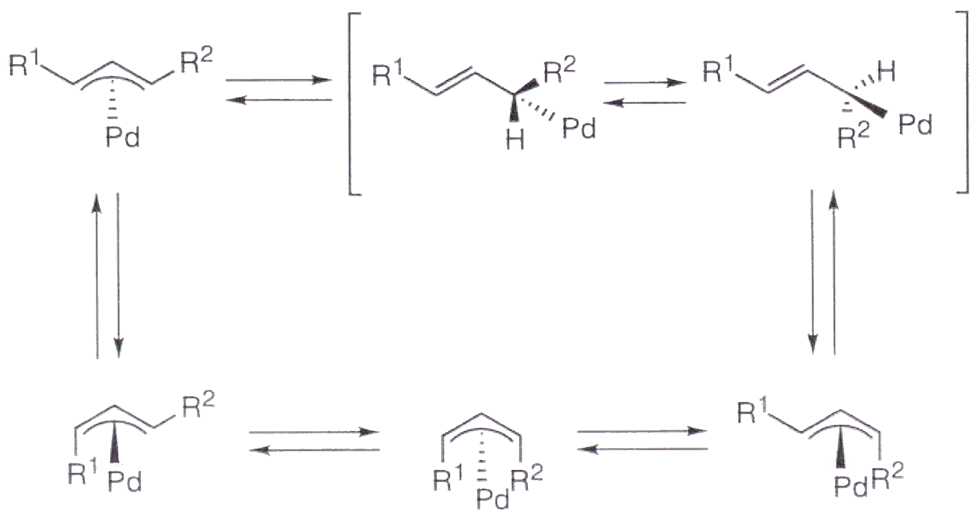
Palladium-Catalyzed Asymmetric Reduction of Racemic Allylic Esters with Formic Acid: Effects of Isomerization of π-Allylpalladium Intermediates on Enantioselectivity

Summary: A new MOP ligand (**1b**), (*R*)-(+)-2-(bis(3-trifluoromethylphenyl)phosphino)-2'-methoxy-1,1'-binaphthyl, was found to be more enantioselective than other MOP ligands for the palladium-catalyzed asymmetric reduction of α,α-disubstituted allylic esters with formic acid. The reduction of *dl*-2-(1-naphthyl)-3-buten-2-yl benzoate gave 3-(1-naphthyl)-1-butene of 90% ee. The higher enantioselectivity of **1b** is ascribed to fast *syn-anti* isomerization of π-allylpalladium intermediates formed by oxidative addition of allylic ester to a palladium(0) species. The rate of *syn-anti* isomerization was measured by the magnetization saturation transfer in ^{1}H NMR.

Introduction

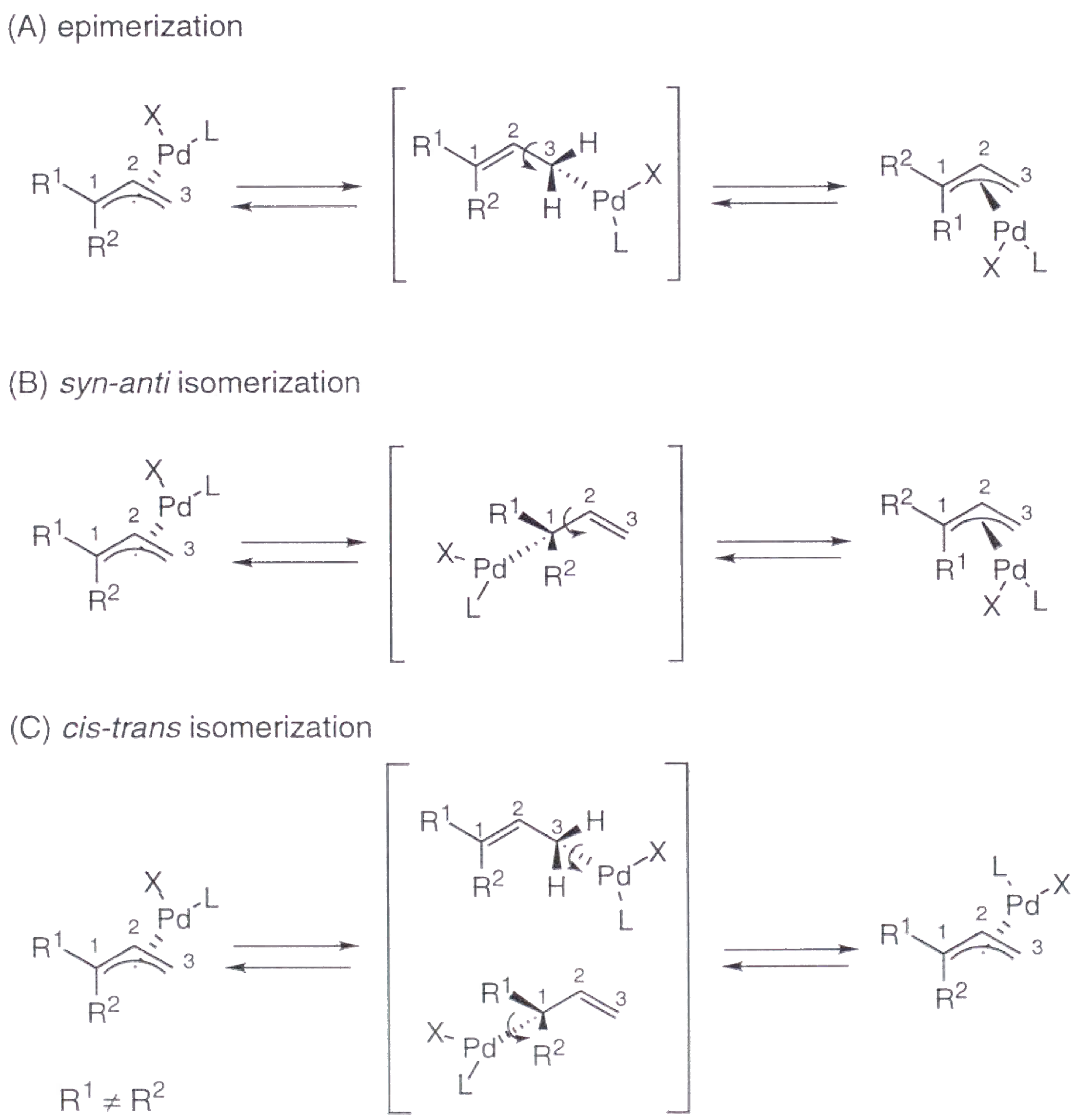
Asymmetric allylic substitutions catalyzed by palladium complexes containing optically active phosphine ligands have attracted significant interest due to their synthetic utility.[1] The catalytic cycle of the reactions involves a π-allylpalladium complex as a key

Scheme1



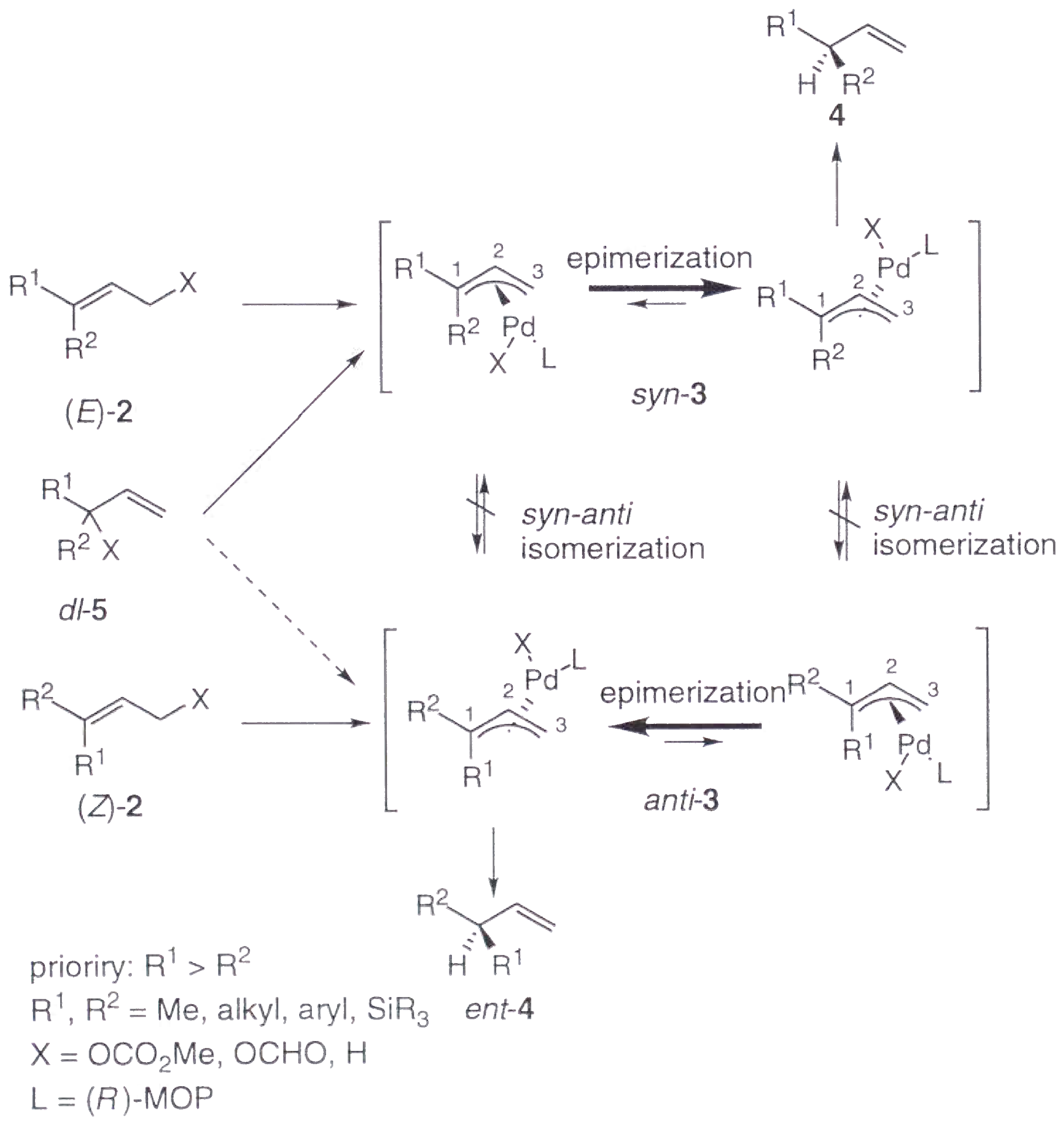
intermediate. Enantioselectivity in the asymmetric allylic substitutions is strongly dependent on the isomerization of π-allylpalladium intermediates which proceeds via well-known σ-π-σ mechanism. When a palladium atom shifts from one face to the other face, a substituent at the terminal position of π-allyl group coordinated to a palladium undergoes *syn-anti* interconversion with respect to the hydrogen at the center position by the σ-π-σ mechanism (Scheme 1). In the π-allylpalladium intermediates bearing π-allyl moiety that contains two different substituents (R^1 and R^2) at the 1-position, a monodentate phosphine ligand (L) and anionic ligand (X), there are three patterns of isomerization. These are (A) epimerization, (B) *syn-anti* isomerization and (C) *cis-trans* isomerization (Scheme 2).

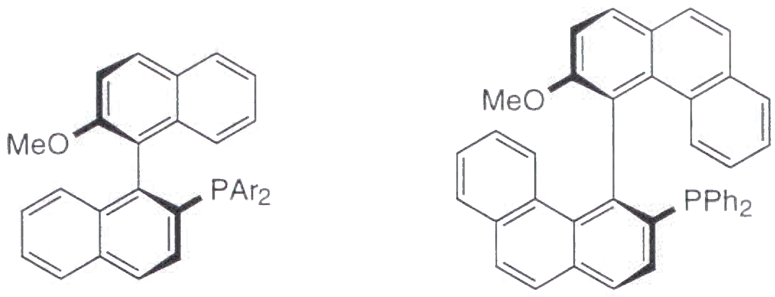
Scheme 2



(A) The epimerization proceeds through a σ-allylpalladium intermediate that forms σ-bond at the C-3 position (*cis* to phosphorous atom). By the rotation around C2-C3 bond in this σ-allylpalladium intermediate, the palladium metal moves to the other face of π-allyl. During this isomerization, *syn* and *anti* substituents on C-1 carbon stay at the original positions, so we call this one epimerization. (B) The *syn-anti* isomerization proceeds through a σ-allylpalladium intermediate that forms the σ-bond at the C-1 position (*trans* to phosphorous atom). The *syn-anti* interconversion takes place through rotation around C1-C2 bond in this σ-allylpalladium intermediate. The isomerization of the substituents from *syn* to *anti* and vice versa leads to the shift of palladium atom from one face to the other. (C) The *cis-trans* isomerization is a exchange of phosphine ligand

Scheme 3





1a: Ar = C_6H_5 ((*R*)-MeO-MOP)
1b: Ar = 3-$CF_3C_6H_4$
1c: Ar = 4-$CF_3C_6H_4$
1d: Ar = 4-$MeOC_6H_4$

1e: (*R*)-MOP-phen

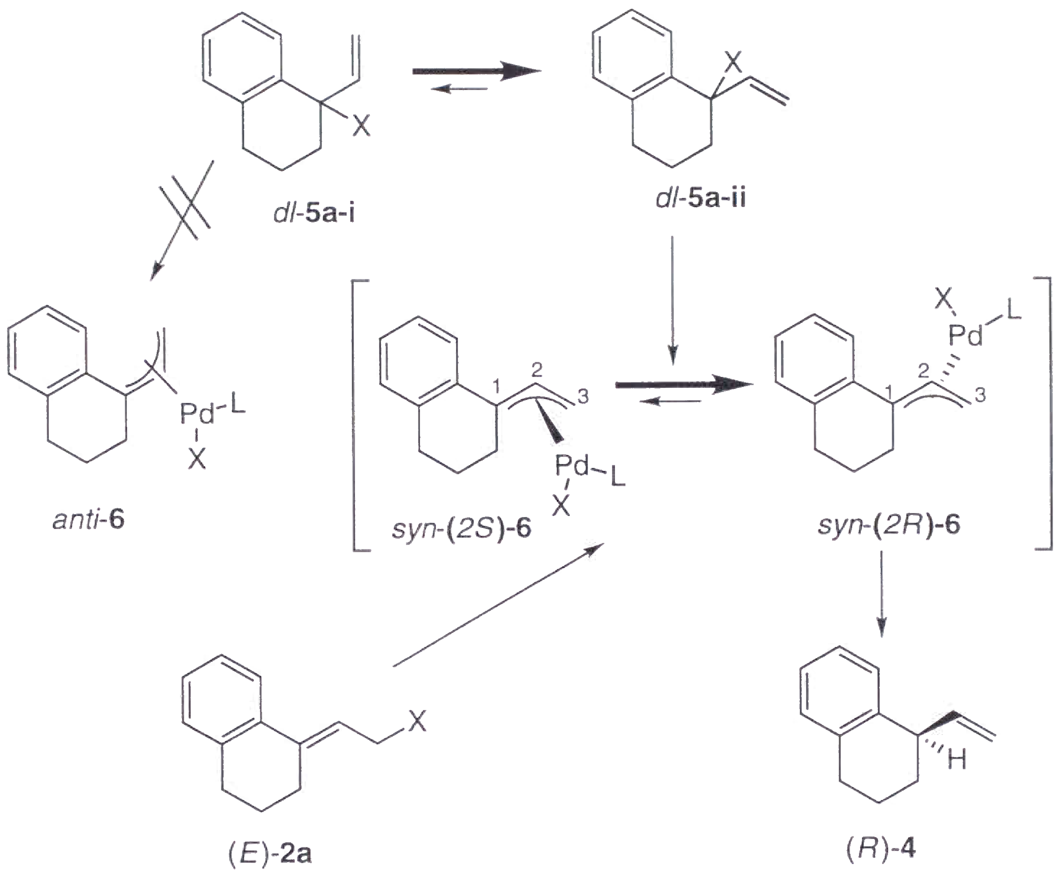
Figure 1. Chiral Monodentate Phosphine Ligands (**1a-e**)

(L) and anionic ligand (X) on the palladium atom. The *cis-trans* interconversion takes place through rotation of palladium-carbon bond in the σ-allylpalladium intermediates. To obtain high stereoselectivity in palladium-catalyzed reaction that proceeds through monophosphine π-allylpalladium intermediates, it is important to control these three isomerizations. Palladium-catalyzed reduction of allylic esters with formic acid proceeds through this type of monophosphine π-allylpalladium intermediate.

Palladium-catalyzed reduction of allylic esters with formic acid developed by Tsuji and co-workers[2] provides a convenient method for regioselective synthesis of less-substituted olefins. Mechanistic studies[3] on the catalytic reduction have revealed that the olefin is produced by reductive elimination from the key intermediate, Pd(II)(p-allyl)(hidrido)(L), which is generated by the decarboxylation of the palladium formate complex, and that the use of monodentate phosphine ligand is essential for the high regioselectivity. Hayashi has already reported[4] that the asymmetric reduction of γ, γ-disubstituted allylic carbonates **2** with formic acid in the presence of a palladium catalyst coordinated with axially chiral monodentate phosphine ligand, (*R*)-2-diphenylphosphino-2'-methoxy-1.1'-binaphthyl ((*R*)-MeO-MOP) (**1a**),[5] or its biphenanthryl analog, (*R*)-MOP-phen[6] gives optically active olefins **4** of up to 91% ee (Scheme 3). The reduction of geometrically pure *E*- or *Z*- allylic esters of 3,3-disubstituted-2-propenols proceeds by way of Pd(II)X(π-allyl)L intermediates **3** where the epimerization is fast but the *syn-anti* isomerization is slow compared with the reductive elimination forming olefin **4** and the stereochemical outcome is mainly determined by the thermodynamic stability of the epimeric π-allylpalladium intermediates.

In Chapter I, it was found that racemic tertiary allylic esters can be also used for the

Scheme 4

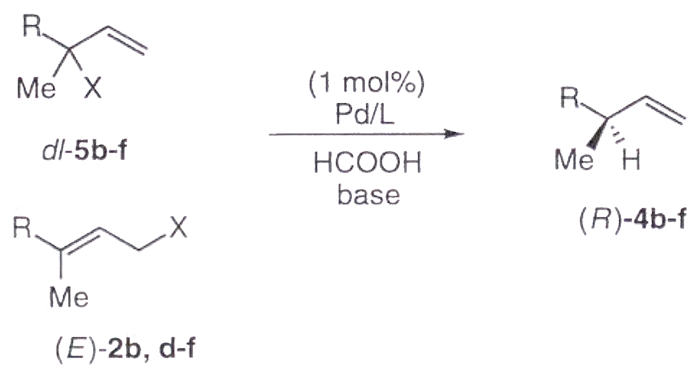


asymmetric reduction if one of the alkyl groups at the α-position is a sterically bulky group. For example, racemic methyl 1-vinyl-1,2,3,4-tetrahydronaphthyl benzoate, obtained from tetralone, gave reduction product with 93% enantiomeric purity. The high enantioselectivity can be accounted for by the selective formation of a π-allylpalladium intermediate that contains the more bulky group at the *syn* position (Scheme 4). However, for the asymmetric reduction of α,α-disubstituted allylic esters where the selectivity in forming *syn* or *anti* π-allylpalladium intermediates is not high, the enantioselectivity was lower. In this chapter the author describes that high enantioselectivity is also attained for such allylic esters by use of new MOP ligand **1b** containing 3-$CF_3C_6H_4$ group on the phosphorous. The ligand **1b** accelerates the *syn*-*anti* isomerization to result in the reductive elimination from thermodynamically more stable *syn* isomer.

Results and Discussion

The results obtained for the asymmetric reduction of α,α-disubstituted allylic esters *dl*-**5** (Scheme 5) are summarized in Table 1, which also contains the data for γ,γ-disubstituted esters (*E*)-**2**. The asymmetric reduction of allyl carbonate *dl*-**5b** that contains sterically bulky 1-naphthyl group at 1-position in the presence of 1 mol % of palladium catalyst coordinated with (*R*)-MeO-MOP (**1a**) proceeded regioselectively to give 94% yield of terminal olefin (*R*)-3-(1-naphthyl)-1-butene (**4b**) of 65% ee (entry 1). Benzoate ester *dl*-**5b'** also underwent the asymmetric reduction to give (*R*)-**4b** in 72% ee (entries 2 and 3). The enantioselectivity was lower in the reaction of sterically less bulky esters, *dl*-**5d**, *dl*-**5e** and *dl*-**5f**, the enantioselectivities being 40% ee, 29% ee and 55% ee, respectively (entries 7, 9 and 11). On the other hand, (*E*)-3,3-disubstituted-2-propenyl esters (*E*)-**2b**, (*E*)-**2d**, (*E*)-**2e** and (*E*)-**2f**, which are regioisomeric esters of *dl*-**5** gave the olefins **4** of 88% ee, 60% ee, 71% ee and 76% ee, respectively (entries 5, 8, 10 and 12). Thus the enantioselectivity is higher for (*E*) esters **2** than for the corresponding *dl* esters **5**. These results are as expected, because (*E*)-**2** should form only *syn* isomer of the π-allylpalladium intermediate at the oxidative addition while *dl*-**5** will form both *syn* and *anti* isomers. The reductive elimination from the anti isomer will produce an olefin of opposite absolute configuration to that from *syn* isomer.

Scheme 5



X = OCO_2Me, OCOMe, OCOPh

b; R = 1-naphthyl
c; R = adamantyl
d; R = Ph
e; R = cyclohexyl
f ; R = 4-methyl-3-pentenyl

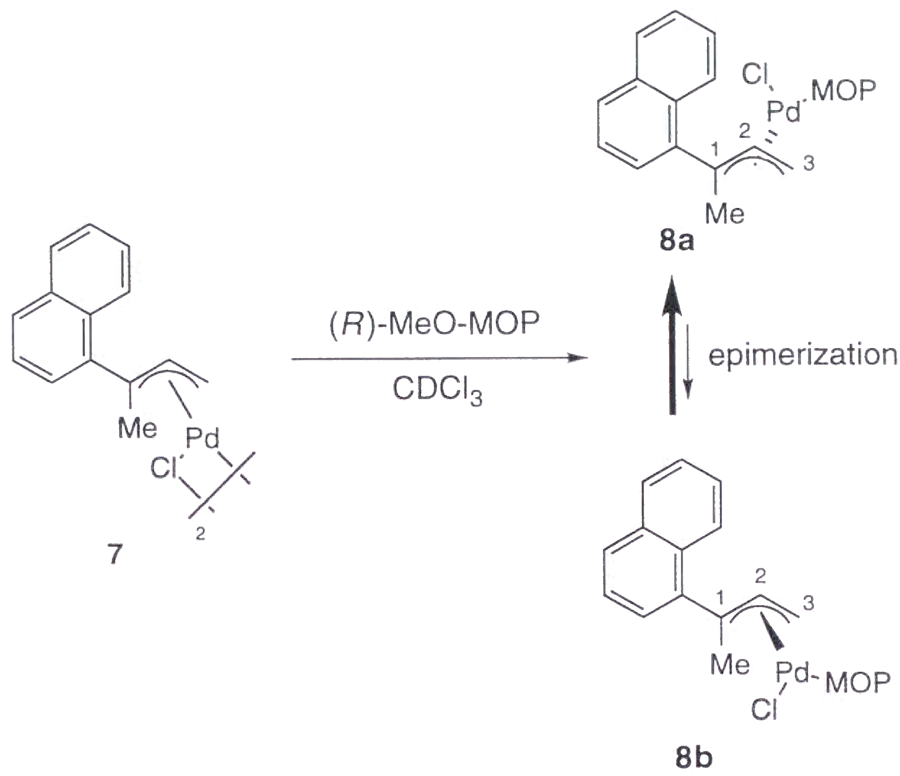
Table 1. Asymmetric Reduction of Racemic Allylic Esters (*dl*-**5b-f**) and (*E*)-3,3-Disubstituted-2-propenyl esters ((*E*)-**2b,d-f**) Catalyzed by Palladium/(*R*)-MeO-MOP Complex[a]

entry	allyl ester	X in **5**	base	conditions time (h)	yield (%)[b] of **4**	% ee of **4** (config)[c]
1	*dl*-**5b**	OCO_2Me	P. S.	12	94	65[c] (*R*)
2	*dl*-**5b'**	OCOPh	P. S.	10	75	72[c] (*R*)
3	*dl*-**5b'**	OCOPh	Et_3N	36	73	72[c] (*R*)
4[d]	*dl*-**5b**	OCO_2Me	P. S.	36	92	71[c] (*R*)
5	(*E*)-**2b**	OCO_2Me	P. S.	144	84	88[c] (*R*)
6	*dl*-**5c**	OCO_2Me	P. S.	36	96	75[f]
7	*dl*-**5d**	OCOMe	P. S.	2	80	40[e] (*R*)
8	(*E*)-**2d**	OCO_2Me	P. S.	19	88	60[e] (*R*)
9	*dl*-**5e**	OCOMe	P. S.	2	99	29[e] (*R*)
10	(*E*)-**2e**	OCO_2Me	P. S.	15	99	71[e] (*R*)
11	*dl*-**5f**	OCO_2Me	P. S.	5	82	55[f] (*S*)
12	(*E*)-**2f**	OCO_2Me	P. S.	14	95	76[f] (*S*)

[a] The reaction was carried out with 2.2 equiv. of formic acid in dioxane (0.5 M) in the presence of 1.2 equiv. of base and 1.0 mol % of catalyst prepared in situ by mixing $Pd_2(dba)_3{\cdot}CHCl_3$ and (*R*)-MeO-MOP (P/Pd = 2/1) at 20 °C. [b] Isolated yield by silica gel column chromatography. [c] Determined by GLC analysis wiyh chiral stationary phase column, CP Cyclodex β236M. [d] Reaction with (*R*)-MOP-phen. [e] Determined by HPLC analysis of anilide of carboxylic acid, obtained by the oxidation ($NaIO_4$–$KMnO_4$) of **4c**, **4d** and **4e** with Sumichiral OA-2000 (hexane/dichloroethane/ethanol = 250/20/1). [f] Determined by HPLC analysis of dianilide of carboxylic acid, obtained by the oxidation ($NaIO_4$–$KMnO_4$) of **4f** with Sumichiral OA-4100 (hexane/dichloroethane/ethanol = 50/15/1).

π-Allylpalladium complex, PdCl{[1-(1-naphthyl)-1-methyl-π-allyl]}(MeO-MOP) (**8**), was prepared by mixing $[PdCl\{1\text{-}(1\text{-naphthyl})\text{-}1\text{-methyl-}\pi\text{-allyl}\}]_2$ (**7**) with 1 equiv. (to Pd) of (*R*)-MeO-MOP and it was characterized by ^1H, ^{13}C and ^{31}P NMR spectra. In $CDCl_3$ at –50 °C the complex exists as a mixture of isomers in a ratio of 3 : 2. These two isomers have substituted carbon (C-1) of the π-allyl *trans* to the phosphorus atom of MeO-MOP and the unsubstituted carbon (C-3) *cis* to phosphorous, which is determined by a large coupling constant (J = 9.8 Hz) between methyl group and phosphorous and no coupling between C-3 protons and phosphorous. Both isomers contain 1-naphthyl and methyl groups *syn* and *anti* positions, respectively, which was determined by NOE's

Scheme 6



between the methyl group on C-1 position and *anti* hydrogen on the C-3 position. Thus, the structures of the isomers are assigned to be **8a** and **8b** shown in Scheme 6. These results reveal that the *syn* isomers are thermodynamically much more stable than *anti* isomers. (*E*)-Allylic ester (*E*)-**5b**, which should form only *syn*-π-allylpalladium intermediate, gave optically active alkene **4b** of 88% ee. In this reaction, the enantioselectivity is determined by the epimerization of *syn*-π-allylpalladium intermediates. On the other hand, the reaction of racemic allyl ester *dl*-**5b** mainly forms the *syn*-π-allylpalladium intermediates but a minor amount of *anti*-π-allylpalladium intermediates were also formed. This *anti*-π-allylpalladium intermediate gives an opposite enantiomer and, as a result, the enantioselectivity in the catalytic reduction was reduced. In order to attain the higher enantioselectivity in the asymmetric reduction of α,α-disubstituted esters **5**, it is necessary to accelerate the *syn-anti* isomerization in the π-allylpalladium intermediates to reach the equilibrium where *syn* isomers are predominant.

Several reaction conditions were examined for the asymmetric reduction of *dl*-2-(1-naphthyl)-3-buten-2-yl ester (*dl*-**5b'**). The results are summarized in Table 2. Under the standard conditions so far used, where 2,2 equiv. (to allyl ester) of formic acid was added in one portion, the enantioselectivity was 73% ee (entry 1). A little higher

Scheme 7

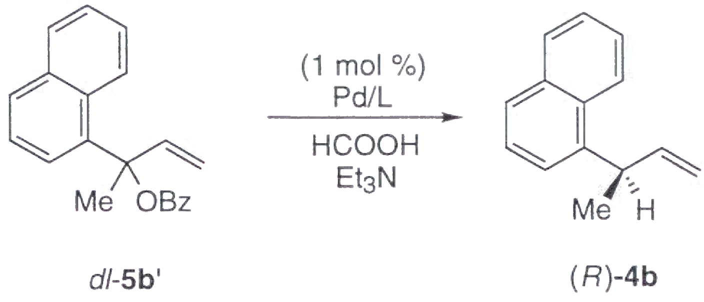


Table 2. Asymmetric Reduction of *dl*-2-(1-Naphthyl)-3-buten-2-yl benzoate (*dl*-**5b'**) and Methyl (*E*)-3-(1-naphthyl)-2-buten-2-butenyl carbonate ((*E*))-**2b** with Formic Acid Catalyzed by Palladium-MOP Complexes[a]

entry	allyl ester	MOP ligand	HCOOH (equiv.)	method[d]	time (days)	yield (%)[b] of **4b**	% ee of **4b**[c] (config)[e]
1	*dl*-**5b'**	**1a**	2.2	A	1.5	81	73 (*R*)
2	*dl*-**5b'**	**1a**	1.1	A	2.0	85	76 (*R*)
3	*dl*-**5b'**	**1a**	1.1	B	3.0	77	80 (*R*)
4	*dl*-**5b'**	**1e**	2.2	A	1.5	91	77 (*R*)
5	*dl*-**5b'**	**1e**	1.1	B	2.0	92	82 (*R*)
6	*dl*-**5b'**	**1d**	2.2	A	4.5	83	69 (*R*)
7	*dl*-**5b'**	**1c**	2.2	A	0.7	76	76 (*R*)
8	*dl*-**5b'**	**1b**	2.2	A	3.5	92	84 (*R*)
9	*dl*-**5b'**	**1b**	1.1	A	3.0	77	86 (*R*)
10	*dl*-**5b'**	**1b**	1.1	B	3.0	86	90 (*R*)
11[f]	(*E*)-**2b**	**1b**	2.2	A	6.0	86	88 (*R*)

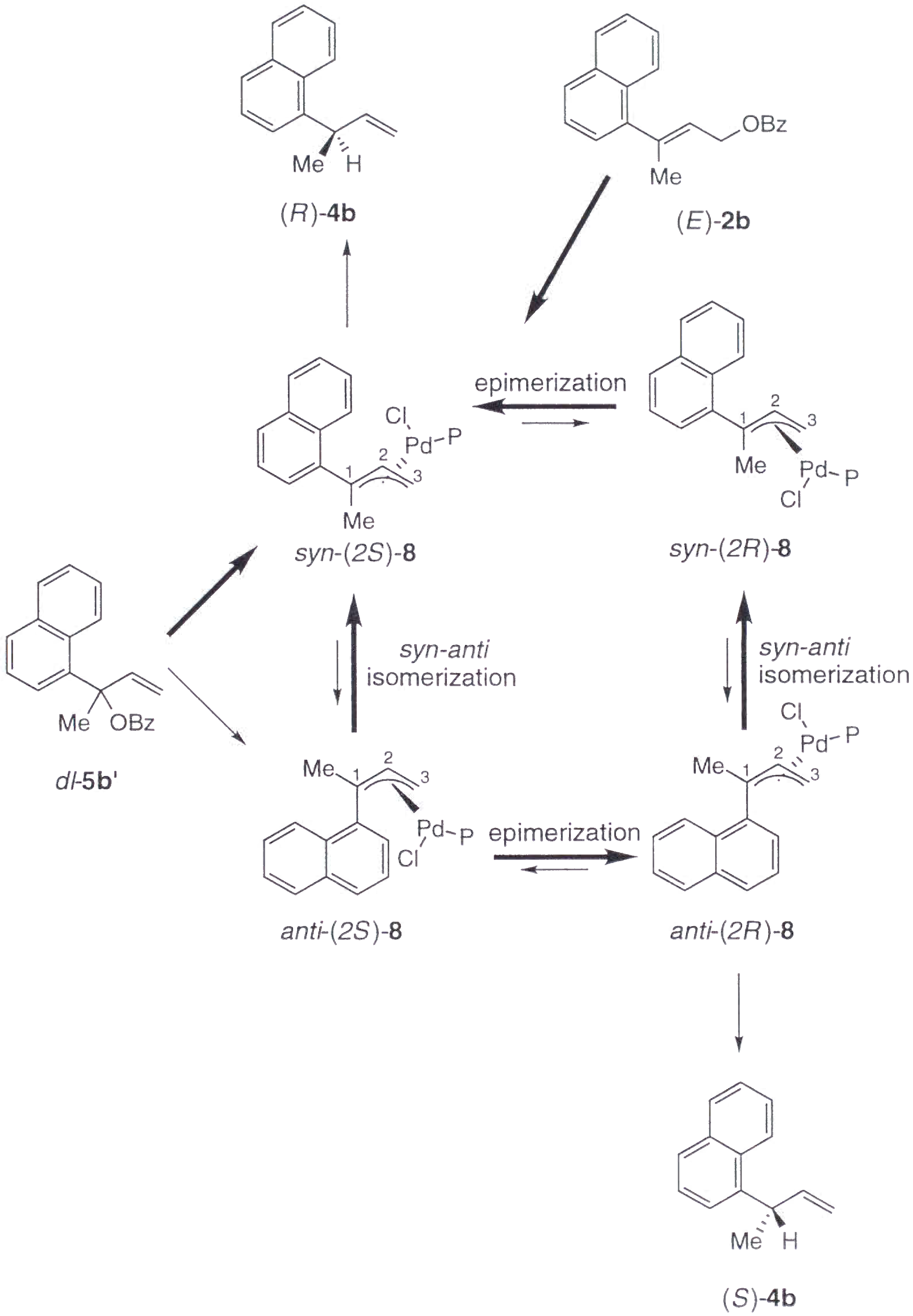
[a] The reaction was carried out with 2.2 or 1.1 equiv. of formic acid in THF-dioxane (1:1) in the presence of 1.2 equiv. of Et_3N and 1.0 mol % of catalyst prepared in situ by mixing $Pd_2(dba)_3 \cdot CHCl_3$ and MOP ligand (P/Pd = 2/1) at 0 °C. [b] Isolated yield by silica gel column chromatography. [c] Determined by GLC analysis with chiral stationary phase column, CP Cyclodex β236M. [d] Method A; Formic acid was added in one portion. Method B; Formic acid was added slowly over 10 h. [e] Specific rotation of **4b** in entry 10 is $[\alpha]_D^{20}$ +16.3 (*c* 0.35, chloroform). [f] The reaction was carried out at 20 °C.

enantioselectivity (76% ee) was observed in the reduction with 1.1 equiv. of formic acid (entry 2). The enantioselectivity was further increased by slow addition of formic acid over a period of 10 h, which gave (*R*)-**4b** of 80% ee (entry 3). These results indicate that the slow addition extends the lifetime of π-allylpalladium intermediates to provide a chance for the *syn-anti* isomerization. However, the enantioselectivity observed here (80% ee) is still lower than that in the reduction of (*E*)-**5b** which gave **4b** of 88% ee (entry 5 in Table 1). It follows that the equilibration to *syn*-π-allylpalladium intermediates is not reached in the reaction of *dl*-**5b'** and a certain amount of *anti* intermediates are still involved even in the reaction under the slow addition conditions. The asymmetric reduction of *dl*-**5b'** was also examined with some other axially chiral monophosphine ligands, (*R*)-MOP-phen (**1e**) and MeO-MOP analogues containing substituents on the diphenylphosphino group, **1b** (Ar = 3-$CF_3C_6H_4$), **1c** (Ar = 4-$CF_3C_6H_4$), and **1d** (Ar = 4-$MeOC_6H_4$). Under the standard conditions, **1e**, **1d**, **1c**, and **1b** gave (*R*)-**4b** of 77% ee, 69% ee, 76% ee, and 84% ee, respectively (entries 4, 6, 7 and 8). Thus, the order of enantioselectivity in the reaction with MeO-MOP analogues is **1b** (Ar = 3-$CF_3C_6H_4$) > **1c** (Ar = 4-$CF_3C_6H_4$) > **1a** (Ar = Ph) > **1d** (Ar = 4-$MeOC_6H_4$). The highest enantioselectivity (90% ee) was obtained in the reaction with **1b** by the slow addition of formic acid, the enantioselectivity being essentially the same as that obtained in the reduction of (*E*)-**2b** catalyzed by palladium/**1b** (entry 11). It is expected that the *syn-anti* isomerization is accelerated by the introduction of trifluoromethyl group on the MeO-MOP ligand and that the reaction of *dl*-**5b'** produces olefin **4b** from *syn*-π-allylpalladium intermediates after the equilibration.

The stereochemical results in the reduction of *dl*-**5b'** and (*E*)-**2b** with MOP are illustrated in Scheme 8. The π-allylpalladium intermediate resulting from (*E*)-**2b** should be *syn*-**8**, which contains 1-naphthyl group at the *syn* position. After the epimerization between *syn*-(*2R*)-**8** and *syn*-(*2S*)-**8**, the product (*R*)-**4b** is formed from thermodynamically more stable *syn*-(*2S*)-**8**. On the other hand, *dl*-**5b'** forms both *syn*-π-allylpalladium intermediate (*syn*-**8**) and *anti*-π-allylpalladium intermediate (*anti*-**8**) at oxidative addition. To attain the high enantioselectivity in the reduction of *dl*-**5b**, the isomerization of *anti*-**8** to *syn*-**8** is necessary. The experimental results indicate that the slow addition of formic acid extends the lifetime of π-allylpalladium intermediates to reach the equilibration and MOP ligand **1b** accelerates the *syn-anti* isomerization.

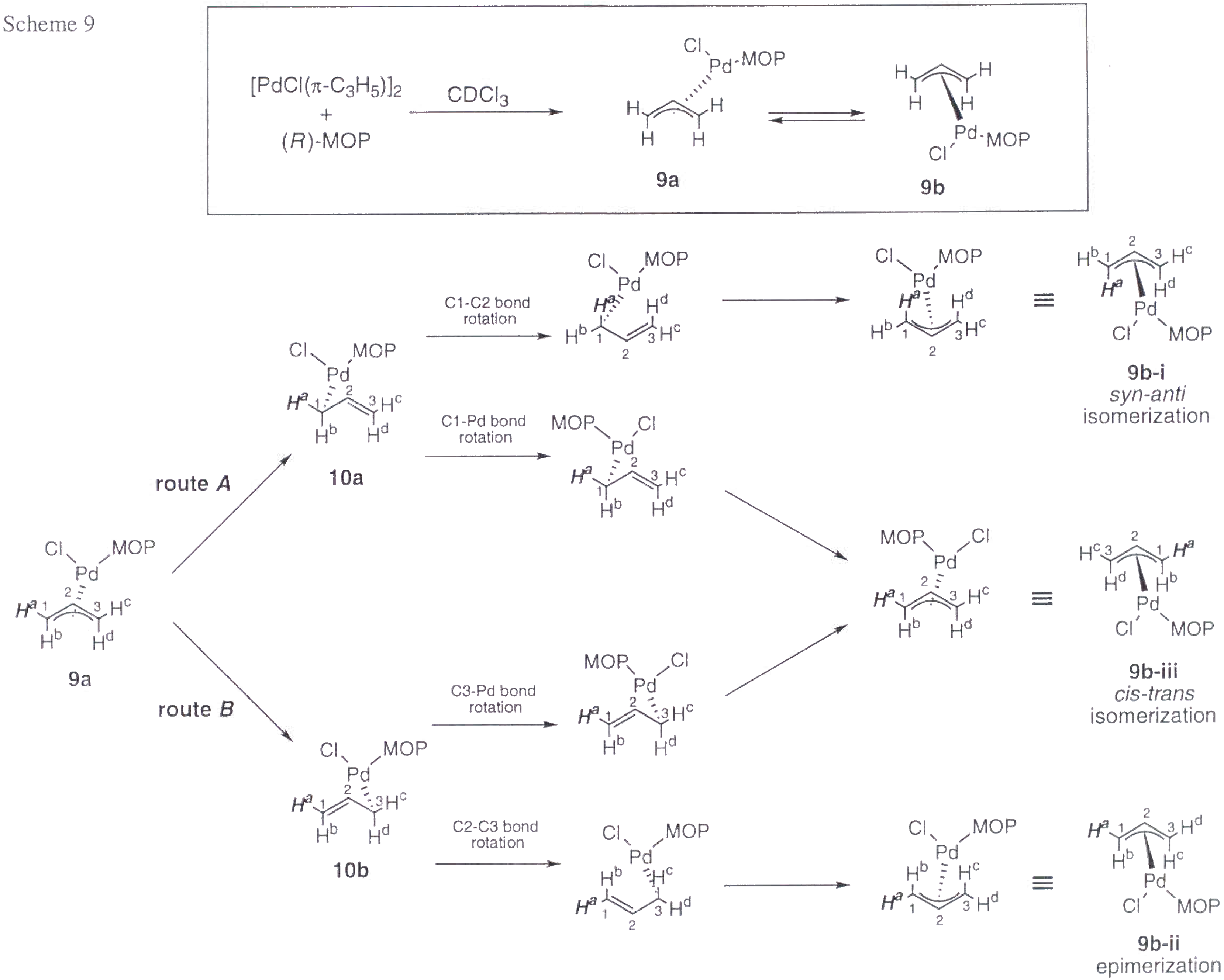
Rate constants for the isomerization of π-allylpalladium complexes coordinated with MOP ligands were measured by the magnetization saturation transfer technique in ^{1}H NMR.[7] As a model of the π-allylpalladium intermediates, we chose nonsubstituted π-allylpalladium complexes PdCl(π-C_3H_5)(MOP) (**9**) where MOP ligands are **1a**, **1b**, and **1d** that showed a remarkable difference in the enantioselectivity for reduction of *dl*-**5b'**.

Scheme 8



Me H
(R)-4b
OBz
Me
(E)-2b
epimerization
Cl
Pd-P
1 2 3
Me
syn-(2S)-8
Me
Pd-P
Cl
syn-(2R)-8
Me OBz
dl-5b'
syn-anti
isomerization
syn-anti
isomerization
Me
Pd-P
Cl
epimerization
Me
Cl
Pd-P
anti-(2S)-8
anti-(2R)-8
Me H
(S)-4b

Scheme 9


[PdCl(π-C_3H_5)]$_2$
+
(R)-MOP
$CDCl_3$
9a
9b
route A
route B
10a
10b
C1-C2 bond rotation
C1-Pd bond rotation
C3-Pd bond rotation
C2-C3 bond rotation
9b-i
syn-anti isomerization
9b-iii
cis-trans isomerization
9b-ii
epimerization

It would be better to use π-allylpalladium-MOP complexes bearing 1,1-disubstituted π-allyl groups, but the *syn-anti* isomerization is too slow to measure the rate by the saturation transfer.

In complex **9a**, *syn* and *anti* protons on the C-1 position of the π-allyl group which is *trans* to phosphorus, are named H^a and H^b, respectively, and *syn* and *anti* protons on the C-3 position are named H^c and H^d, respectively. The isomerization which corresponds to the *syn-anti* isomerization of π-(1,1-disubstituted allyl)palladium, (B) in Scheme 2, is that proceeds through route *A*. By this conversion of **9a** to **9b-i**, protons H^a and H^b on the C-1 position exchange their *syn* and *anti* positions while H^c and H^d on the C-3 position stay at the original positions. By the isomerization which corresponds to the epimerization, (A) in Scheme 2, **9a** is converted into **9b-ii** through route *B*, where H^a and H^b stay at the original positions while H^c and H^d are exchanged. In the *cis-trans* isomerization, (C) in Scheme 2, all protons remain on the original positions, but palladium moves from one π-allyl face to the other. As a result, it appears that protons H^a and H^c exchange their positions. It is possible to measure the rate constants of the three isomerizations by the magnetization saturation transfer technique in ^{1}H NMR because the H^a proton on **9a** shifts to the different positions on **9b** depending on the type of isomerization. The rate constants of the isomerization of π-allylpalladium complexes **9** are summarized in Table 4. In the complex coordinated with (*R*)-MeO-MOP (**1a**), the rate constants for *syn-anti* isomerization, epimerization, and *cis-trans* isomerization were 0.4 s^{-1}, 8.0 s^{-1}, and 2.0 s^{-1}, respectively. The rate of *syn-anti* isomerization was strongly dependent on the MOP ligands coordinated to palladium. Thus, the rate constants (k_1) for the palladium complex of **1b** (Ar = 3-$CF_3C_6H_4$) and **1d** (Ar = 4-

Table 3. Rate Constants (*k*) for Exchange of π-Allylpalladium Complexes [PdCl(π-C_3H_5)L] (**9a** and **9b**); *syn-anti* Isomerization (k_1), Epimerization (k_2) and *cis-trans* Isomerization (k_3)[a] .

entry	MOP ligand (L)	k_1 (s^{-1}) *syn-anti* isomerization	k_2 (s^{-1}) epimerization	k_3 (s^{-1}) *cis-trans* isomerization
1	**1b** (Ar = 3-$CF_3C_6H_4$)	1.7	3.1	3.3
2	**1a** (Ar = Ph) (MeO-MOP)	0.4	8.0	2.0
3	**1d** (Ar = 4-$MeOC_6H_4$)	0.08	17	1.3

[a] The rate conatants were measured by saturation of H^a proton in **9a** at 0 °C in $CDCl_3$.

$MeOC_6H_4$) are 1.7 s^{-1} and 0.08 s^{-1}, respectively. The isomerization with **1b** is fastest, four times faster than that with **1a** and twenty times faster than that with **1d**. The order of the rate constants (k_2) for the epimerization was reverse, slowest with **1b** and fastest with **1d**, through the difference was not so large as the rate constants for the *syn-anti* isomerization.

The fast rate of the *syn-anti* isomerization observed for the π-allylpalladium complex **9** coordinated with **1b** (Ar = 3-$CF_3C_6H_4$) is in good agreement with the high enantioselectivity in the catalytic asymmetric reduction of α,α-disubstituted allylic ester *dl*-**5b'**. The *syn* and *anti* π-allylpalladium intermediates **8** formed by the oxidative addition of *dl*-**5** to palladium(0) coordinated with **1b** undergo the *syn-anti* isomerization, faster than those of other MOP ligands, to reach the equilibration where *syn* intermediates are predominant. The *syn* intermediates will produce the reduction product **4b** of high enantiomeric excess. The slow addition of formic acid will also increase the enantioselectivity by providing a chance for the isomerization to *syn*-intermediates.

Experimental Section

General. All manipulations were carried out under a nitrogen atmosphere. Nitrogen gas was dried by passage through P_2O_5 (Merck, SICAPENT). NMR spectra were recorded on a JEOL JNM-EX270 spectrometer (270 MHz for ^1H and 109 MHz for ^{31}P), JEOL JNM-AL400 spectrometer (400 MHz for ^1H NMR), or JEOL JNM LA500 spectrometer (500 MHz for ^1H, 125 MHz for ^{13}C and 202 MHz for ^{31}P). Chemical shifts are reported in δ ppm referenced to an internal $SiMe_4$ standard for ^1H NMR, and to an external 85% H_3PO_4 standard for ^{31}P NMR. Residual chloroform (δ 77.0 for ^{13}C) was used as internal reference for ^{13}C NMR. ^1H, ^{13}C and ^{31}P NMR spectra were recorded in $CDCl_3$ at 25 °C unless otherwise noted. HPLC analysis was performed on a Shimazu LC-6A liquid chromatograph system and a JASCO PU-980 liquid chromatograph system with chiral stationary phase column Sumitomo Chemical Co. Ltd., Sumipax OA series. GLC analysis was performed on a HEWLETT PACKARD HP 6890 series with a chiral stationary phase column, CP Cyclodex β-236M (50 m). Optical rotation were measured on a JASCO DIP-370 polarimeter.

Materials. THF was dried over sodium benzophenone ketyl and distilled prior to use. $[PdCl(\pi\text{-}C_3H_5)]_2$,[8] $Pd_2(dba)_3\cdot CHCl_3$,[9] (*R*)-MeO-MOP,[5] **1d** (Ar = 4-$MeOC_6H_4$),[5b] (*R*)-MOP-phen,[6] (*E*)-3-cyclohexyl-2-butenol,[10] (*E*)-3-phenyl-2-butenol[11] and ethyl 3-(1-naphthyl) crotonate[12] were prepared according to the reported procedures.

New MOP analogue **1b** (Ar = 3-$CF_3C_6H_4$) and **1c** (Ar = 4-$CF_3C_6H_4$) were prepared by the modified procedure of MOP synthesis (see below).

Preparation of New MOP Analogues 1b (Ar = 3-$CF_3C_6H_4$) and 1c (Ar = 4-$CF_3C_6H_4$): New MOP analogues were prepared from (*R*)-2-hydroxy-2'-methoxybinaphthyl by the sequence of (1) sulfonylation, (2) palladium-catalyzed phosphinylation, and (3) reduction.

(*R*)-(–)-2-Methoxy-2'-((trifluoromethanesulfonyl)oxy)-1,1'-binaphthyl. To a solution of (*R*)-2-hydroxy-2'-methoxybinaphthyl[13] (10.6 g, 35.3 mmol) and pyridine (3.6 g, 45.5 mmol) in $CHCl_3$ (100 mL) at 0 °C was added dropwise trifluoromethanesulfonic anhydride (14.3 g, 50.7 mmol). The mixture was stirred at 0 °C for 2 h. The reaction mixture was evaporated. The residue was diluted with EtOAc and washed with 5% hydrochloric acid, saturated sodium bicarbonate and brine, dried over anhydrous sodium sulfate and evaporated. The residue was chromatographed on silica gel (hexane/EtOAc = 1/1) to give 13.5 g (89%) of (*R*)-(–)-2-methoxy-2'-((trifluoromethanesulfonyl)oxy)-1,1'-binaphthyl: $[\alpha]_D^{20}$ –92.5 (*c* 1.7, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 3.82 (s, 3H), 7.00–8.20 (m, 12H). Anal. Calcd for $C_{22}H_{15}F_3SO_4$: C, 61.11; H, 3.50. Found: C,60.88; H, 3.51.

(*R*)-(+)-2-(Bis(3-trifluoromethylphenyl)phosphinyl)-2'-methoxy-1,1'-binaphthyl. To a mixture of (*R*)-(–)-2-((trifluoromethanesulfonyl)oxy)-2'-methoxy-1,1'-binaphthyl (1.03 g, 2.61 mmol), bis(3-trifluoromethylphenyl)phosphine oxide (1.35 g, 3.99 mmol), palladium diacetate (115 mg, 0.51 mmol) and 1,4-bis(diphenylphosphino)butane (dppb) (228 mg, 0.54 mmol) were added 40 mL of dimethyl sulfoxide and diisopropylethylamine (1.8 mL, 10.2 mmol) and the mixture was heated with stirring at 100 °C for 12 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure to give a dark brown residue. The residue was diluted with EtOAc, washed with water, dried over anhydrous sodium sulfate and evaporated. The residue was chromatographed on silica gel (hexane/EtOAc = 1/1) to give 1.36 g (80%) of (*R*)-(+)-2-(bis(3-trifluoromethylphenyl)phosphinyl)-2'-methoxy-1,1'-binaphthyl: $[\alpha]_D^{20}$ +116.1 (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 3.68 (s, 3H), 6.79–8.06(m, 20H). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 26.9. Anal. Calcd for $C_{35}H_{23}F_6O_2P$: C, 67.75; H, 3.74. Found: C, 68.01; H, 3.77.

(*R*)-(+)-2-(Bis(3-trifluoromethylphenyl)phosphino)-2'-methoxy-1,1'-binaphthyl (1b). To a mixture of (*R*)-(+)-2-(bis(3-trifluoromethyl-phenyl)phosphinyl)-2'-methoxy-1,1'-binaphthyl (700 mg, 1.13 mmol) and Et_3N (1.14 g, 11.3 mmol) in toluene (10 mL) was added Cl_3SiH (765 mg, 5.65 mmol) at 0 °C. The reaction mixture was stirred at 120 °C for 30 h. After being cooled to room temperature, the mixture was diluted with ether and quenched with a small amount of saturated sodium bicarbonate. The resulting suspension was filtered through Celite, and the solid was washed with ether. The combined organic layer was dried over anhydrous magnesium sulfate and evaporated. The crude product was chromatographed on silica gel (hexane/EtOAc = 9/1) to give 624 mg (92%) of (*R*)-(+)-2-(bis(3-trifluoromethylphenyl)phosphino)-2'-methoxy-1,1'-binaphthyl (**1b**): $[\alpha]_D^{20}$ +47.7 (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 3.48 (s, 3H), 6.85–8.03 (m, 20H). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ –12.0. Anal. Calcd for $C_{35}H_{23}F_6OP$: C, 69.54; H, 3.84. Found: C,69.38; H, 3.89.

(*R*)-(+)-2-(Bis(4-trifluoromethylphenyl)phosphinyl)-2'-methoxy-1,1'-binaphthyl: $[\alpha]_D^{20}$ +96.3 (*c* 2.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 3.68 (s, 3H), 6.78–8.06 (m, 20H). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 27.1. Anal. Calcd for $C_{35}H_{23}F_6O_2P$: C, 67.75; H, 3.74. Found: C, 68.01; H, 3.41. **(*R*)-(+)-2-(Bis(4-trifluoromethylphenyl)phosphino)-2'-methoxy-1,1'-binaphthyl (1c):** $[\alpha]_D^{20}$ +61.1 (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 3.43 (s, 3H), 6.83–8.02 (m, 20H). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ –12.5. Anal. Calcd for $C_{35}H_{23}F_6OP$: C, 69.54; H, 3.84. Found: C,69.32; H, 4.04.

Preparation of 3,3-Disubstituted Propenyl Esters ((*E*)-2b,d,e and f): Methyl (*E*)-3-(1-naphthyl)-2-butenyl carbonate ((*E*)-**2b**), methyl (*E*)-3-phenyl-2-butenyl carbonate ((*E*)-**2d**), methyl (*E*)-3-cyclohexyl-2-butenyl carbonate ((*E*)-**2e**) and geranyl methyl carbonate ((*E*)-**2f**) were obtained by treatment of the corresponding alcohols with methyl chloroformate and pyridine.[14] (*E*)-3-(1-Naphthyl)-2-butenol was prepared from the corresponding alcohol which was readily prepared by reduction of ethyl 3-(1-naphthyl) crotonate[12] with $LiAlH_4$, and used without purification. A typical procedure is given for the preparation of methyl (*E*)-3-cyclohexyl-2-butenyl carbonate ((*E*)-**2e**). Experimental procedures: To a solution of (*E*)-3-cyclohexyl-2-butenol and pyridine (522 mg, 6.6 mmol) in benzene (10 mL) was added methyl chloroformate (467 mg, 4.9 mmol) dropwise at 0 °C and stirred for 1.5 h. The reaction was quenched with brine and extracted with ether. The organic layer was washed with saturated sodium bicarbonate solution, dried over anhydrous sodium sulfate and evaporated. The crude product was purified by silica gel column chromatography (hexane/ EtOAc = 10/1) to give 657 mg (94%) of methyl (*E*)-3-cyclohexyl-2-butenyl carbonate ((*E*)-**2e**): ^1H NMR ($CDCl_3$) δ 1.15–1.92 (m, 11H), 1.70 (s, 3H), 3.79 (s, 3H), 4.66 (d, *J* = 7.0 Hz, 2H), 5.36 (t, *J* = 7.0 Hz, 1H). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.49. Found: C, 67.78; H, 9.47. **Methyl (*E*)-3-(1-Naphthyl)-2-butenyl Carbonate ((*E*)-2b):** ^1H NMR ($CDCl_3$) δ 2.16 (s, 3H), 3.78 (s, 3H), 4.91 (d, *J* = 6.7 Hz, 2H), 5.71 (t, *J* = 6.7 Hz, 1H), 7.23–7.91 (m, 7H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 19.2, 54.6, 64.5, 123.6, 124.6, 125.2, 125.3, 125.6, 125.8, 127.3, 128.2, 130.5, 133.6, 141.6, 142.2, 155.7. Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.99; H, 6.18. **Methyl (*E*)-3-Cyclohexyl-2-butenyl Carbonate** ((*E*)-**2d**): ^{1}H NMR ($CDCl_3$) δ 2.13 (s, 3H), 3.80 (s, 3H), 4.85 (d, *J* = 6.9 Hz, 2H), 5.91 (t, *J* = 6.9 Hz, 1H), 7.24–7.42 (m, 5H). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.73; H, 6.82. **Geranyl Methyl Carbonate ((*E*)-2f)**[14]: ^{1}H NMR ($CDCl_3$) δ 1.60 (s, 3H), 1.68 (s, 3H), 1.71 (s, 3H), 2.02–2.18 (m, 4H), 3.77 (s, 3H), 4.63 (d, *J* = 7.0 Hz, 2H), 5.07 (m, 1H), 5.38 (t, *J* = 7.0 Hz, 1H).

Preparation of Racemic 1,1-Disubstituted Propenyl Esters (*dl*-**5b-f**). A typical procedure is given for *dl*-2-(1-naphthyl)-3-butene-2-yl benzoate (*dl*-**5b'**). To a solution of vinylmagnesium bromide (7.2 mL of 0.9 M, 6.5 mmol) in diethyl ether at 0 °C was added dropwise a solution of 1'-acetonaphthone (1.0 g, 5.9 mmol) in THF (30 mL). The mixture was stirred at room temperature for 12 h. It was quenched with 0.5% sulfuric acid solution and extracted with ether. The ether extracts were dried over anhydrous sodium sulfate. Evaporation of the solvent gave a crude product. To a solution of this crude allyl alcohol and 1,10-phenanthroline (ca. 5 mg) in THF (10 mL) was added 1.5 M *n*-butyllithium in hexane (4.7 mL, 7.1 mmol) at –78 °C and stirred for 0.5 h. To this reaction mixture was added benzoyl chloride (993 mg, 7.1 mmol). The mixture was allowed to warm to room temperature and stirred for 1 h. The reaction was quenched with saturated sodium bicarbonate solution and extracted with ether. The organic layer was washed with saturated sodium bicarbonate solution and brine, dried over anhydrous sodium sulfate and evaporated. The crude product was purified by alumina column chromatography (hexane/Et_3N = 10/1) to give 1.3 g (73%) of *dl*-2-(1-naphthyl)-3-butene-2-yl benzoate (*dl*-**5b'**): ^{1}H NMR ($CDCl_3$) δ 2.26 (s, 3H), 5.27 (d, J = 17.6 Hz, 1H), 5.33 (d, J = 17.6 Hz, 1H), 6.56 (dd, J = 10.7 and 17.6 Hz, 1H), 7.28–8.41 (m, 12H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 25.1, 114.5, 123.9, 124.2, 124.6, 125.4, 126.0, 127.1, 127.7, 128.5, 128.9, 129.8, 130. 2, 131.0, 132. 1, 133.3, 134.6, 138.2, 142.0, 143.1, 164.4. Anal. Calcd for $C_{21}H_{18}O_2$: C, 83.42; H, 6.00. Found: C, 83.50; H, 5.97. ***dl*-Methyl 2-(1-Naphthyl)-3-butene-2-yl Carbonate (*dl*-5b):** ^{1}H NMR ($CDCl_3$) δ 2.14 (s, 3H), 3.54 (s, 3H), 5.18 (d, J = 17.4 Hz, 1H), 5.24 (d, J = 10.7Hz, 1H), 6.44 (dd, J = 10.7 and 17.4 Hz, 1H), 7.41–8.37 (m, 7H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 26.1, 54.2, 85.8, 114.9, 124.6, 124.8, 125.2, 126.5, 129.0, 129.4, 130.3, 134.6, 137.4, 141.8, 153.3. Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 75.23; H, 5.96. ***dl*-Methyl 2-Adamantyl-3-buten-2-yl Carbonate (*dl*-5c):** ^{1}H NMR ($CDCl_3$) δ 1.59 (s, 3H), 1.60–1.80 (m, 15H), 1.95–2.05 (m, 3H), 3.72 (s, 3H), 5.01 (d, *J* = 16.5 Hz, 1H), 5.26 (d, *J* = 9.5 Hz, 1H), 5.92 (dd, *J* = 9.5, 16.5 Hz, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 28.4, 35.8, 36.9, 39.5, 53.9, 89.2, 115.0, 138.7, 154.2. Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C,72.60; H, 9.30. ***dl*-2-Phenyl-3-buten-2-yl Acetate (*dl*-5d):** ^{1}H NMR ($CDCl_3$) δ 1.87 (s, 3H), 2.05 (s, 3H), 5.22 (d, *J* = 9.5 Hz, 1H), 5.25 (d, *J* = 16.0 Hz, 1H), 6.26 (dd, *J* = 9.5 and 16.0 Hz, 1H), 7.21–7.38 (m, 5H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 21.6, 24.2, 85.6, 117.1, 124.6, 126.6, 128.0, 128.2, 144.4, 169.9. Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 68.00; H, 7.20. ***dl*-2-Cyclohexyl-3-buten-2-yl Acetate (*dl*-5e):** ^{1}H NMR ($CDCl_3$) δ 0.82–1.86 (m, 11H), 1.57 (s, 3H), 2.02 (s, 3H), 5.10 (d, *J* = 16.5 Hz, 1H), 5.16 (d, *J* = 9.5 Hz,1H), 5.97 (dd, *J* = 9.5, 16.5 Hz, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 21.0, 24.9, 26.5, 27.0, 27.3, 47.9, 75.1, 111.8, 144.3, 170.0. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.62; H, 9.96. ***dl*-Methyl Linalyl Carbonate (*dl*-5f):** ^{1}H NMR ($CDCl_3$) δ 1.64 (s, 3H), 1.66 (s, 3H), 1.70 (s, 3H), 0.92 (t, *J* = 7.0 Hz, 3H), 1.90–2.00 (m, 2H), 2.10–2.20 (m, 3H), 3.80 (s, 3H), 5.17–5.22 (m, 1H), 5.24 (d, *J* = 9.5 Hz, 1H), 5.34 (d, *J* = 16.2 Hz, 1H), 5.79 (dd, *J* = 9.5 and 16.2 Hz, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 17.5, 22.0, 22.8, 25.2, 39.2, 53.5, 83.9, 113.6, 123.3, 131.4, 140.8, 153.5. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.49. Found: C, 68.16; H, 9.78.

Catalytic Asymmetric Reduction of Racemic Allylic Esters *dl*-5: Typical procedures are given for the reaction of *dl*-2-(1-naphthyl)-3-buten-2-yl benzoate (*dl*-5b') (entries 8 and 10 in Table 2). **Method A** (entry 8): To a solution of $Pd_2(dba)_3$•$CDCl_3$ (3.4 mg, 0.0033 mmol) and ligand **1b** (8.1 mg, 0.013 mmol) in THF/dioxane (0.15 mL/0.15 mL) was added *dl*-2-(1-naphthyl)-3-buten-2-yl benzoate (***dl*-5b'**) (101.3 mg, 0.34 mmol) in THF/dioxane (0.15 mL/0.15 mL) and Et_3N (40.4 mg, 0.40 mmol). Formic acid (16.1 mg, 0.35 mmol) was added and the mixture was stirred at 0 °C. The reaction was monitored by TLC and diluted with hexane. The catalyst was removed by filtration through a short silica gel (hexane). The filtrate was evaporated to give 47.0 mg (77%) of (*R*)-3-(1-naphthyl)-1-butene ((***R*)-4b**).

Method B (entry 10): To a solution of $Pd_2(dba)_3$•$CDCl_3$ (5.1 mg, 0.0049 mmol) and ligand **1b** (12.2 mg, 0.020 mmol) in THF/dioxane (0.25 mL/0.25 mL) was added *dl*-2-(1-naphthyl)-3-butene-2-yl benzoate (***dl*-5b'**) (152.9 mg, 0.51 mmol) in THF/dioxane (0.25 mL/0.25 mL) and Et_3N (60.2 mg, 0.60 mmol). Formic acid (24.3 mg, 0.53 mmol) was added slowly over 10 h at 0 °C and the mixture was stirred at 0 °C. The reaction was monitored by TLC and dilute with hexane. The catalyst was removed by filtration through a short silica gel (hexane). The filtrate was evaporated to give 79.3 mg (86%) of (*R*)-3-(1-naphthyl)-1-butene ((***R*)-4b**):[15] ^{1}H NMR ($CDCl_3$, 400 MHz, RT) δ 1.51 (d, *J* = 6.8 Hz, 1H), 4.31 (quintet, *J* = 6.8 Hz, 1H), 5.12 (dt, *J* = 11.7, 1.5 Hz, 1H), 5.13 (dt, *J* = 17.6, 1.5 Hz, 1H), 6.16 (ddd, *J* = 6.8, 11.7, 17.6 Hz, 1H), 7.04–8.54 (m, 7H). $[\alpha]_D^{20}$ +16.3 (*c* 0.35, $CDCl_3$); 90% ee. The enantiomeric purity was determined by GLC analysis with CP Cyclodex β236M. The absolute configuration was assigned to be (*R*)-(+) by correlation with known (*S*)-(+)-2-(1-naphthyl)propionic acid. ^{1}H NMR and analytical data for other reduction products **4c-f** are shown below. **3-Adamantyl-1-butene**[16] (**4c**) (75% ee): $[\alpha]_D^{20}$ +3.5 (*c* 1.0, chloroform) ^{1}H NMR ($CDCl_3$) δ 0.90 (d, *J* = 7.3 Hz, 3H), 1.20–2.00 (m, 16H), 1.95–2.05 (m, 3H), 4.87–4.96 (m, 2H), 5.26 (d, *J* = 10.5 Hz, 1H), 5.38 (d, *J* = 17.5 Hz, 1H), 5.92 (dd, *J* = 10.5 and 17.5 Hz, 1H). **(*R*)-3-Phenyl-1-butene** (**(*R*)-4d**) (60% ee): ^{1}H NMR ($CDCl_3$) δ 1.39 (d, *J* = 6.8 Hz, 3H), 2.48 (quintet, *J* = 6.8 Hz, 1H), 5.00–5.08 (m, 2H), 6.02 (ddd, *J* = 6.8, 10.5 and 16.0 Hz, 1H), 7.19–7.34 (m, 5H). $[\alpha]_D^{22}$ −2.2 (c 0.74, chloroform). *lit.*[17] (*R*)-(−): $[\alpha]_D^{22}$ −6.39 (neat). **(*R*)-3-Cyclohexyl-1-butene** (**(*R*)-4e**) (71% ee): ^{1}H NMR ($CDCl_3$) δ 0.98 (d, *J* = 6.9 Hz, 3H), 0.92–1.78 (m, 11H), 1.91–2.04 (m, 1H), 4.88–4.94 (m, 2H), 5.68 (m, 1H). $[\alpha]_D^{20}$ +3.6 (c 0.9, chloroform). *lit.*[18] (*R*)-(+): $[\alpha]_D^{24}$ +4.1 (c 0.67, chloroform). **(*S*)-3,7-Dimethyl-1,6-octadiene** (**(*S*)-4f**) (76% ee): ^{1}H NMR ($CDCl_3$) δ 0.98 (d, *J* = 7.0 Hz, 3H), 1.27–1.36 (m, 2H), 1.60 (s, 3H), 1.67 (s, 3H), 1.96 (q, *J* = 7.0 Hz, 2H), 2.12 (heptet, *J* = 7.0 Hz, 1H), 4.90 (d, *J* = 10.1 Hz, 1H), 4.92 (d, *J* = 17.1 Hz, 1H), 5.05–5.15 (m, 1H), 5.70 (ddd, *J* = 17.1, 10.1 and 7.0 Hz, 1H). $[\alpha]_D^{23}$ +7.0 (c 1.10, chloroform). *lit.*[19] (*R*)-(−): $[\alpha]_D$ −9.82 (c 6.18, chloroform).

Determination of the Absolute Configuration of 3-(1-Naphthyl)-1-butene ((*R*)-4b**).** To a solution of 3-(1-naphthyl)-1-butene (**(*R*)-4b**) (80 mg, 0.44 mmol; 61% ee) in *t*-BuOH (8 mL) and water (20 mL) were added $KMnO_4$ (175 mg, 1.11 mmol), $NaIO_4$ (1.52 g, 7.11 mmol) and K_2CO_3 (396 mg, 2.87 mmol), and the mixture was adjusted to pH 8 with 3 N aq NaOH. After stirring at r.t. for 2 h, the mixture was acidified with conc. hydrochloric acid to pH 1 and sodium hydrogen sulfite was added to reduce MnO_2. The mixture was extracted with ether, and the ether layer was extracted with 3 N aq. NaOH. The aqueous solution was acidified with conc. hydrochloric acid and extracted with ether. The ether extracts were dried ($MgSO_4$) and evaporation of the solvent gave 2-(1-naphthyl)propionic acid (17 mg). $[\alpha]_D^{20}$ +47.1 (*c* 0.65, ethanol). *lit.*[20] (*S*)-(+)-2-(1-naphthyl)propionic acid (96% ee): $[\alpha]_D^{20}$ +120.0 (*c* 1.0, ethanol).

Determination of absolute configuration and enantiomeric Purities of 4c-f: Olefins **4d-f** were converted into *N*-phenyl-2-adamantylpropanamide, *N*-phenyl-2-phenylpropanamide,[21] *N*-phenyl-2-cyclohexylpropanamide[22] and *N,N'*-diphenyl-2-methylpentane-1,5-dicarboxamide,[23] respectively, by oxidation with $NaIO_4/KMnO_4$ followed by treatment of the resulting carboxylic acids with aniline and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (WSC). The conditions for the determination of the enantiomeric purities of anilides with chiral stationary phase columns were as follows. *N*-phenyl-2-adamantylpropanamide: Sumichiral OA-2500I; hexane/1,2-dichloroethane/-EtOH = 1000/20/1; (+) isomer eluted faster than (–) isomer. *N*-Phenyl-2-cyclohexyl-propanamide and *N*-phenyl-2-phenylpropanamide: Sumichiral OA-2000; hexane/1,2-dichloroethane/EtOH = 250/20/1; *S* isomers eluted faster than *R* isomers. *N,N'*-Diphenyl-2-methylpentane-1,5-dicarboxamide: Sumichiral OA-4100; hexane/1,2-dichloroethane/EtOH = 50/15/1; *R* isomer eluted faster than *S* isomer. A typical procedure for the conversion is given for the reaction of **2f**. To a solution of (*S*)-**2f** (61 mg, 0.44 mmol) in *t*-BuOH (10 mL) and water (20 mL), were added $KMnO_4$ (185 mg, 1.17 mmol), $NaIO_4$ (1.46 g, 6.86 mmol) and K_2CO_3 (366 mg, 2.64 mmol), and the mixture was adjusted to pH 8 with 3 N aq NaOH. After stirring at room temperature for 2 h, the mixture was acidified with conc. hydrochloric acid to pH 1 and sodium hydrogen sulfite was added to reduce MnO_2. The mixture was extracted with ether layer was extracted with 3 N aq NaOH. The aqueous solution was acidified with conc. hydrochloric acid and extracted with ether. The ether extracts were dried ($MgSO_4$) and evaporation of the solvent gave 2-methylpentanedioic acid (38 mg). To a solution of the carboxylic acid (10 mg) obtained above in THF (0.5 mL), were added aniline (15 mg, 0.16 mmol) and WSC (30 μL), and the mixture was stirred at 40 °C for 1 h. Conc. hydrochloric acid was added and the mixture was extracted with EtOAc. Evaporation of the solvent followed by silica gel column chromatography (hexane/EtOAc = 1/1) gave *N,N'*-diphenyl-2-methylpentane-1,5-dicarboxamide (11 mg).

Preparation of [PdCl{1-(1-naphthyl)-1-methyl-π-allyl}]$_2$ (7): Palladium chloride (900.4 mg, 5.0 mmol) and lithium chloride (430.2 mg, 10.1 mmol) was dissolved in hot water (1.5 mL) and to this solution were added ethanol (3 mL), 2-(1-naphthyl)-3-buten-2-ol (1.0 g, 5.0 mmol) in THF (15 mL) and aqueous hydrochloric acid (0.8 mL, 12 N). Carbon monoxide was passed through the solution at room temperature and, after 1 h, a clear yellow orange solution was obtained. The reaction mixture began to precipitate as orange-yellow crystals. After 4 h under carbon monoxide, the solvent was removed under reduced pressure and the residue was dissolved in $CHCl_3$ which was washed with water and dried over anhydrous sodium sulfate and evaporated to give 940 mg (58%) of [PdCl[π-(1-naphthyl)-1-methylallyl]]$_2$: ^{1}H NMR ($CDCl_3$) δ 1.79 (brs, 3H), 2.60 (brs, 1H), 3.95 (brs, 1H), 5.91 (brs, 1H), 7.41–8.66 (m, 7H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 202 Hz, RT) δ 28.8, 58.6, 95.1, 108.5, 125.0, 125.6, 125.8, 126.2, 127.6, 127.8, 128.5, 131.9, 133.7, 137.7. Anal. Calcd for $C_{28}H_{26}Cl_2Pd_2$: C, 52.04; H, 4.06. Found: C, 51.84; H, 4.10.

NMR Study of PdCl{1-(1-naphthyl)-1-methyl-π-allyl}((*R*)-MeO-MOP) (8). In an NMR sample tube were placed (*R*)-MeO-MOP (**1a**) (13.8 mg, 0.030

mmol) and [PdCl{1-(1-naphthyl)-1-methyl-π-allyl}]$_2$ (**7**) (9.6 mg, 0.015 mmol). The tube was filled with nitrogen and $CDCl_3$ (0.5 mL) was added. ^{1}H NMR, ^{31}P NMR and ^{13}C NMR spectra were measured. **major isomer**: ^{1}H NMR ($CDCl_3$, 500 MHz, RT) δ 1.74 (d, J = 12.7 Hz, 1H, anti-H on C^3), 2.11 (d, J_{H-P}= 9.8 Hz, Me), 2.55 (d, J = 7.3 Hz, 1H, syn-H on C^3), 3.14 (s, 3H, OMe), 5.08 (dd, J = 7.3, 12.7 Hz, 1H, H on C^2), 6.22–8.72 (m, 29H, aromatic). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 Hz, RT) δ 27.5 (Me), 54.5 (C^3), 54.9 (OMe), 112.3 (d, J_{C-P} = 2.1 Hz, C^2), 112.3 (d, J_{C-P} = 24.8 Hz, C^1), 113.5–138.0 (aromatic). ^{31}P{^{1}H} NMR ($CDCl_3$, 202 MHz, RT) δ 28.3. **minor isomer**: ^{1}H NMR ($CDCl_3$, 500 MHz, RT) δ 2.21 (d, J_{H-P}= 9.8 Hz, 1H, Me), 2.26 (d, J = 12.7 Hz, anti-H on C^3), 2.75 (d, J = 7.3 Hz, 1H, syn-H on C^3), 3.55 (s, 3H, OMe), 5.70 (dd, J = 7.3, 12.7 Hz, 1H, H on C^2), 6.22–8.72 (m, 29H, aromatic). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 Hz, RT) δ 27.8 (Me), 53.5 (C^3), 55.1 (OMe), 111.7 (d, J_{C-P} = 3.1 Hz, C^2), 113.9 (d, J_{C-P} = 23.8 Hz, C^1), 111.9–137.6 (aromatic). ^{31}P{^{1}H} NMR ($CDCl_3$, 202 MHz, RT) δ 32.4.

NMR Study of [PdCl(π-C_3H_5)]L (9a and 9b). A typical procedure is given for the study of **[PdCl(π-C_3H_5)]((*R*)-MeO-MOP)**. In an NMR sample tube were placed (*R*)-MeO-MOP (12.8 mg, 0.027 mmol) and [PdCl(π-C_3H_5)]$_2$ (5.0 mg, 0.014 mmol). The tube was filled with nitrogen and $CDCl_3$ (0.5 mL) was added. ^{1}H NMR, ^{31}P NMR and ^{13}C NMR spectra were measured. **[PdCl(π-C_3H_5)]L (L = 1a (*R*)-MeO-MOP)**: major isomer: ^{1}H NMR ($CDCl_3$, 500 MHz, –20 °C) δ 0.82 (d, J = 11.7 Hz, 1H, anti-H on C^3), 2.03 (dd, J = 10.7 Hz, J_{H-P} = 13.2 Hz, 1H, anti-H on C^1), 2.10 (d, J = 6.4 Hz, 1H, syn-H on C^3), 3.65 (s, 3H, OMe), 4.13 (dd, J = 4.9 Hz, J_{H-P} = 7.3 Hz, 1H, syn-H on C^1), 4.99 (m, 1H, H on C^2), 6.88–7.90 (m, 22H, aromatic). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 Hz, –20 °C) δ 55.4 (OMe), 64.7 (C^3), 81.3 (d, J_{C-H} = 31.0, C^1), 117.9 (d, J_{C-H} = 4.1, C^2), 113.9–155.7 (aromatic). ^{31}P{^{1}H} NMR ($CDCl_3$, 202 MHz, –20 °C) δ 20.2. minor isomer: ^{1}H NMR ($CDCl_3$, 500 MHz, –20 °C) δ 1.48 (d, J = 12.2 Hz, 1H, anti-H on C^3), 2.80 (d, J = 6.4 Hz, 1H, syn-H on C^3), 2.99 (dd, J = 8.8 Hz, J_{H-P} = 13.7 Hz, 1H, anti-H on C^1), 3.24 (m, 1H, H on C^2), 3.27 (s, 3H, OMe), 3.99 (dd, J = 6.8 Hz, J_{H-P} = 4.9 Hz, 1H, syn-H on C^1), 6.88–7.90 (m, 22H, aromatic). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 Hz, –20 °C) δ 54.9 (OMe), 60.6 (C^3), 80.0 (d, J_{C-H} = 30.0, C^1), 117.8 (d, J_{C-H} = 4.1, C^2), 113.9–155.7 (aromatic). ^{31}P{^{1}H} NMR ($CDCl_3$, 202 MHz, –20 °C) δ 17.8. **[PdCl(π-C_3H_5)]L (L = 1d) (Ar = 4-$MeOC_6H_4$)**: major isomer: ^{1}H NMR ($CDCl_3$, 500 MHz, –20 °C) δ 1.18 (d, J = 11.7 Hz, 1H, anti-H on C^3), 2.35 (m, 2H, anti-H on C^1 and syn-H on C^3), 3.74 (s, 3H, OMe), 3.79 (s, 6H, OMe), 4.26 (dd, J = 5.9 Hz, J_{H-P} = 7.2 Hz, 1H, syn-H on C^1), 5.48 (m, 1H, H on C^2), 6.76–8.16 (m, 20H, aromatic). ^{13}C{^{1}H} NMR ($CDCl_3$, 125

Hz, –20 °C) δ 55.1 (OMe), 55.5 (OMe), 63.3 (C^3), 80.5 (d, $J_{C\text{-}H}$ = 32.1, C^1), 117.4 (d, $J_{C\text{-}H}$ = 5.2, C^2), 112.8–160.3 (aromatic). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 202 MHz, –20 °C) δ 16.5. minor isomer: 1H NMR (CDCl3, 500 MHz, –20 °C) δ 1.76 (d, J = 12.2 Hz, 1H, anti-H on C^3), 2.95 (d, J = 6.9 Hz, 1H, syn-H on C^3), 3.13 (dd, J = 8.8 Hz, $J_{H\text{-}P}$ = 13.7 Hz, 1H, anti-H on C^1), 3.43 (s, 3H, OMe), 3.79 (m, 1H, H on C^2), 3.8 (s, 6H, OMe), 4.14 (dd, J = 5.9 Hz, $J_{H\text{-}P}$ = 7.0 Hz, 1H, syn-H on C^1), 6.76–8.16 (m, 20H, aromatic). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 Hz, –20 °C) δ 54.9 (OMe), 55.1 (OMe), 69.5 (C^3), 79.5 (d, $J_{C\text{-}H}$ = 30.0 Hz, C^1), 117.1 (d, $J_{C\text{-}H}$ = 5.2 Hz, C^2), 113.9–155.7 (aromatic). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 202 MHz, –20 °C) δ 14.2. **[PdCl(π-C_3H_5)]L (L = 1b) (Ar = 3-$CF_3C_6H_4$)**: major isomer: ^1H NMR ($CDCl_3$, 500 MHz, –20 °C) δ 1.00 (d, J = 12.2 Hz, 1H, anti-H on C^3), 2.20 (d, J = 7.0 Hz, 1H, syn-H on C^3), 2.32 (dd, J = 10.7 Hz, $J_{H\text{-}P}$ = 13.4 Hz, 1H, anti-H on C^1), 3.76 (s, 3H, OMe), 4.36 (dd, J = 7.3 Hz, $J_{H\text{-}P}$ = 9.4 Hz, 1H, syn-H on C^1), 5.16 (m, 1H, H on C^2), 6.97–8.00 (m, 20H, aromatic). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 Hz, –20 °C) δ 55.4 (OMe), 64.7 (C^3), 81.3 (d, $J_{C\text{-}H}$ = 31.0 Hz, C^1), 117.9 (d, $J_{C\text{-}H}$ = 5.2 Hz, C^2), 113.7–155.6 (aromatic). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 202 MHz, –20 °C) δ 19.8. minor isomer: ^1H NMR ($CDCl_3$, 500 MHz, –20 °C) δ 1.71 (d, J = 12.2 Hz, 1H, anti-H on C^3), 2.90 (d, J = 6.4 Hz, 1H, syn-H on C^3), 3.20 (dd, J = 9.1 Hz, $J_{H\text{-}P}$ = 13.7 Hz, 1H, anti-H on C^1), 3.41 (s, 3H, OMe), 3.63 (m, 1H, H on C^2), 4.23 (dd, J = 7.0 Hz, $J_{H\text{-}P}$ = 9.4 Hz, 1H, syn-H on C^1), 6.97–8.00 (m, 20H, aromatic). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 Hz, –20 °C) δ 55.0 (OMe), 60.6 (C^3), 80.0 (d, $J_{C\text{-}H}$ = 29.0, C^1), 117.9 (d, $J_{C\text{-}H}$ = 7.2, C^2), 113.7–155.6 (aromatic). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 202 MHz, –20 °C) δ 17.1.

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Chapter III

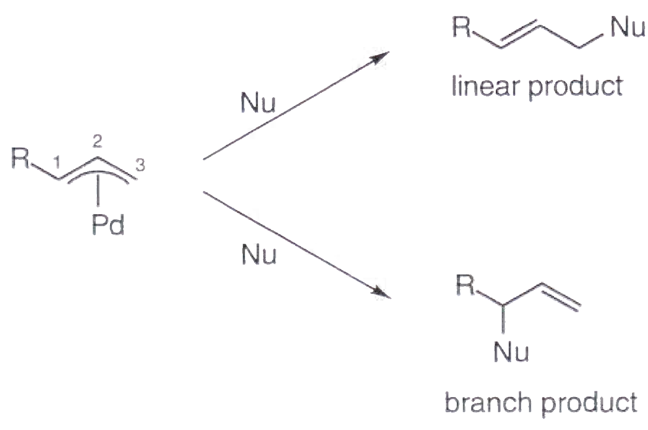
Regio- and Enantio-selective Allylic Alkylation Catalyzed by a Chiral Monophosphine–palladium Complex

Summary: Allylic alkylation of racemic 1-arylprop-2-enyl acetates [ArCH(OAc)CH=CH_2] with the sodium enolate of dimethyl methylmalonate in the presence of a palladium catalyst coordinated with (*R*)-2-diphenylphosphino-2'-methoxy-1,1'-binaphthyl [(*R*)-MeO-MOP] proceeds with high branch selectivity (90%) to give chiral products [ArC*H(Nu)CH=CH_2] of up to 87% ee.

Introduction

Palladium-catalyzed allylic substitution reactions including catalytic asymmetric reactions have attracted considerable attention owing to their synthetic utility and mechanistic interest.[1] One of the major problems in developing the catalytic asymmetric substitutions in 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 C-1 position produces linear isomer rather than branch isomer.[1] It follows that the reaction can not be extended to asymmetric synthesis because the linear isomer lacks the chiral carbon center. The regioselectivity in forming the branch isomer is usually very low except for methyl as the substituent.[2] Here we report that the use of 2-

Scheme 1



diphenylphosphino-2'-methoxy-1,1'-binaphthyl (MeO-MOP),[3] which is a sterically bulky chiral monophosphine ligand, for allylic alkylation of 1-aryl-2-propenyl acetates **1** reversed the regiochemistry to give branch isomers **2** with high selectivity and it realized the asymmetric synthesis (up to 87% ee) in this new allylic alkylation system.

Results and discussion

The results obtained for the allylic substitution of racemic 1-aryl-2-propenyl acetates *dl*-**1** in the presence of palladium-phosphine complexes (Scheme 2) are summarized in Table 1. The reaction of *dl*-1-phenyl-2-propenyl acetate (**1a**) with sodium salt of dimethyl methylmalonate in THF at –20 °C in the presence of 2 mol % of palladium catalyst generated from [PdCl(π-C_3H_5)]$_2$) and 1,2-bis(diphenylphosphino)ethane (dppe) gave linear isomer (*E*)-**3a** with 93% regioselectivity (entry 1). The linear-selectivity (79%–85% regioselectivity) was also observed in the reaction with a palladium catalyst coordinated with triphenylphosphine (entries 2 and 3). It is

Scheme 2

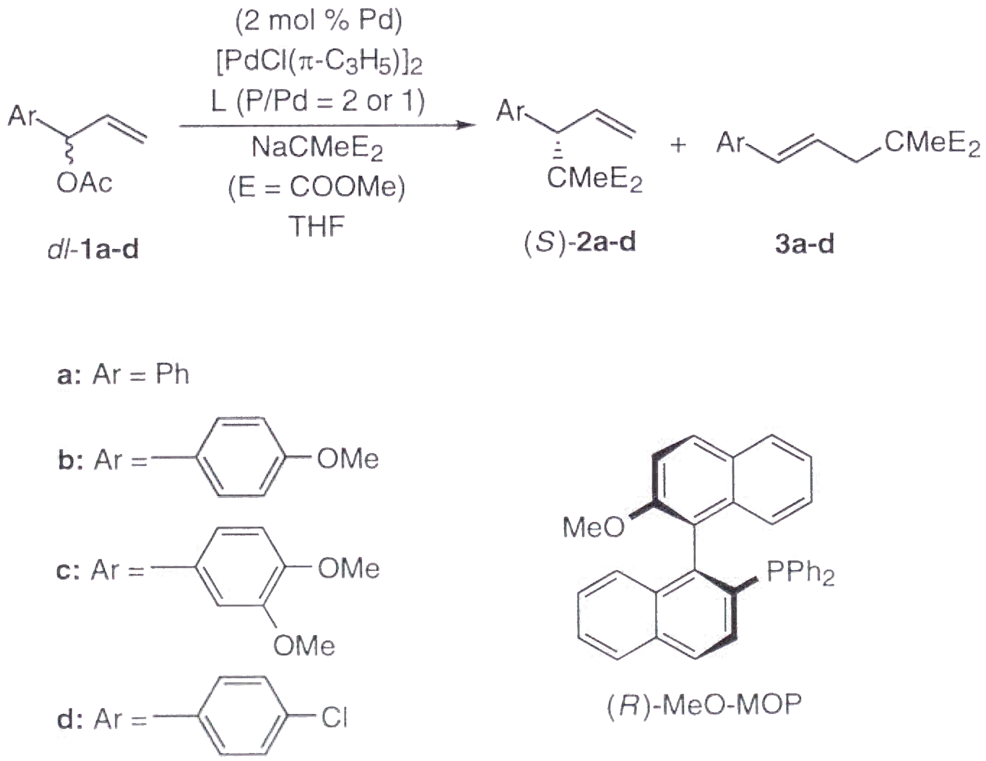


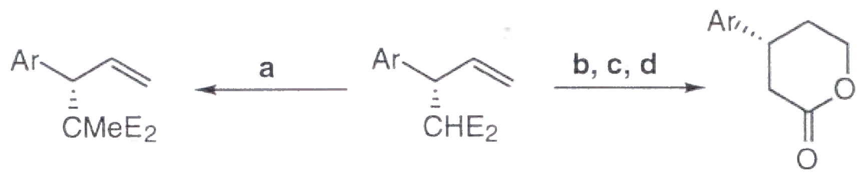
Table 1 Regio- and Enantioselective Allylic Alkylation of Acetate **1** Catalyzed by Palladium-phosphine Complexes[a]

entry	allyl ester	ligand (ratio P/Pd)	temp (°C)	time (h)	yield (%)[b] **2** and **3**	ratio[c] **2/3**	% ee (config.)
1	**1a**	dppe (2/1)	–20	4	92	7/93	—
2	**1a**	PPh_3 (2/1)	–20	4	99	15/85	—
3	**1a**	PPh_3 (1/1)	–20	24	63	21/79	—
4	**1a**	(*R*)-MeO-MOP (2/1)	–20	6	99	79/21	68[d]
5	**1a**	(*R*)-MeO-MOP (1/1)	–20	6	99	79/21	68[d]
6	**1a**	(*R*)-MeO-MOP (1/1)	–30	6	97	82/18	86[d,e]
7	**1b**	dppe (2/1)	–20	2	96	27/73	—
8	**1b**	PPh_3 (2/1)	–20	6	97	30/70	—
9	**1b**	PPh_3 (1/1)	–20	24	58	28/72	—
10	**1b**	(*R*)-MeO-MOP (2/1)	–20	2	97	86/14	76[f] (*S*)
11	**1b**	(*R*)-MeO-MOP (1/1)	–20	2	99	85/15	76[f] (*S*)
12	**1b**	(*R*)-MeO-MOP (1/1)	–30	2	96	90/10	87[f] (*S*)[e]
13	**1c**	(*R*)-MeO-MOP (1/1)	–30	2	99	89/11	85[g,e]
14	**1d**	(*R*)-MeO-MOP (1/1)	–30	2	93	80/20	82[g,e]

[a] All reactions were carried out in THF under nitrogen: THF (1.0 mL), allylic acetate (0.20 mmol), $NaCMe(COOMe)_2$ (0.40 mmol), $[PdCl(\pi\text{-}C_3H_5)]_2$ (0.002 mmol), and phosphine ligand. [b] Isolated yield by silica gel column chromatography. [c] The ratio was determined by ^1H NMR analysis of the products. [d] Determined by GLC analysis with CP Cyclodex β236M after decarbomethoxylation of one of the two carbomethoxy groups. [e] Specific rotation of **2a** (entry 6), **2b** (entry 12), **2c** (entry 13) and **2d** (entry 14) are $[\alpha]_D^{20}$ +46.4, +50.3, +45.0 and +56.3 (*c* 0.8-1.8, chloroform), respectively. [f] Determined by HPLC analysis with Chiralpak AD (hexane/2-propanol = 9/1). [g] Determined by HPLC analysis with Chiralcel OD-H (hexane/2-propanol = 9/1).

noteworthy that the reaction catalyzed by palladium-PPh_3 requires two equivalents of triphenylphosphine (to Pd) for the allylic substitution to proceed smoothly. With one equivalent of triphenylphosphine, the reaction stops at about 60% conversion. The opposite regioselectivity was observed in the same substitution reaction of **1a** by use of MeO-MOP as a ligand, which gave branch isomer **2a** with 79% regioselectivity at –20 °C (entries 4 and 5). With the palladium–MeO-MOP catalyst, the ratio of phosphine to palladium did not affect either activity or regioselectivity. Higher regioselectivity in forming branch isomer was observed in the reaction of 1-aryl-2-propenyl acetates **1b**,

Scheme 3



(*S*)-(+)-**2b** $[\alpha]_D^{20}$ +40.7 (*c* 1.7, chloroform)

(*R*)-(+)-**5** $[\alpha]_D^{20}$ +15.9 (*c* 1.0, chloroform)

(*R*)-(–)-**4** $[\alpha]_D^{20}$ –6.2 (*c* 1.0, chloroform)

Ar = 4-MeOC$_6$H$_4$, E = CO$_2$Me

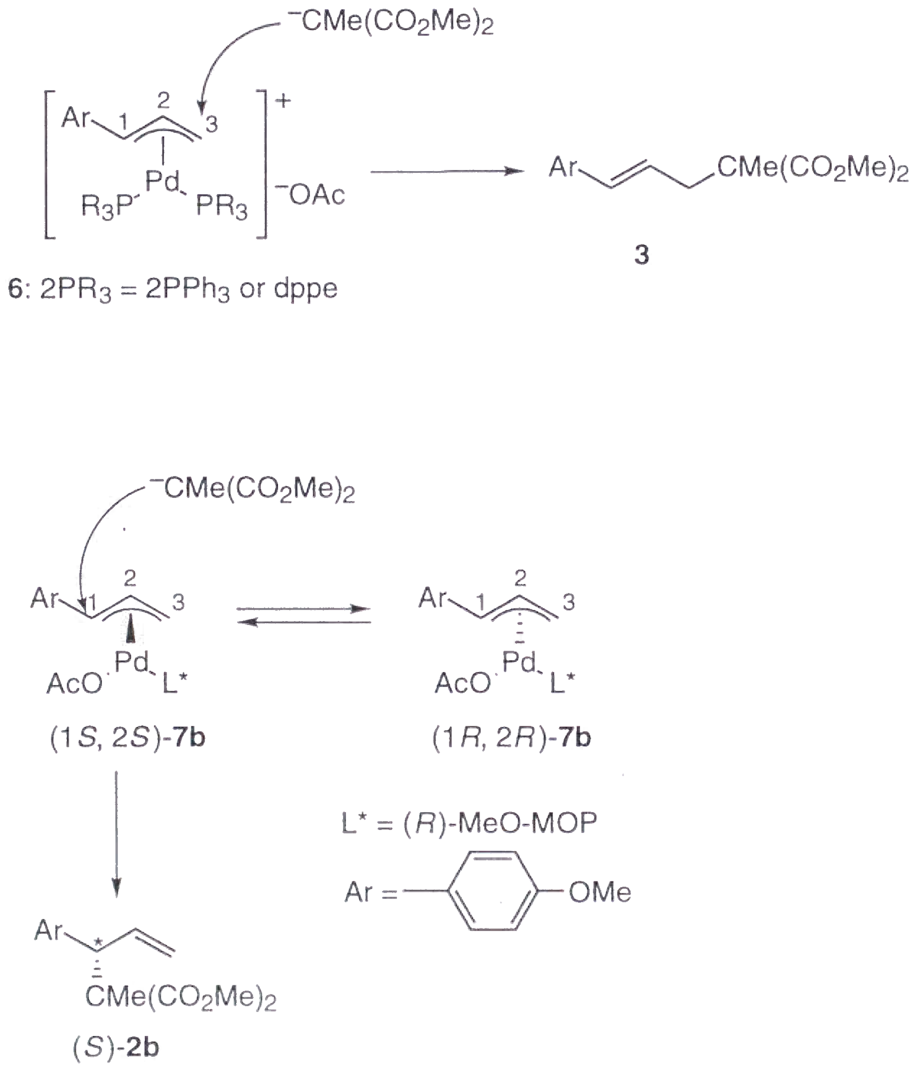
(a) MeI, NaOMe, MeOH, reflux, 86%; (b) LiCl, DMSO, H$_2$O,120 °C;
(c) BH$_3$•THF, THF; (d) *p*-TsOH, PhH (58% over 3 steps)

1c and **1d** that containmethoxy group(s) or chloride on the aromatic ring (entries 10-14). At the reaction temperature of –30 °C, 1-(4-methoxyphenyl)-2-propenyl acetate (**1b**) gave branch isomer **2b** with 90% regioselectixity (entry 12). The enantiomeric purity of **2b** determined by a chiral stationary phase column (Chiralpak AD) was 87% ee and its absolute configuration was assigned to be (+)-(*S*) by correlation with known (*R*)-(–)-4-(4-methoxyphenyl)-tetrahydro-2*H*-pyran-2-one[4] (**4**) by way of (*R*)-(+)-dimethyl (1-aryl-2-propenyl)-malonate (**5**) (Scheme 3). Here again the palladium catalyst containing dppe or triphenylphosphine gave linear isomer **3b** preferentially (entries 7-9). The reaction of allylic acetate **1c** in the presence of MeO-MOP at –30 °C also gave the corresponding alkylation product **2c** of 85% ee with high branch-selectivity (enrty 13). Thus, chiral monodentate phosphine ligand, MeO-MOP, is playing a key role on the high branch-selectivity in the catalytic allylic alkylation of 1-aryl-2-propenyl acetates. The present type of asymmetric alkylation is considered to be difficult with chelating bisphosphine ligands so far used mostly for the asymmetric allylic alkylation which proceeds by way of palladium intermediate containing 1,3-disubstituted π-allyl such as 1,3-diphenyl.[1,5]

The preferential formation of linear isomers in the allylic alkylation of **1** catalyzed by palladium–dppe or palladium–PPh$_3$ is as expected because cationic [π-(1-aryl)]bis(phosphine)palladium(II) intermediate **6** formed by oxdative addition of **1** to bis(phosphine)palladium(0) will undergo the nucleophilic attack on the less hindered end of the π-allyl, namely, C-3 position of π-(1-aryl)allyl group (Scheme 4). It gives the thermodinamically more stable product **3** where the double bond is conjugated with aromatic ring. On the other hand, the reaction with MeO-MOP ligand should proceed via neutral [π-(1-aryl)allyl](acatato)(phosphine)palladium(II) intermediate **7** because the steric bulkiness of MOP ligand does not allow the palladium to form a cationic bis(phosphine) complex which is analogous to **6**.

The π-allylpalladium complex **7b** (Ar = 4-MeO-C_6H_4) was prepared by mixing [π-(1-aryl)allyl](acatato)palladium(II) dimer with one equivalent (to Pd) of (*R*)-MeO-MOP and it was characterized by ^{31}P and ^{1}H NMR spectra. In $CDCl_3$ at −50 °C the complex exists as a mixture of isomers in a ratio of 9:1 (see experimental section). The main isomer has substituted carbon (C-1) of the π-allyl *trans* to phosphorou atom of MeO-MOP and the unsubstituted carbon (C-3) *cis* to phosphorous, which is determined by a large coupling constant (J = 8.2 Hz) between C-1 proton and phosphorus and no

Scheme 4



coupling between C-3 proton and phosphorus. Our structural studies of related PdCl(π-allyl)(MeO-MOP) complexes[6] also showed that the unsubstituted π-allyl carbon adopts *cis* position to phosphorus. The nucleophile attacks the C-1 carbon which is more weakly bonded to palladium due to a stronger trans influence of phosphine ligand to give branch product preferentially. The stoichiometric reaction of π-allylpalladium complex **7b** with sodium enolate of dimethyl methylmalonate in THF –20 °C gave (*S*)-**2b** of 90% ee with 88% regioselectivity, which is in good agreement with the catalytic reactions in terms of both regio- and enantioselectivity.

Experimental Section

General. All manipulations were carried out under a nitrogen atmosphere. Nitrogen gas was dried by passage through P_2O_5 (Merck, SICAPENT). NMR spectra were recorded on a JEOL JNM-EX270 spectrometer (270 MHz for ^1H and 109 MHz for ^{31}P), JEOL JNM-AL400 spectrometer (400 MHz for ^1H NMR), or JEOL JNM LA500 spectrometer (500 MHz for ^1H, 125 MHz for ^{13}C and 202 MHz for ^{31}P). Chemical shifts are reported in δ ppm referenced to an internal $SiMe_4$ standard for ^1H NMR, and to an external 85% H_3PO_4 standard for ^{31}P NMR. Residual chloroform (δ 77.0 for ^{13}C) was used as internal reference for ^{13}C NMR. ^1H, ^{13}C and ^{31}P NMR spectra were recorded in $CDCl_3$ at 25 °C unless otherwise noted. Preparative medium pressure liquid chromatography (MPLC) was performed with a silica gel prepacked column Si-10 (Kusano). HPLC analysis was performed on a Shimazu LC-6A liquid chromatograph system and a JASCO PU-980 liquid chromatograph system with chiral stationary phase column Daicel Co. Ltd., Chiralpak AD and Chiralcel OD-H. GLC analysis was performed on a HEWLETT PACKARD HP 6890 series with a chiral stationary phase column, CP Cyclodex β-236M (50 m). Optical rotations were measured on a JASCO DIP-370 polarimeter. Preparative medium pressure liquid chromatography (MPLC) was performed with a silica gel prepacked column Si-10 (Kusano).

Materials. THF was dried over sodium benzophenone ketyl and distilled prior to use. $[PdCl(\pi\text{-}C_3H_5)]_2$,[7] (*R*)-MeO-MOP[3] and 1-aryl-2-propenyl acetates (**1a**, **1b** and **1d**)[8,9] were prepared according to the reported procedures.

Preparation of 1-(3,4-Dimethoxyphenyl)-2-propenyl Acetate (1c). To a solution of vinylmagnesium bromide (85 mL of 0.8 M, 68.0 mmol) in THF at 0 °C was added dropwise a solution of 3,4-dimethoxybenzaldehyde (10 g, 60.2 mmol) in THF (30 mL). The mixture was stirred at room temperature for 3 h. It was quenched with saturated ammonium chloride solution and extracted with ether. The ether extracts were washed with saturated sodium hydrogen carbonate solution, and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a crude 1-(3,4-dimethoxyphenyl)-2-propenol. To a solution of this crude alcohol, pyridine (6.0 mL, 74.4 mmol) and a catalytic amount of 4-dimethylaminopyridine in ether (50 mL) was added acetic anhydride (7.0 mL, 74.5 mmol). The mixture was stirred at room temperature for 12 h, quenched with water, and extracted with ether. The organic phase was washed with 10% $CuSO_4$ solution, water and brine, dried over anhydrous sodium sulfate and evaporated. The residue was chromatographed on alumina (hexane/Et_3N = 6/1) to give 11.1 g (79%) of 1-(3, 4-dimethoxyphenyl)-2-propenyl acetate (**1c**): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.10 (s, 3H), 3.86 (s, 3H), 3.88 (s, 3H), 5.23 (d, *J* = 11.3 Hz, 1H), 5.29 (d, *J* = 15.8 Hz, 1H), 6.01 (ddd, *J* = 5.5, 11.3, 15.8 Hz, 1H), 6.22 (d, *J* = 5.5 Hz, 1H), 6.83–6.94 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.1, 55.7, 75.8, 110.4, 110.9, 116.4, 119.8, 131.2, 136.2, 148.9, 169.8. Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 66.29; H, 7.00.

Palladium-Catalyzed Allylic Alkylation of 1. The reaction conditions and results are shown in Table 1. **A typical procedure is given for the reaction of 1-(4-Methoxyphenyl)-2-propenyl acetate (1b)** (entry 12). To a solution of $[PdCl(\pi\text{-}C_3H_5)]_2$ (1.26 mg, 0.0035 mmol) and (*R*)-MeO-MOP (6.5 mg, 0.014 mmol) in THF (0.1 mL) was added a solution of sodium salt of dimethyl methylmalonate (100 mg, 0.69 mmol) prepared from dimethyl methylmalonate and sodium hydride in THF (1.4 mL). Allyl acetate **1b** (71 mg, 0.35 mmol) was added and the mixture was stirred at 20 °C for 12 h. The catalyst was removed by filtration through a short silica gel pad (ether). The crude filtrate was chromatographed on silica gel (EtOAc/hexane = 1/6) to give 97 mg (96%) of a mixture of dimethyl ((*E*)-3-(4-methoxyphenyl)-2-propenyl)methylmalonate (**3b**) and dimethyl (1-(4-methoxyphenyl)-2-propenyl)methylmalonate (**2b**). The ratio of **2b** to **3b** was determined to be 90 to 10 by ^{1}H NMR. The regioisomers **3b** and **4b** were separable by MPLC (eluent: EtOAc/hexane = 1/6). **Dimethyl (1-(4-Methoxyphenyl)-2-propenyl)methylmalonate (2b):** (87% ee) $[\alpha]_D^{20}$ +50.3 (*c* 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.51 (s, 3H), 3.71 (s, 3H), 3.79 (s, 3H), 3.87 (s, 3H), 4.19 (d, *J* = 8.3 Hz, 1H), 5.09 (d, *J* = 16.8 Hz, 1H), 5.14 (d, *J* = 11.3, 1H), 6.32 (ddd, *J* = 8.3, 11.3, 16.8 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.3, 52.3, 53.7, 55.1, 58.9, 113.5, 117.4, 130.5, 131.0, 137.1, 158.6, 171.3, 171.5. Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 66.00; H, 6.85. **Dimethyl ((*E*)-3-(4-Methoxyphenyl)-2-propenyl)methylmalonate (3b):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.59 (s, 3H), 2.74 (dd, *J* = 7.8, 1.0 Hz, 2H), 3.73 (s, 6H), 3.80 (s, 3H), 5.93 (dt, *J* = 15.6, 7.8 Hz, 1H), 6.38 (d, J = 15.6 Hz, 1H), 6.82 (d, J = 6.4 Hz, 2H), 7.25 (d, J = 6.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.0, 39.5, 52.5, 54.0, 55.2, 111.0, 113.9, 121.8, 127.3, 133.5, 159.0, 172.4. Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.80; H, 7.11. ^1H NMR and analytical data for other allylic alkylation products **2** and **3** are shown below. **Dimethyl (1-Phenyl-2-propenyl)methylmalonate (2a):** (86% ee) $[\alpha]_D^{20}$ +46.4 (c 1.6, $CHCl_3$); ^1H NMR ($CDCl_3$, 270 MHz) δ 1.43 (s, 3H), 3.62 (s, 3H), 3.72 (s, 3H), 4.10 (d, J = 8.6 Hz, 1H), 5.11 (d, J = 16.8 Hz, 1H), 5.12 (d, J = 10.0, 1H), 6.32 (ddd, J = 8.6, 10.0, 16.8 Hz, 1H), 7.18–7.34 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.4, 52.3, 52.4, 54.5, 58.9, 117.8, 127.1, 128.2, 129.5, 136.9, 139.1, 171.3, 171.5. Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.70; H, 6.95. **Dimethyl ((*E*)-3-Phenyl-2-propenyl)methylmalonate (3a):** ^1H NMR ($CDCl_3$, 270 MHz) δ 1.46 (s, 3H), 2.77 (dd, J = 7.8, 1.0 Hz, 2H), 3.73 (s, 6H), 6.08 (dt, J = 15.6, 7.8 Hz, 1H), 6.45 (d, J = 15.6 Hz, 1H), 7.19–7.34 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.0, 39.5, 52.5, 54.0, 124.1, 126.2, 127.4, 128.5, 134.1, 137.1, 172.3. Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.55; H, 7.01. **Dimethyl (1-(3,4-Dimethoxyphenyl)-2-propenyl)methylmalonate (2c):** (85% ee) $[\alpha]_D^{20}$ +45.0 (c 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.43 (s, 3H), 3.64 (s, 3H), 3.71 (s, 3H), 3.85 (s, 3H), 3.86 (s, 3H), 4.07 (d, J = 8.5 Hz, 1H), 5.10 (d, J = 16.5 Hz, 1H), 5.12 (d, J = 8.5 Hz, 1H), 6.30 (dt, J = 16.5, 8.5 Hz, 1H), 6.79 (s, 1H), 6.79 (d, J = 7.9 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.5, 52.4, 54.2, 55.8, 59.0, 110.8, 112.8, 117.5, 121.63, 131.5, 137.0, 148.0, 148.4, 171.3, 171.6. Anal. Calcd for $C_{17}H_{22}O_6$: C, 63.34; H, 6.88. Found: C, 63.33; H, 7.10. **Dimethyl ((*E*)-3-(3,4-Dimethoxyphenyl)-2-propenyl)methylmalonate (3c):** ^1H NMR ($CDCl_3$, 500 MHz) δ 1.46 (s, 3H), 2.75 (d, J = 7.3 Hz, 2H), 3.73 (s, 6H), 3.87 (s, 3H), 3.89 (s, 3H), 5.94 (dt, J = 15.2, 7.3 Hz, 1H), 6.37 (d, J = 15.2 Hz, 1H), 6.79 (d, J = 9.1 Hz, 2H), 6.88 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.0, 39.5, 52.4, 54.0, 55.8, 55.9, 108.9, 111.1, 119.2, 122.0, 133.8, 148.0, 172.4. Anal. Calcd for $C_{17}H_{22}O_6$: C, 63.34; H, 6.88. Found: C, 63.22, ; H, 7.00. **Dimethyl (1-(4-Chlorophenyl)-2-propenyl)methylmalonate (2d):** (82% ee) $[\alpha]_D^{20}$ +56.3 (c 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.42 (s, 3H), 3.63 (s, 3H), 3.70 (s, 3H), 4.11 (d, J = 8.8 Hz, 1H), 5.09 (d, J = 17.1 Hz, 1H), 5.15 (d, J = 10.3, 1H), 6.26 (ddd, J = 8.8, 10.3, 17.1 Hz, 1H), 7.22 (d, J = 8.7 Hz, 2H), 7.25 (d, J = 8.7 Hz, 2H). Anal. Calcd for $C_{15}H_{17}O_4Cl$: C, 60.71; H, 5.77. Found: C, 60.57; H, 5.89. **Dimethyl ((*E*)-3-(4-Chlorophenyl)-2-propenyl)methylmalonate (3d):** ^1H NMR ($CDCl_3$, 500 MHz) δ 1.45 (s, 3H), 2.75 (d, J = 7.3 Hz, 2H), 3.73 (s, 6H), 6.07 (dt, J = 15.6, 7.3 Hz, 1H), 6.39 (d, J = 15.6 Hz, 1H), 7.25 (s, 4H). Anal. Calcd for $C_{15}H_{17}O_4Cl$: C, 60.71; H, 5.77. Found: C, 60.57; H, 5.93.

Determination of the Absolute Configuration of 5: Reaction conditions are shown in Scheme 3. Dimethyl (1-(4-methoxyphenyl)-2-propenyl)malonate (**5**) (74% ee (+)) was converted into the known (*R*)-(–)-4-(4-methoxyphenyl)tetrahydro-2*H*-pyran-2-one (**4**)[10]by the following procedures, (1) decarbomethoxylation, (2) hydroboration and (3) lactonaization. Experimental procedures: To a solution of lithium chloride (500 mg, 11.8 mmol) in dimethyl sulfoxide (2.5 mL) and water (0.5 mL) was added dimethyl (1-(4-methoxyphenyl)-2-propenyl)malonate (50 mg, 0.18 mmol). The mixture was stirred at 120 °C for 18 h. The mixture was diluted with ether and extracted with ether. The ether layer was dried over magnesium sulfate and evaporated. The residue was dissolved in THF (5 mL) and cooled to 0 °C. To the solution was added BH_3•THF (0.5 mL of 1.0 M, 0.5 mmol) and the mixture was stirred at room temperature for 3 h. It was quenched with 3 N NaOH (0.5 mL), water (0.5 mL) and 30% hydrogen peroxide (1.0 mL), and stirred for 1 h. The mixture was extracted with ether and the extracts were dried over anhydrous sodium sulfate and evaporated. To the crude product dissolved in benzene (2 mL), was added a catalytic amount of *p*-toluenesulfonic acid. The mixture was stirred at room temperature for 5 min. Removal of solvent followed by preparative TLC on silica gel (hexane/EtOAc = 6/1) gave 22 mg (58% over 3 steps) of 4-(4-methoxyphenyl)tetrahydro-2*H*-pyran-2-one (**4**): ^1H NMR ($CDCl_3$, 400 MHz) δ 1.78–3.40 (m, 5H), 3.77 (s, 3H), 4.32 (m, 2H), 6.81 (d, J = 9.2 Hz, 2H), 7.12 (d, J = 9.2 Hz, 2H). The absolute configuration of **5** was determined to be (*R*)-(+) by comparison of the rotation value. (*R*)-(–)-4-(4-methoxyphenyl)tetrahydro-2*H*-pyran-2-one (**4**): $[\alpha]_D^{20}$ –6.2 (*c* 1.0 $CHCl_3$) (*lit.*[7] (*R*)-(–)-**4**: $[\alpha]_D^{20}$ –6.98 (*c* 0.96, $CHCl_3$).

Determination of the Absolute Configuration of 2b: Dimethyl (1-(4-methoxyphenyl)-2-propenyl)malonate (**5**) (74% ee (*R*)) was converted into dimethyl (1-(4-methoxyphenyl)-2-propenyl)methylmalonate (**2b**) by methylation with MeI and NaOMe. Experimental procedures: To a solution of dimethyl (1-(4-methoxyphenyl)-2-propenyl)malonate (**5**) (20 mg, 0.07 mmol) in THF (1.0 mL) was added sodium methoxide (8 mg, 0.14 mmol) and methyl iodide (40 mg, 0.29 mmol) at 0 °C. The mixture was refluxed for 14 h. After being cooled to room temperature, the mixture was extracted with ether and the extracts were dried over anhydrous sodium sulfate. Removal of solvent followed by preparative TLC on silica gel (hexane/ether = 5/1) gave 19 mg, (86%) of dimethyl (1-(4-methoxyphenyl)-2-propenyl)methylmalonate (**2b**) (74% ee): $[\alpha]_D^{20}$ +40.7 (*c* 1.7, $CHCl_3$). The absolute configuration of **2b** was determined to be (*S*)-(+) by comparison of the rotation value. The condition for the determination of the enantiomeric purities of **2b:** chiralpak AD; hexane/2-propanol = 9/1; *S* isomer eluted faster than *R* isomer.

Preparation of [π-(1-(4-Methoxyphenyl)allyl)](acetato)palladium(II)

Dimer: Palladium chloride (788 mg, 2.8 mmol) and lithium chloride (377 mg, 8.9 mmol) were dissolved in hot water (1.5 mL) and to this solution were added ethanol (3 mL), 1-(4-methoxyphenyl)-2-propenol (500 mg, 3.0 mmol) in THF (15 mL) and aqueous hydrochloric acid (0.3 mL, 12 N). Carbon monoxide was passed through the solution at room temperature and, after 5 h, a yellow orange solution was obtained. The reaction mixture began to precipitate as yellow orange crystals. After 4 h under carbon monoxide, the solvent was removed under reduced pressure and the residue was dissolved in $CHCl_3$ which was washed with water and dried over anhydrous sodium sulfate and evaporated to give 511 mg (58%) of $[PdCl\{\pi$-(1-(4-methoxyphenyl)allyl$\}]_2$: Anal. Calcd for $C_{20}H_{22}Cl_2O_2Pd_2$: C, 41.55; H, 3.84. Found: C, 41.53; H, 4.00. To a solution of $[PdCl\{\pi$-(1-(4-methoxyphenyl)allyl$\}]_2$ (120.2 mg, 0.21 mmol) in benzene (10 mL) was added 76.5 mg (0.46 mmol) of silver acetate at room temperature, and the mixture was stirred at room temperature for 14 h. Filtration followed by evaporation of the filtrate gave 119 mg (92%) of [π-(1-(4-methoxyphenyl)allyl)](acetato)palladium(II) dimer which was used for the following experiment without further purification.

NMR Study and NMR Data of [π-(1-(4-Methoxyphenyl)allyl]-(acetato)(MeO-MOP)palladium(II) (7). In an NMR sample tube were placed [π-(1-(4-methoxyphenyl)allyl)](acetato)palladium(II) dimer (5.0 mg, 0.008 mmol) and (*R*)-MeO-MOP (7.5 mg, 0.016 mmol). The tube was filled with nitrogen, and $CDCl_3$ (0.5 mL) was added. ^{1}H, ^{13}C and ^{31}P NMR spectra were measured at –50 °C. The ratio of isomers was 9:1. Major isomer: ^{1}H NMR ($CDCl_3$, 500 MHz, –50 °C) δ 1.51 (s, 3H), 1.56 (d, J = 11.6 Hz, 1H, *anti*-H on C-3), 2.66 (d, J = 6.3 Hz, 1H, *syn*-H on C-3), 3.03 (s, 3H), 3.28 (m, 1H, H on C-2), 3.89 (s, 3H), 5.41 (dd, $J_{H\text{-}H}$ = 13.5 Hz, $J_{H\text{-}P}$ = 8.2 Hz, 1H, H on C-1), 6.87–8.10 (m, 26H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 Hz, –50 °C) δ 24.9, 47.9, 54.2, 65.6 (C-3), 77.5 ($J_{C\text{-}P}$ = 7.7 Hz, C-2), 98.8 ($J_{C\text{-}P}$ = 22.8 Hz, C-1), 108.4–158.5 (aromatic), 176.3. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 202 Hz, –50 °C) δ 23.2 (s). Minor isomer: $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 202 Hz, –50 °C) δ 24.8 (s).

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Chapter IV

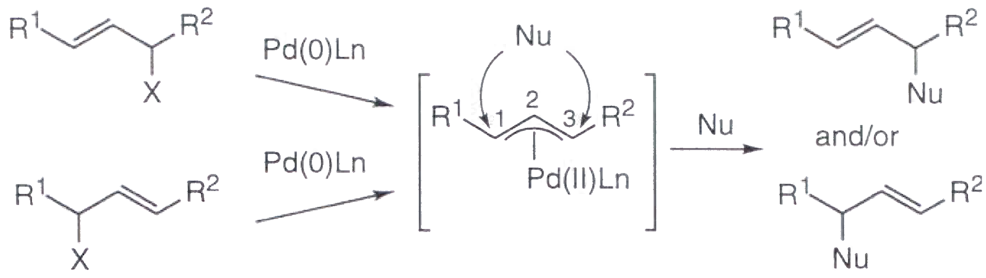
Retention of Regiochemistry of Allylic Esters in Palladium-Catalyzed Allylic Alkylation in the Presence of a MOP Ligand

Summary: In the palladium-catalyzed allylic alkylation of (*E*)-3-substituted-2-propenyl acetates (**1**), 1-substituted-2-propenyl acetates (**2**), and 1- or 3-deuterio-2-cyclohexenyl acetate (**5**), which proceeds through 1,3-unsymmetrically substituted π-allylpalladium intermediates, selective substitution at the position originally substituted with acetate was observed by use of a sterically bulky monodentate phosphine ligand, 2-diphenylphosphino-2'-methoxy-1,1'-binaphthyl (MeO-MOP). Studies of the structure of π-allylpalladium complexes generated by mixing [PdCl(π-cyclohexenyl)]$_2$ with one or two equivalents of MeO-MOP (L**) revealed that cationic bisphosphine complex $[Pd(L^{**})_2(\pi\text{-cyclohexenyl})]^+Cl^-$ is not formed even in the presence of excess ligand but neutral monophosphine complex PdCl(L**)(π-cyclohexenyl) (**11**) is formed leaving excess ligand free and that the exchange of the coordination site of Cl and L** in **11** is much slower than that in triphenylphosphine complex $PdCl(PPh_3)$(π-cyclohexenyl) (**13**). The slow exchange can rationalize the retention of regiochemistry in the allylic alkylation catalyzed by palladium/MeO-MOP complex.

Introduction

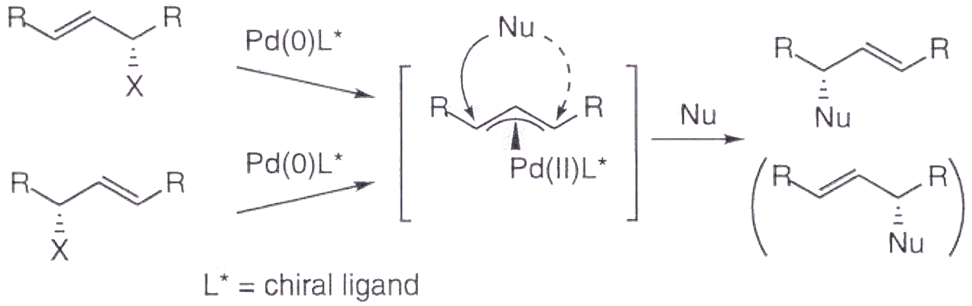
Palladium-catalyzed allylic substitution reactions including catalytic asymmetric reactions have attracted considerable attention owing to their synthetic utility andmechanistic interest.[1] The allylic substitutions proceed by way of a π-allylpalladium(II) intermediate which is formed by oxidative addition of an allylic ester to a palladium(0) species. It has been generally accepted that, in the allylic substitution which proceeds through 1,3-unsymmetrically substituted π-allylpalladium(II) intermediate, the regiochemistry of starting allylic ester is lost at the formation of the π-allylpalladium(II) intermediate and the regiochemistry in the substitution product is determined at the attack of nucleophile on the π-allylpalladium (Scheme 1). Similarly, inthe asymmetric allylic substitution which proceeds through a meso type π-allyl-palladium(II) intermediate, the enantioselectivity is usually determined at the nucleophilic

Scheme 1

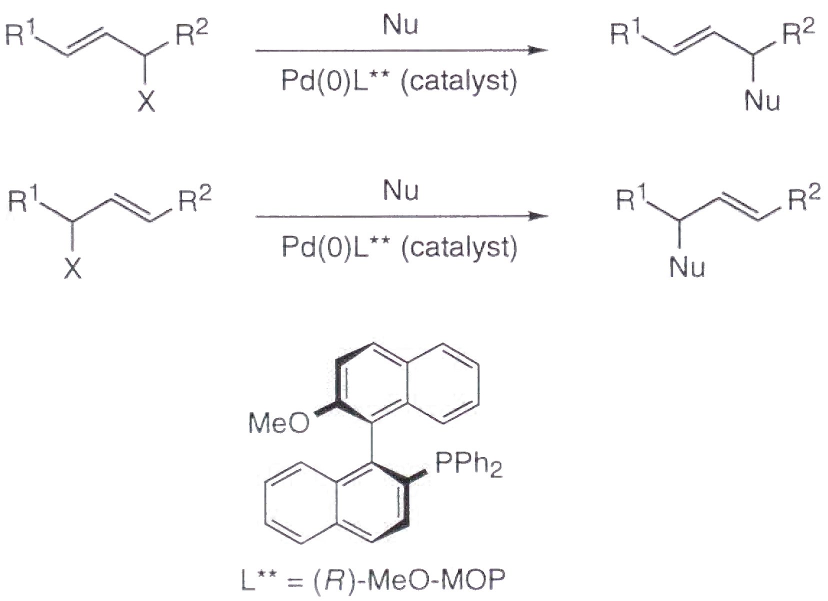


attack on either of diastereotopic π-ally carbons on he π-allylpalladium(II) intermediate which is not concerned with the absolute configuration of starting allylic ester any more (Scheme 2). Recently, Trost found[2] an interesting phenomenon that the absolute configuration of a starting allyl ester has an effect on the structure of π-allylpalladium

Scheme 2



Scheme 3



intermediate in his asymmetric alkylation, though the effect is modest. We report here a new type of palladium-catalyzed allylic alkylation where the regiochemistry of the starting allyl esters is retained in the alkylation products (Scheme 3). The retention of the regiochemistry is observed with a sterically bulky monodentate phosphine ligand, 2-diphenylphosphino-2'-methoxy-1,1'-binaphthyl (MeO-MOP).[3]

Results

Palladium-Catalyzed Allylic Alkylation. In the presence of 2 mol % of palladium catalyst generated in situ by mixing $[PdCl(\pi\text{-}C_3H_5)]_2$ with 2-diphenylphosphino-2'-methoxy-1,1'-binaphthyl (MeO-MOP)[3], γ-substituted allyl acetates **1** and α-substituted allyl acetates **2** were allowed to react with sodium salt of dimethyl methylmalonate in THF at 20 °C for 20 h (Scheme 4). The results are summarized in Table 1, which also contains the data obtained with some other phosphine ligands for comparison. An interesting new regiochemistry, which has not been observed before in allylic substitution reactions by way of 1,3-unsymmetrically substituted π-allylpalladium intermediates, was found in the allylic alkylation catalyzed by a palladium complex coordinated with MeO-MOP. Thus, the alkylation of (*E*)-3-phenyl-2-propenyl acetate (**1a**) in the presence of palladium/MeO-MOP catalyst (P/Pd = 2/1) gave linear product, dimethyl ((*E*)-3-phenyl-2-propenyl)methylmalonate (**3a**), as a major product. The ratio of **3a** to branch isomer, dimethyl (1-phenyl-2-propenyl)-methylmalonate (**4a**), was 79 to 21 (entry 1). On the other hand, the alkylation of

Scheme 4

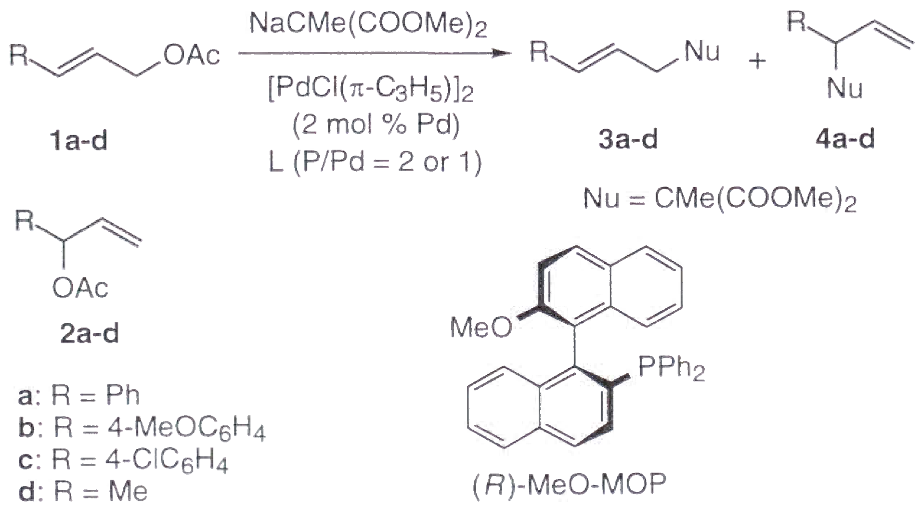


Table 1. Allylic Alkylation of Acetates **1** and **2** with $NaCMe(COOMe)_2$ Catalyzed by Palladium-Phosphine Complexes[a]

entry	substrate	ligand (ratio P/Pd)	yield[b] (%) of **3** and **4**	ratio[c] **3**/**4**
1	**1a** (R = Ph)	(*R*)-MeO-MOP (2/1)	99	79/21
2	**2a** (R = Ph)	(*R*)-MeO-MOP (2/1)	96	23/77
3	**2a** (R = Ph)	(*R*)-MeO-MOP (1/1)	95	23/77
4	**1a** (R = Ph)	dppe (2/1)	99	89/11
5	**2a** (R = Ph)	dppe (2/1)	94	89/11
6	**1a** (R = Ph)	PPh_3 (2/1)	99	91/9
7	**2a** (R = Ph)	PPh_3 (2/1)	99	92/8
8	**2a** (R = Ph)	PPh_3 (1/1)	66	91/9
9	**1b** (R = 4-$MeOC_6H_4$)	(*R*)-MeO-MOP (2/1)	99	71/29
10	**2b** (R = 4-$MeOC_6H_4$)	(*R*)-MeO-MOP (2/1)	93	16/84
11	**1b** (R = 4-$MeOC_6H_4$)	PPh_3 (2/1)	99	75/25
12	**2b** (R = 4-$MeOC_6H_4$)	PPh_3 (2/1)	99	76/24
13	**1c** (R = 4-ClC_6H_4)	(*R*)-MeO-MOP (2/1)	89	81/11
14	**2c** (R = 4-ClC_6H_4)	(*R*)-MeO-MOP (2/1)	99	35/65
15	**1c** (R = 4-ClC_6H_4)	PPh_3 (2/1)	88	93/7
16	**2c** (R = 4-ClC_6H_4)	PPh_3 (2/1)	93	94/6
17	**1d** (R = Me)	(*R*)-MeO-MOP (2/1)	92	95/5
18	**2d** (R = Me)	(*R*)-MeO-MOP (2/1)	94	38/62
19	**1d** (R = Me)	dppe (2/1)	92	78/22
20	**2d** (R = Me)	dppe (2/1)	94	76/24
21	**1d** (R = Me)	PPh_3 (2/1)	91	81/19
22	**2d** (R = Me)	PPh_3 (2/1)	93	82/18

[a] All reactions were carried out in THF at 20 °C for 12 h under nitrogen: THF (1.0 mL), allylic acetate (0.20 mmol), $NaCMe(COOMe)_2$ (0.40 mmol), $[PdCl(\pi\text{-}C_3H_5)]_2$ (0.002 mmol), and phosphine ligand. [b] Isolated yield by silica gel column chromatography. [c] The ratio was determined by ^1H NMR analysis of the products.

1-phenyl-2-propenyl acetate (**2a**), which is a regioisomeric allyl ester of **1a**, catalyzed by the palladium/MeO-MOP complex under the same reaction conditions, gave branch isomer **4a** preferentially, the ratio of **3a** to **4a** being 23 to 77 (entry 2). The same catalytic activity and regioselectivity were observed in the reaction of **2a** catalyzed by a palladium catalyst consisting of MeO-MOP and palladium in a ratio of 1 to 1 (entry 3). The results obtained above for the reaction of **1a** and **2a** clearly show that the alkylation took place preferentially at the position originally substituted with the leaving acetate. The regiochemistry of starting allyl ester is retained in the product in the palladium-catalyzed alkylation in the presence of MeO-MOP ligand. The retention of regiochemistry observed here is quite unusual in the palladium-catalyzed allylic substitution reactions. The allylic substitution of γ-substituted allyl acetates **1** and α-substituted allyl acetates **2** usually gives products consisting of the regioisomers in the same ratio, because the π-allylpalladium intermediate formed by the oxidative addition of **1** and **2** is considered to be the same. Actually, the alkylation of **1a** and **2a** in the presence of palladium catalyst coordinated with 1,2-bis(diphenylphosphino)ethane (dppe) or triphenylphosphine (P/Pd = 2/1) gave the alkylation products in the same ratio irrespective of the regiochemistry of the starting allylic esters (entries 4-7). It is noteworthy that the reaction catalyzed by palladium/PPh_3 requires two equiv (to Pd) of phosphine ligand. With one equiv of phosphine ligand, a deposit of palladium black was observed and the reaction stops at 66% conversion (entry 8), though the regioselectivity is the same. Similar regiochemical results were obtained in the allylic alkylation of allyl acetates substituted at α or γ position with aryl groups, 4-methoxyphenyl (**1b** and **2b**) and 4-chlorophenyl (**1c** and **2c**) (entries 9-16). The palladium/MeO-MOP catalyst gave the alkylation products in a different ratio of regioisomers while palladium/PPh_3 catalyst gave the products of the same ratio starting from a pair of regioisomeric allyl acetates, irrespective of the electron-donating or -withdrawing characters of the aryl substituents. The retention of regiochemistry was also observed in the alkylation of methyl-substituted allyl esters **1d** and **2d** in the presence of palladium/MeO-MOP catalyst, linear ester **1d** giving linear product **3d** with high selectivity while branch ester **2d** giving branch product **4d** as a major product (entries 17 and 18). Here again, the regiochemistry was lost in the reaction catalyzed by palladium complexes of dppe and triphenylphosphine (entries 19-22).

The substitution at the carbon originally substituted with acetate was also observed in the reaction of specifically deuterated cyclohexenyl acetates **5** (Scheme 5). Thus, the alkylation of 3-deuterated acetate **5**-3-d_1 and 1-deuterated acetate **5**-1-d_1 with sodium salt of dimethyl methylmalonate in the presence of palladium/MeO-MOP catalyst took place with high selectivity (83% at 20 °C) at the position originally substituted with acetate giving **6a** and **7a**, respectively (entries 1 and 2 in Table 2). Deuterium isotope effects were not observed in the present alkylation. The reaction carried out at 0 °C in the presence of 0.5 equiv of lithium chloride increased the regioselectivity up to 88% (entries 3 and 4). Use of dppe or triphenylphosphine ligand in place of MeO-MOP gave a one to one mixture of **6a** and **7a**, starting with either **5**-3-d_1 or **5**-1-d_1 (entries 5-8), indicating

Scheme 5

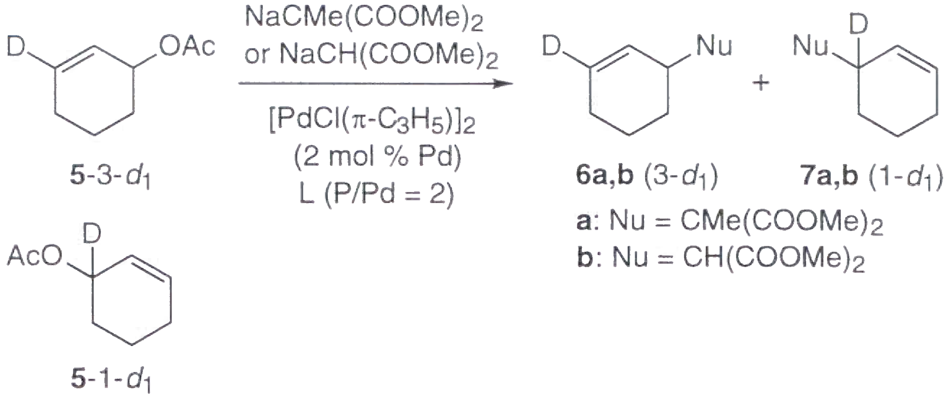


Table 2. Allylic Alkylation of 2-Cyclohexenyl Acetates **5** with Nucleophiles, $NaCMeE_2$ and $NaCHE_2$ (E = COOMe), Catalyzed by Palladium-Phosphine Complexes[a]

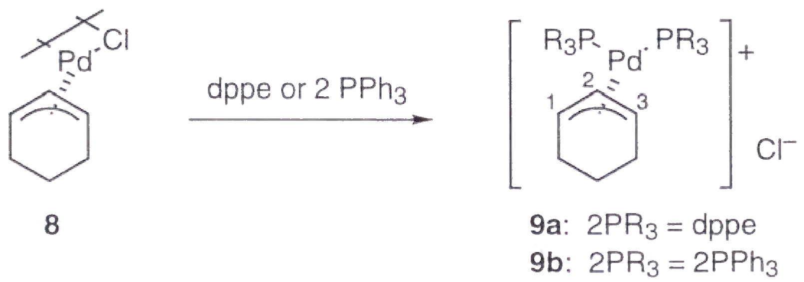
entry	acetate	ligand (Nu)	yield[b] (%) (ratio P/Pd)	**6** and **7**	ratio[c] **6**/**7**
1	**5**-3-d_1	$CMeE_2$	(*R*)-MeO-MOP (2/1)	95	83/17
2	**5**-1-d_1	$CMeE_2$	(*R*)-MeO-MOP (2/1)	85	17/83
3[d]	**5**-3-d_1	$CMeE_2$	(*R*)-MeO-MOP (2/1)	90	88/12
4[d]	**5**-1-d_1	$CMeE_2$	(*R*)-MeO-MOP (2/1)	93	12/88
5	**5**-3-d_1	$CMeE_2$	dppe (2/1)	80	49/51
6	**5**-1-d_1	$CMeE_2$	dppe (2/1)	94	53/47
7	**5**-3-d_1	$CMeE_2$	PPh_3 (2/1)	91	51/49
8	**5**-1-d_1	$CMeE_2$	PPh_3 (2/1)	91	50/50
9	**5**-1-d_1	CHE_2	(*R*)-MeO-MOP (2/1)	87	18/82
10	**5**-1-d_1	CHE_2	PPh_3 (2/1)	89	45/55

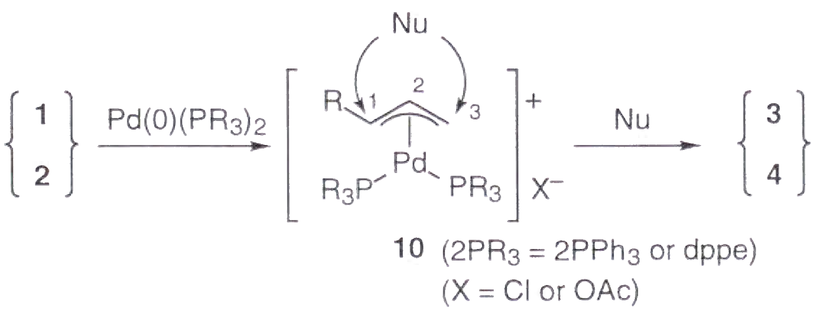
[a] All reactions were carried out in THF at 20 °C for 12 h under nitrogen unless otherwise noted: THF (1.0 mL), allylic acetate (0.20 mmol), $NaCMe(COOMe)_2$ or $NaCH(COOMe)_2$ (0.40 mmol), $[PdCl(\pi\text{-}C_3H_5)]_2$ (0.002 mmol), and phosphine ligand. [b] Isolated yield by silica gel column chromatography. [c] The ratio was determined by ^1H NMR analysis of the products. [d] Carried out at 0 °C in the presence of 0.5 equiv of LiCl.

that the regiochemical integrity of cyclohexenyl acetates **5**-3-d_1 and **5**-1-d_1 is lost before the nucleophilic attack in the case of dppe or PPh_3 as a ligand. In the allylic alkylation with dimethyl malonate catalyzed by palladium/MeO-MOP, the alkylation also took place at the carbon substituted with acetate (entry 9).

Structure and Isomerization of π-Allylpalladium-Phosphine Complexes. It has been reported that π-allylpalladium(II) complexes adopt cationic square planar structure on coordination with a chelating bisphosphine ligand or two molecules of monophosphine ligand.[4] We have examined the coordination number of phosphine ligand for (π-cyclohexenyl)palladium system (Scheme 6). Addition of one equiv of dppe (P/Pd = 2/1) to $[PdCl(\pi\text{-cyclohexenyl})]_2$ (**8**) in THF or $CDCl_3$ gave cationic bisphosphine complex $[Pd(\pi\text{-cyclohexenyl})(dppe)]^+Cl^-$ (**9a**) in a quantitative yield. Similarly, a cationic bisphosphine complex $[Pd(\pi\text{-cyclohexenyl})(PPh_3)_2]^+Cl^-$ (**9b**) was formed selectively on addition of two equiv of PPh_3 (P/Pd = 2/1) to **8**. The formation of the cationic bisphosphine complexes was readily assigned by ^1H and ^{31}P NMR spectroscopic studies.[5] ^1H NMR for π-cyclohexenyl moiety showed a symmetric structure in both **9a** and **9b** (see Experimental Section). The palladium-catalyzed allylic substitution in the presence of dppe or two equivalents of triphenylphosphine should contain cationic π-allylpalladium complex **10** which is a common intermediate formed by the oxidative addition of either allylic ester **1** or **2**. It is likely that the π-allylpalladium intermediate **10** does not have original regiochemical characters of allylic esters any more. Hence, it is reasonable that allyl esters **1** and **2** gave the alkylation products **3** and **4** with the same regioselectivity (see Scheme 1).

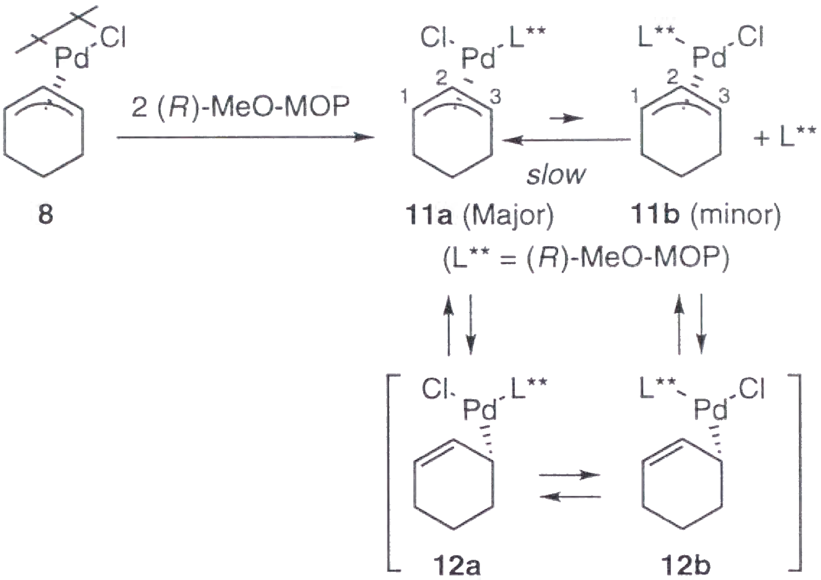
Scheme 6





On the other hand, the reaction of **8** with 2 equiv (to Pd) of (*R*)-MeO-MOP gave neutral monophosphine complex $[PdCl(\pi\text{-cyclohexenyl})(MeO\text{-}MOP)]$ (**11**) leaving one molecule of MeO-MOP ligand free from palladium (Scheme 7). The same neutral

Scheme 7



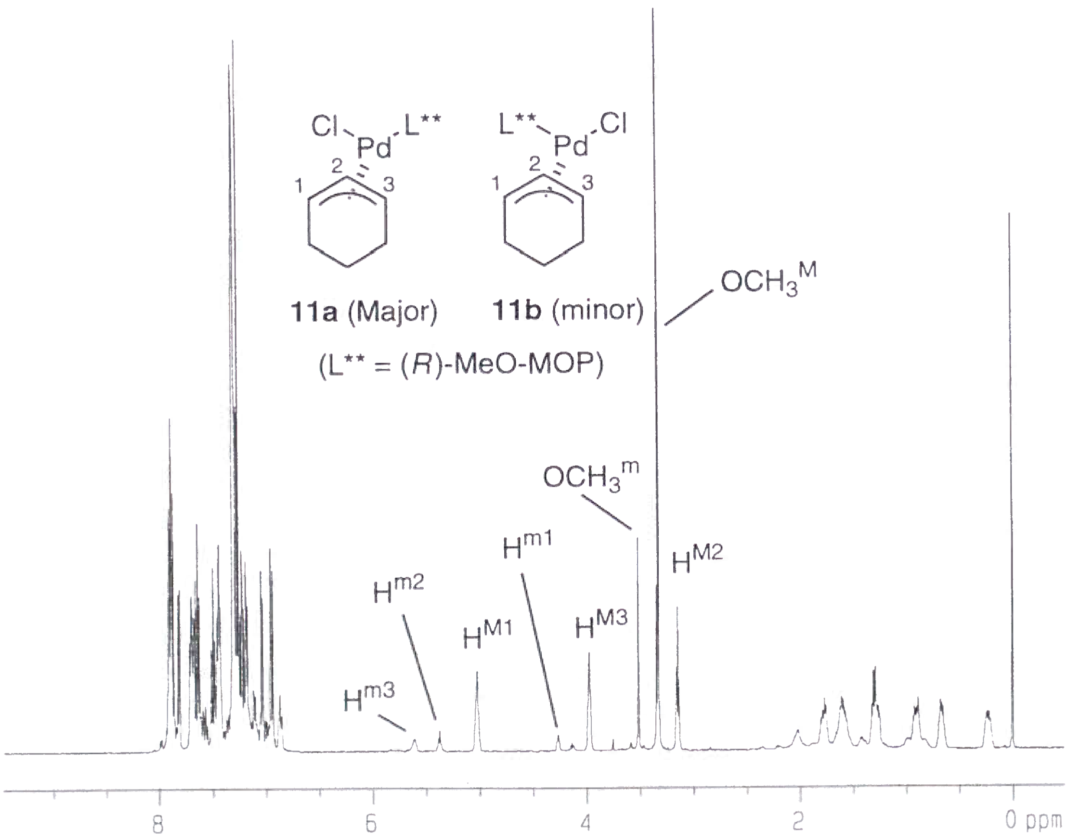


Figure 1. [1]H NMR spectrum of PdCl(π-cyclohexenyl)((*R*)-MeO-MOP) (**11**) in $CDCl_3$ at 20 °C. Complex **11** consists of major and minor isomers in a ratio of 6 to 1. H^M: major isomer **11a**. H^m: minor isomer **11b**.

monophosphine complex **11** was formed by mixing **8** with 1 equiv (to Pd) of MeO-MOP. With MeO-MOP ligand, the π-allylpalladium cannot accommodate two molecules of phosphine ligand because of the steric bulkiness of MeO-MOP ligand.[6] The complex **11** consists of a pair of diastereoisomers **11a** and **11b** in a ratio of 6 to 1 at 20 °C in $CDCl_3$ (Figure 1). π-Allyl protons were fully asigned by $^{31}P,^{1}H$-correlation spectrum (Figure 2). The protons which have correlation peaks with ^{31}P signals are asigned as those on the π-allyl carbons *trans* to phosphorus (H^1 proton of major isomer and H^3 proton in minor isomer). The major isomer is tentatively asigned to be **11a**, which has axial chirality *R* around π-allyl–palladium bond axis,[7] on the basis of our structural studies of related PdCl(π-allyl)((*R*)-MeO-MOP) complexes.[8] The unusual high field shift (δ 3.15 ppm) of H^2 proton of the major isomer supports the structure **11a**.[8] In ^{1}H 2-D NOESY spectrum of **11** (Figure 3) obtained by mixing **8** with 1 equiv (to Pd) of MeO-MOP in $CDCl_3$ at 20 °C, cross-peaks arising from exchange were observed between isomers **11a** and **11b** for allylic protons, H^1, H^2, H^3, and methoxy groups on MeO-MOP ligand. The allylic proton *trans* to phosphorus in the major isomer (H^1 in **11a**: δ 5.02) found a cross-peak for the allylic proton *cis* to phosphorus in the minor isomer (H^1 in **11b**: δ 4.26), and that *cis* to phosphorus in the major isomer (H^3 in **11a**: δ 3.98) found a cross-peak for that *trans* to phosphorus in the minor isomer (H^3 in **11b**: δ 5.61). Thus, the isomerization between **11a** and **11b** is formally recognized to be *trans-cis* isomerization, exchange of coordination site of the phosphine ligand and chloride.

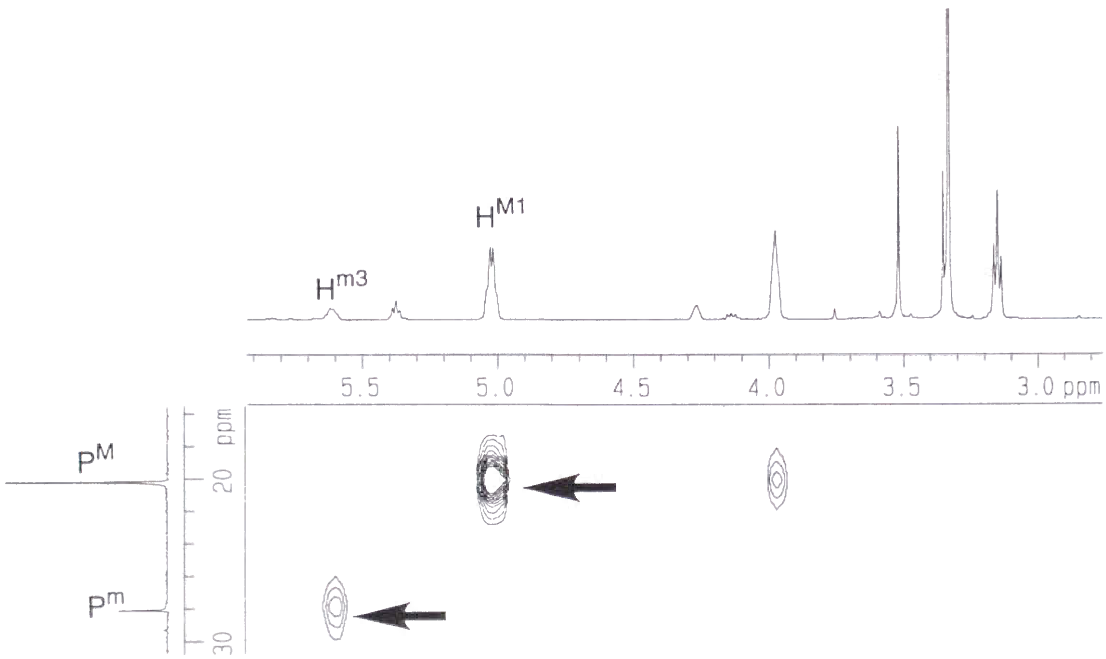


Figure 2. $^{31}P,^{1}H$–Correlation spectrum of **11** showing the π-allyl region. Strong correlation peaks due to $^{31}P–^{1}H$ couplings are observed for H^1 in the major isomer **11a** and H^3 in the minor isomer **11b**.

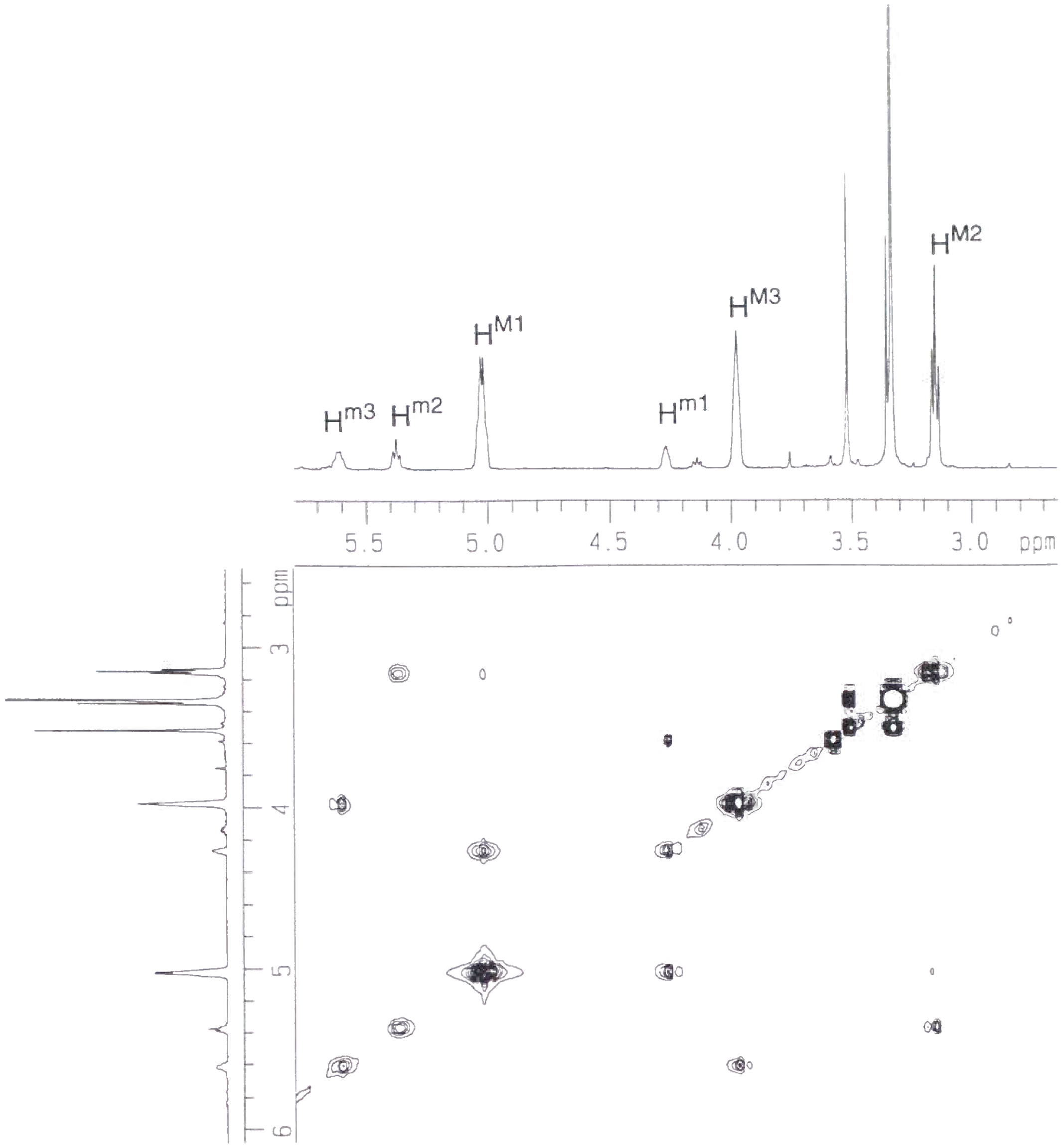


Figure 3. 2-D NOESY spectrum of **11** showing the π-allyl region. Strong correlation peaks are observed between H^{M1} and H^{m1}, between H^{M2} and H^{m2}, and between H^{M3} and H^{m3}.

The rate of isomerization between **11a** and **11b** was measured by a magnetization saturation transfer technique in ^{1}H NMR[9] (Table 3). The rate constant, $k_{(\mathbf{11a}\rightarrow\mathbf{11b})}$, obtained by saturation of H^1 proton in **11b** at 20 °C in $CDCl_3$ was 0.5 s^{-1} and the rate constant, $k_{(\mathbf{11b}\rightarrow\mathbf{11a})}$, obtained by saturation of H^1 proton in **11a** was 3.2 s^{-1} (entry 1). The isomerization rate in THF-d_8 was a little slower than that in $CDCl_3$, $k_{(\mathbf{11b}\rightarrow\mathbf{11a})}$ being 2.8 s^{-1} (entry 2). At –15 °C, the rate constant $k_{(\mathbf{11a}\rightarrow\mathbf{11b})}$ was decreased to 0.08 s^{-1} (entry 3). The isomerization rate was not affected by addition of an excess of MOP ligand (entry 4), indicating that the isomerization is taking place intramolecularly, probably by way of σ-allylpalladium intermediates **12** which can undergo the *trans-cis* isomerization by bond rotation around palladium carbon bond axis.

Table 3. Rate Constants ($k_{(\mathbf{11a}\rightarrow\mathbf{11b})}$ and $k_{(\mathbf{11b}\rightarrow\mathbf{11a})}$) for Isomerization of π-Allylpalladium Complexes [PdCl(π-cyclohexenyl)((*R*)-MeO-MOP)] (**11a** and **11b**)

entry	ratio P/Pd	temp (°C)	solvent	$k_{(\mathbf{11a}\rightarrow\mathbf{11b})}$[a] ($s^{-1}$)	$k_{(\mathbf{11b}\rightarrow\mathbf{11a})}$[b] ($s^{-1}$)	ratio[c] **11a/11b**
1	1/1	20	$CDCl_3$	0.5	3.2	6/1
2	1/1	20	THF-d_8	0.3	2.8	9/1
3	1/1	–15	$CDCl_3$	0.08	–	8/1
4	2/1	20	$CDCl_3$	0.6	2.9	6/1

[a] Measured by saturation of H^1 proton in **11b**. [b] Measured by saturation of H^1 proton in **11a**. [c] The ratio was determined by integration in ^1H and ^{31}P NMR spectra.

Addition of 0.9 equiv (to Pd) of triphenylphosphine to $[PdCl(\pi\text{-cyclohexenyl})]_2$ (**8**) gave monophosphine complex, $[PdCl(\pi\text{-cyclohexenyl})(PPh_3)]$ (**13**) and a small amount (0.1 equiv) of starting **8**. The isomerization of **13** is asslow as that of MeO-MOP analog **11** in the absence of an excess of PPh_3 (Scheme 8). The rate constants for the isomerization, which were measured by the saturation transfer technique using exchange between H^1 (δ 5.81 in **13a**) and H^3 (δ 4.14 in **13a**) protons, were 1.4 s^{-1} and 0.08 s^{-1} at 20 °C and –15 °C, respectively (entries 1 and 2 in Table 4). The isomerization was found to be greatly accelerated by addition of an excess of triphenylphosphine. In the presence of 0.1 equiv excess of triphenylphosphine, the rate of isomerization was 3.4 s^{-1} at –15 °C, faster by forty times than that in the absence of excess triphenylphosphine

Scheme 8

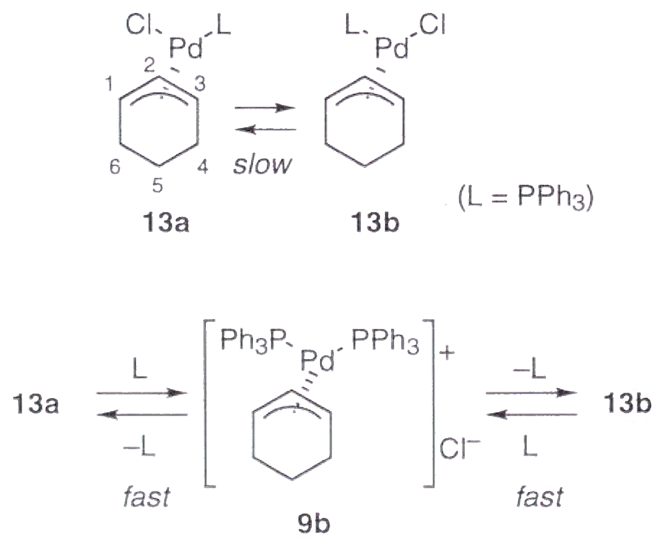


Table 4. Rate Constants for *trans-cis* Isomerization of π-Allylpalladium Complex [PdCl(π-cyclohexenyl)(PPh_3)] (**13**)

entry	ratio P/Pd	temp (°C)	solvent	$k_1{}^a$ (s^{-1})	$k_2{}^b$ (s^{-1})
1	0.9/1	20	$CDCl_3$	1.4	1.2
2	0.9/1	–15	$CDCl_3$	0.08	0.09
3	1.1/1	–15	$CDCl_3$	3.4	4.2

[a] Measured by saturation of H^1 proton in **13a**. [b] Measured by saturation of H^3 proton in **13a**.

(entry 3). At 20 °C, the isomerization is so fast on the NMR time scale that nonequivalent allylic protons H^1 and H^3 in **13** appear as very broad signals (Figure 4). The signal broadening was also observed for the protons on C^4 and C^6 carbons of complex **13**. At lower temperature, the isomerization is slower and ^1H NMR spectrum in the presence of 10% excess triphenylphosphine ligand showed formation of monophsphine complex **13** and 0.1 equiv of cationic bisphosphine complex **9b**. The great acceleration of the isomerization by the addition of triphenylphosphine demonstrates that the fast isomerization of PPh_3 complex **13** takes place by an associative mechanism via cationic bisphosphine complex **9b** or a five coordinated species. Thus, the difference between MeO-MOP complex **11** and triphenylphosphine complex **13** is that the *trans-cis* isomerization of **11** is much slower than that of **13** in the presence of an excess of the phosphine ligand.

Discussion

The retention of the regiochemistry in the catalytic alkylation of cyclohexenyl acetates **5** in the presence of MeO-MOP ligand (Scheme 5) must be related to the slow isomerization of the π-allylpalladium intermediates **14** coordinated with MeO-MOP ligand (Scheme 9). It is reasonable that the nucleophilic attack takes place selectively on either of π-allyl carbons C^1 and C^3, most probably on the carbon *trans* to the phosphine ligand because of its stronger *trans* influence than acetate or chloride.[10] Provided that the oxidative addition of **5**-3-d_1 and **5**-1-d_1 to a palladium(0) species coordinated with MeO-MOP takes place selectively in forming *cis*-**14** and *trans*-**14**, respectively, the slow isomerization between *cis*-**14** and *trans*-**14** can rationalize the retention of the regiochemistry observed in the catalytic alkylation. Attempts to isolate and characterize π-allylpalladium intermediates **14** formed by oxidative addition of **5**-3-d_1 or **5**-1-d_1 to a

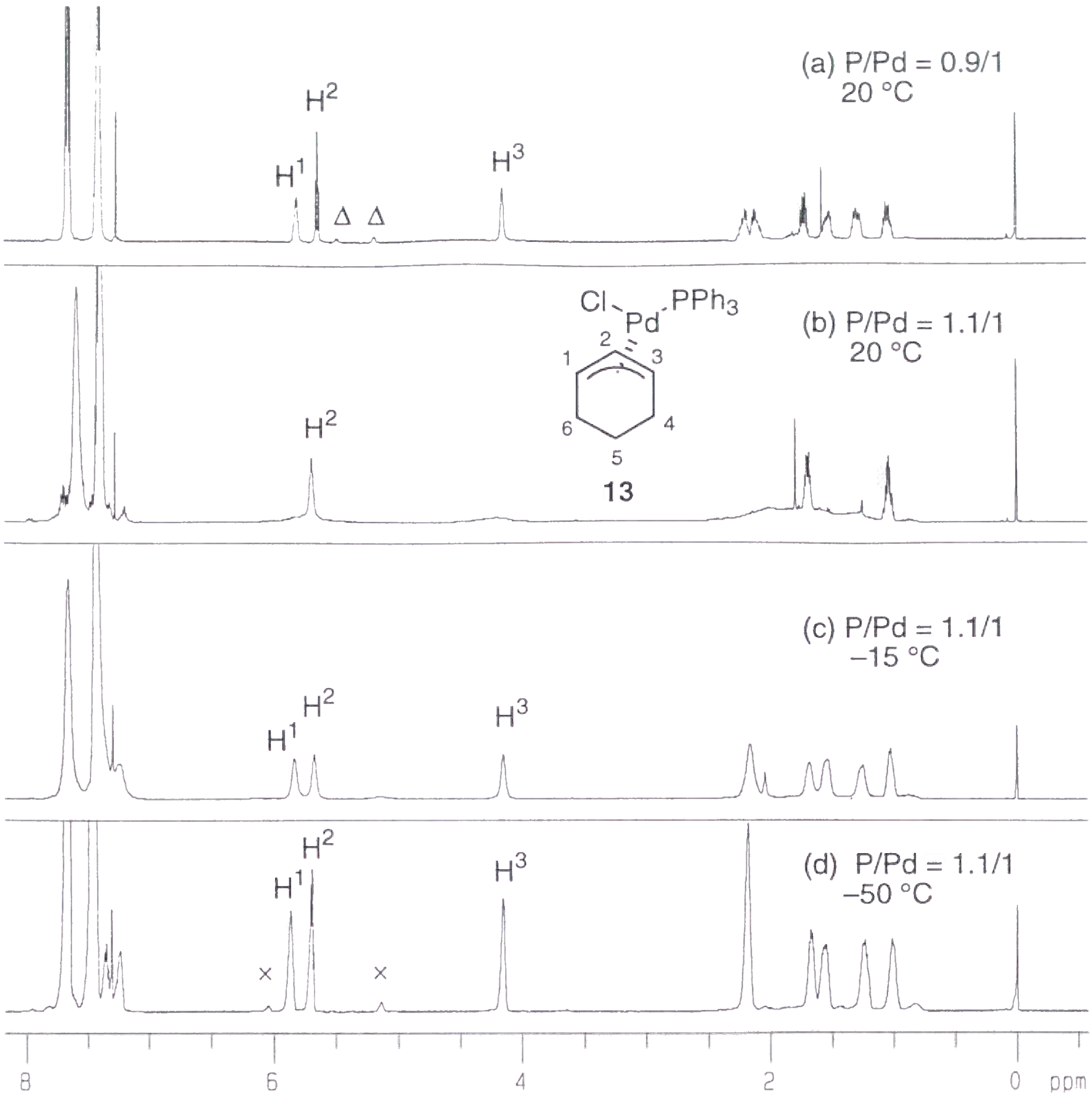
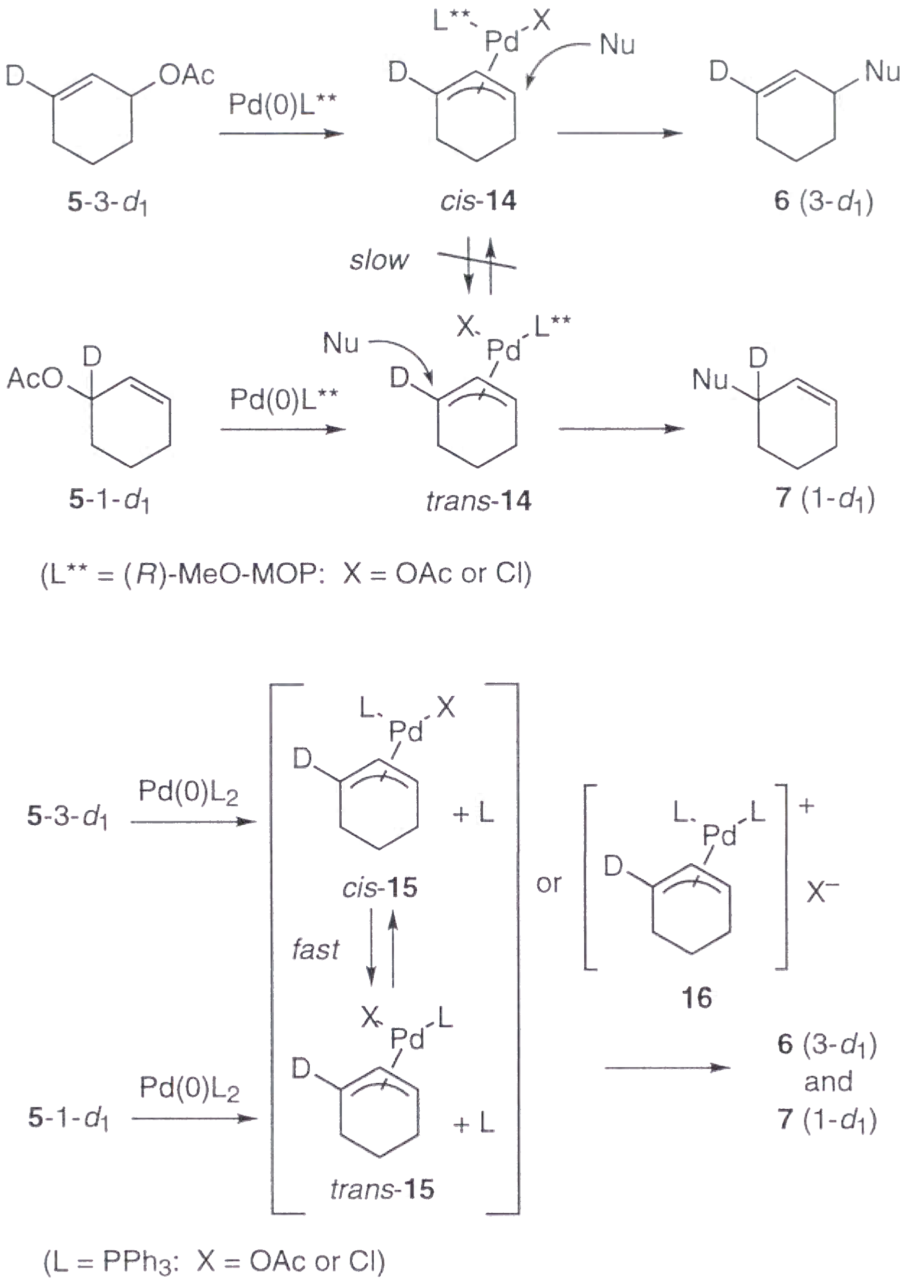


Figure 4. ^{1}H NMR spectra for PdCl(π-cyclohexenyl)(PPh_3) (**13**) generated by mixing [PdCl(π-cyclohexyenyl)]$_2$ (**8**) with triphenylphosphine in $CDCl_3$: The ratios of PPh_3 to Pd are 0.9/1 in (a) and 1.1/1 in (b), (c), and (d). Peaks indicated by Δ are for π-allyl protons of **8** and those indicated by × are for π-allyl protons of cationic bisphosphine complex [Pd(π-cyclohexenyl)(PPh_3)$_2$]$^+$Cl$^-$ (**9b**).

Pd(0)/MeO-MOP species before *trans-cis* isomerization are not successful because the isomerization is not so slow that they are characterized before the isomerization. It is noteworthy that the palladium(0) complex coordinated with one molecule of MeO-MOP, which was generated by addition of sodium dimethyl malonate to a mixture of [PdCl(π-cyclohexenyl)]$_2$ (**8**) and MeO-MOP (P/Pd = 1/1) in THF, is stable in solution for days at room temperature. The coordination of naphthyl group was found in the palladium(0) complex coordinated with MeO-MOP which was demonstrated by low field shifts of the

Scheme 9



protons of 7' and 8' positions of MeO-MOP ligand in ^{1}H NMR.[11] It is well-known that palladium(0) complexes usually require at least two molecules of the phosphine ligand even with sterically demanding tertiary phosphines such as tri(cyclohexyl)phosphine.[12] The catalytic allylic alkylation in the presence of triphenylphosphine ligand should contain palladium(0) species coordinated with two molecules of the phosphine ligand even if the initial ratio at the generation of the catalyst was P/Pd = 1/1. A deposit of palladium black which was observed in the catalytic reaction (entry 8 in Table 1) increases the ratio of P/Pd to more than 1. Thus, the catalytic cycle of the allylic alkylation catalyzed by palladium/triphenylphosphine system involves a cationic bisphosphine intermediate $[Pd(\pi\text{-allyl})(PPh_3)_2]^+$ (**16**) or combination of a neutral monophosphine intermediate $[PdX(\pi\text{-allyl})(PPh_3)]$ (**15**) and an excess of the phosphine. The bisphosphine complex **16** does not have the regiochemical characters of the starting allylic esters and the monophosphine complex **15** undergoes the fast isomerization in the presence of an excess of the phosphine which will lose the original regiochemistry. On the other hand, palladium/MeO-MOP system involves only monophosphine intermediate [PdX(π-allyl)(MeO-MOP)] (**14**) which does not undergo the fast isomerization even in the presence of excess ligand.[13]

Experimental Section

General. All manipulations were carried out under a nitrogen atmosphere. Nitrogen gas was dried by passage through P_2O_5 (Merck, SICAPENT). NMR spectra were recorded on a JEOL JNM-EX270 spectrometer (270 MHz for ^1H and 109 MHz for ^{31}P), JEOL JNM-AL400 spectrometer (400 MHz for ^1H NMR), or JEOL JNM LA500 spectrometer (500 MHz for ^1H, 125 MHz for ^{13}C and 202 MHz for ^{31}P). Chemical shifts are reported in δ ppm referenced to an internal $SiMe_4$ standard for ^1H NMR, and to an external 85% H_3PO_4 standard for ^{31}P NMR. Residual chloroform (δ 77.0 for ^{13}C) was used as internal reference for ^{13}C NMR. ^1H, ^{13}C, and ^{31}P NMR spectra were recorded in $CDCl_3$ at 25 °C unless otherwise noted. Preparative medium pressure liquid chromatography (MPLC) was performed with a silica gel prepacked column Si-10 (Kusano).

Materials. THF was dried over sodium benzophenone ketyl and distilled prior to use. $[PdCl(\pi\text{-}C_3H_5)]_2$,[14] [PdCl(π-cyclohexenyl)]$_2$,[15] (*R*)-MeO-MOP[3] 1-aryl-2-propenyl acetates,[16,17] (*E*)-3-aryl-2-propenyl acetates[14,18] and 3-dueterio-2-cyclohexen-1-ol[19] were prepared according to the reported procedures.

Preparation of Allylic Acetates (5-1-d_1) and (5-3-d_1). 1-Deuterio-2-cyclohexenyl Acetate (5-1-d_1). To a solution of $LiAlD_4$ (1.12 g, 26.7 mmol) in ether (60 mL) was slowly added a solution of 2-cyclohexen-1-one (5.03 g, 52.3 mmol) in ether (20 mL) at 0 °C. The reaction mixture was stirred at room temperature for 2 h and diluted with ether. Addition of $NaSO_4 \cdot 10H_2O$ followed by filtration through a pad of Celite and evaporation of the solvent gave a quantitative yield of crude 1-dueterio-2-cyclohexene-1-ol. To a solution of this crude alcohol, pyridine (8.43 mL, 104 mmol) and a catalytic amount of 4-dimethylaminopyridine in ether (50 mL) was added acetic anhydride (12.3 mL, 130 mmol). The mixture was stirred at room temperature for 12 h, quenched with water, and extracted with ether. The organic phase was washed with 10% $CuSO_4$ solution, water and brine, dried over anhydrous magnesium sulfate and evaporated. The residue was chromatographed on silica gel (hexane/EtOAc = 5/1) to give 5.81 g (79%) of 1-deuterio-2-cyclohexenyl acetate (**5**-1-d_1): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.62–2.03 (m, 6H), 2.05 (s, 3H), 5.23–5.27 (m, 1H), 5.70 (m, 1H). MS *m/z*, 141 (M^+, 10), 99 (81), 79 (100).

3-Deuterio-2-cyclohexenyl Acetate (5-3-d_1). To a solution of 3-dueterio-2-cyclohexen-1-ol[17] (3.13 g, 31.9 mmol), pyridine (3.7 mL, 46 mmol) and a catalytic amount of 4-dimethylaminopyridine in ether (30 mL) was added acetic anhydride (5.8 ml, 61 mmol). The mixture was stirred at room temperature for 12 h, quenched with water, and extracted with ether. The organic phase was washed with 10% $CuSO_4$ solution, water and brine, dried over anhydrous magnesium sulfate and evaporated. The crude product was purified by silica gel column chromatography (hexane/EtOAc = 5/1) to give 4.46 g (99%) of 3-deuterio-2-cyclohexenyl acetate (**5**-3-d_1): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.62–2.03 (m, 6H), 2.05 (s, 3H), 5.69–5.72 (m, 1H), 5.94–5.98 (m, 1H). MS *m/z*, 141 (M^+, 5), 99 (51), 80 (100).

Palladium-Catalyzed Allylic Alkylation of 1 and 2. The reaction conditions and results are shown in Table 1. A typical procedure is given for the reaction of 1-(4-methoxyphenyl)-2-propenyl acetate (**2b**). To a solution of $[PdCl(\pi\text{-}C_3H_5)]_2$ (0.90 mg, 0.0025 mmol) and (*R*)-MeO-MOP (5.1 mg, 0.011 mmol) in THF (0.1 mL) was added a solution of sodium salt of dimethyl methylmalonate prepared from dimethyl methylmalonate (73 mg, 0.50 mmol) and sodium hydride in THF (1.0 mL). Allyl acetate **2b** (56 mg, 0.27 mmol) was added and the mixture was stirred at 20 °C for 12 h. The catalyst was removed by filtration through a short silica gel pad (ether). The filtrate was evaporated and the residue was chromatographed on silica gel (hexane/EtOAc = 6/1) to give 74 mg (99%) of a mixture of dimethyl ((*E*)-3-(4-methoxyphenyl)-2-propenyl)methylmalonate (**3b**) and dimethyl (1-(4-methoxyphenyl)-2-propenyl)methylmalonate (**4b**). The ratio of **3b** to **4b** was determined to be 16 to 84 by ^{1}H NMR. Analytically pure samples of **3b** and **4b** were obtained by MPLC (hexane/EtOAc = 6/1). **Dimethyl ((*E*)-3-(4-Methoxyphenyl)-2-propenyl)methylmalonate (3b):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.59 (s, 3H), 2.74 (dd, J = 7.8, 1.0 Hz, 2H), 3.73 (s, 6H), 3.80 (s, 3H), 5.93 (dt, J = 15.6, 7.8 Hz, 1H), 6.38 (d, J = 15.6 Hz, 1H), 6.82 (d, J = 6.4 Hz, 2H), 7.25 (d, J = 6.4 Hz, 2H). Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.80; H, 7.11. **Dimethyl (1-(4-Methoxyphenyl)-2-propenyl)-methylmalonate (4b):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.51 (s, 3H), 3.71 (s, 3H), 3.79 (s, 3H), 3.87 (s, 3H), 4.19 (d, J = 8.3 Hz, 1H), 5.09 (d, J = 16.8 Hz, 1H), 5.14 (d, J = 11.3, 1H), 6.32 (ddd, J = 8.3, 11.3, 16.8 Hz, 1H), 6.90 (d, J = 8.3 Hz, 2H), 7.25 (d, J = 8.3 Hz, 2H). Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 66.00; H, 6.85.

^{1}H NMR and analytical data for other allylic alkylation products **3** and **4** are shown below. **Dimethyl ((*E*)-3-Phenyl-2-propenyl)methylmalonate (3a):** ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.46 (s, 3H), 2.77 (dd, J = 7.8, 1.0 Hz, 2H), 3.73 (s, 6H), 6.08 (dt, J = 15.6, 7.8 Hz, 1H), 6.45 (d, J = 15.6 Hz, 1H), 7.19–7.34 (m, 5H). Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.55; H, 7.01. **Dimethyl (1-Phenyl-2-propenyl)methylmalonate (4a):** ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.43 (s, 3H), 3.62 (s, 3H), 3.72 (s, 3H), 4.10 (d, J = 8.6 Hz, 1H), 5.11 (d, J = 16.8 Hz, 1H), 5.12 (d, J = 10.0, 1H), 6.32 (ddd, J = 8.6, 10.0, 16.8 Hz, 1H), 7.18–7.34 (m, 5H). Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.70; H, 6.95. **Dimethyl ((*E*)-3-(4-Chlorophenyl)-2-propenyl)methylmalonate (3c):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.45 (s, 3H), 2.75 (d, J = 7.3 Hz, 2H), 3.73 (s, 6H), 6.07 (dt, J = 15.6, 7.3 Hz, 1H), 6.39 (d, J = 15.6 Hz, 1H), 7.25 (s, 4H). Anal. Calcd for $C_{15}H_{17}O_4Cl$: C, 60.71; H, 5.77. Found: C, 60.57; H, 5.93. **Dimethyl (1-(4-Chlorophenyl)-2-propenyl)methylmalonate (4c):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.42 (s, 3H), 3.63 (s, 3H), 3.70 (s, 3H), 4.11 (d, J = 8.8 Hz, 1H), 5.09 (d, J = 17.1 Hz, 1H), 5.15 (d, J = 10.3, 1H), 6.26 (ddd, J = 8.8, 10.3, 17.1 Hz, 1H), 7.22 (d, J = 8.7 Hz, 2H), 7.25 (d, J = 8.7 Hz, 2H). Anal. Calcd for $C_{15}H_{17}O_4Cl$: C, 60.71; H, 5.77. Found: C, 60.57; H, 5.89. **Dimethyl ((*E*)-2-Butenyl)methylmalonate (3d):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.38 (s, 3H), 1.65 (dd, J = 1.0, 6.9 Hz, 3H), 2.54 (d, J = 7.3 Hz, 2H), 3.71 (s, 6H), 5.29 (qdt, J = 1.0, 15.1, 7.3 Hz, 1H), 5.51 (dq, J = 15.1, 6.9 Hz, 1H). Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.80; H, 8.33. **Dimethyl (1-Methyl-2-propenyl)methylmalonate (4d):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.98 (d, J = 6.8 Hz, 3H), 1.29 (s, 3H), 2.93 (dq, J = 8.3, 6.8 Hz, 1H), 3.63 (s, 3H), 3.64 (s, 3H), 4.93 (d, J = 10.7 Hz, 1H), 5.00 (d, J = 18.1 Hz, 1H), 5.70 (ddd, J = 8.3, 10.7, 18.1 Hz, 1H). Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.71; H, 8.00.

Palladium-Catalyzed Allylic Alkylation of 2-Cyclohexenyl Acetates (5-1-d_1) and (5-3-d_1). The reaction conditions and results are shown in Table 2. The ratio of regioisomers **6** and **7** was determined by ^{1}H NMR studies of the mixture of **6** and **7**. **Dimethyl (3-Duterio-2-cyclohexenyl)methylmalonate (6a):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.26–1.32 (m, 1H), 1.34 (s, 3H), 1.51–1.62 (m, 2H), 1.78–1.81 (m, 1H), 1.95–1.98 (m, 2H), 3.04 (m, 1H), 3.71 (s, 3H), 3.72 (s, 3H), 5.48 (brs, 1H). **Dimethyl (1-Duterio-2-cyclohexenyl)methylmalonate (7a):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.26–1.31 (m, 1H), 1.34 (s, 3H), 1.51–1.62 (m, 2H), 1.77–1.81 (m, 1H), 1.95–1.98 (m, 2H), 3.71 (s, 3H), 3.72 (s, 3H), 5.48 (m, 1H), 5.78

(m, 1H). **Dimethyl (3-Duterio-2-cyclohexenyl)malonate (6b):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.34–1.43 (m, 1H), 1.54–1.61 (m, 1H), 1.70–1.80 (m, 2H), 1.97–2.04 (m, 2H), 2.88–2.94 (m, 1H), 3.29 (m, 1H), 3.74 (s, 6H), 5.53 (brs, 1H). **Dimethyl (1-Duterio-2-cyclohexenyl)malonate (7b):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.34–1.43 (m, 1H), 1.54–1.61 (m, 1H), 1.70–1.80 (m, 2H), 1.97–2.04 (m, 2H), 3.73 (s, 3H), 3.74 (s, 3H), 5.12 (m, 1H), 5.78 (m, 1H).

NMR Study of [Pd(π-cyclohexenyl)(dppe)]$^{+}$Cl^{-} (9a). In an NMR sample tube were placed dppe (11.3 mg, 0.028 mmol) and [PdCl(π-cyclohexenyl)]$_2$ (6.3 mg, 0.014 mmol). The tube was filled with nitrogen, and $CDCl_3$ (0.5 mL) was added. ^{1}H NMR and ^{31}P NMR spectra were measured at 25 °C. ^{1}H NMR ($CDCl_3$, 500 MHz, 25 °C) δ 1.06–1.08 (m, 1H), 1.22–1.31 (m, 3H), 2.15–2.20 (m, 2H), 2.57–2.64 (m, 2H), 3.02-3.06 (m, 2H), 5.81 (t, J = 6.8 Hz, 1H), 5.97 (brd, $J_{H\text{-}P}$ = 4.9 Hz, 2H), 7.29–7.59 (m, 20H). ^{31}P{^{1}H} NMR ($CDCl_3$, 202 MHz, 25 °C) δ 46.7.

NMR Study of [Pd(π-cyclohexenyl)(PPh$_3$)$_2$]$^{+}$Cl^{-} (9b). In an NMR sample tube were placed PPh_3 (11.8 mg, 0.045 mmol) and [PdCl(π-cyclohexenyl)]$_2$ (4.9 mg, 0.011 mmol). The tube was filled with nitrogen and $CDCl_3$ (0.5 mL) was added. ^{1}H NMR and ^{31}P NMR spectra were mesured at –30 °C. ^{1}H NMR ($CDCl_3$, 500 MHz, –30 °C) δ 0.89–1.58 (m, 6H), 5.15 (brs, 2H), 6.09 (brs, 1H), 7.24–7.54 (m, 30H). ^{31}P{^{1}H} NMR ($CDCl_3$, 202 MHz, –30 °C) δ 22.2.

Isolation of [PdCl(π-cyclohexenyl)(MeO-MOP)] (11a). A solution of (*R*)-MeO-MOP (21.2 mg, 0.045 mmol) and [PdCl(π-cyclohexenyl)]$_2$ (10.1 mg, 0.023 mmol) in benzene (0.8 mL) was placed in a small open bottle (5 mL), and the bottle was placed in a reagent bottle (25 mL) which contained ether (3 mL). After 1 day, yellow crystals 13.5 mg (43%) were formed owing to dispersion of the solvents. Anal. Calcd for $C_{39}H_{34}OClPPd$: C, 67.73; H, 5.86. Found: C, 68.01; H, 5.15.

NMR Study of [PdCl(π-cyclohexenyl)(MeO-MOP)] (11a+11b). (*R*)-MeO-MOP (21.2 mg, 0.045 mmol) and [PdCl(π-cyclohexenyl)]$_2$ (10.0 mg, 0.023 mmol) were placed in an NMR sample tube. The tube was filled with nitrogen, and $CDCl_3$ (0.5 mL) was added. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra were measured at 20 °C. The ratio of major isomer **11a** to minor isomer **11b** is 6 to 1. The rate of isomerization was measured by a saturation transfer experiment in ^{1}H NMR. The results are shown in Table 3. Major isomer (**11a**): ^{1}H NMR ($CDCl_3$, 500 MHz, 20 °C) δ 0.20–0.25 (m, 1H), 0.63–0.71 (m, 1H), 0.87–0.94 (m, 1H), 1.28–1.33 (m, 1H), 1.57–1.63 (m, 1H), 1.75–1.81 (m, 1H), 3.15 (brt, J = 6.4 Hz, 1H), 3.33 (s, 3H), 3.98 (brs, 1H), 5.02 (brd, $J_{H\text{-}P}$ = 5.4 Hz, 1H), 6.86–8.00 (m, 22H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, 25 °C) δ 54.9 (CH_3), 75.4 (C^3), 94.4 (d, J_{C-P} = 29.0 Hz, C^1), 107.6 (d, J_{C-P} = 5.2 Hz, C^2). ^{31}P{^{1}H} NMR ($CDCl_3$, 202 MHz, 25 °C) δ 20.8. Minor isomer (**11b**): ^{1}H NMR

($CDCl_3$, 500 MHz, 25 °C) 0.86-2.03 (m, 6H), 3.52 (s, 3H), 4.26 (brs, 1H), 5.37 (brt, J = 6.8 Hz, 1H), 5.61 (brd, $J_{H\text{-}P}$ = 5.8 Hz, 1H), 6.86–8.00 (m, 22H). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 202 MHz, 25 °C) δ 28.7.

NMR Study and Isolation of [PdCl(π-cyclohexenyl)(PPh_3)] (13). PPh_3 (5.3 mg, 0.020 mmol) and [PdCl(π-cyclohexenyl)]$_2$ (5.0 mg, 0.011 mmol) were placed in an NMR sample tube. The tube was filled with nitrogen, and $CDCl_3$ (0.5 mL) was added. ^1H NMR, ^{13}C NMR and ^{31}P NMR spectra were measured at 20 °C. The spectra at 20 °C are shown below. The rate of isomerization was measured by a saturation transfer experiment in ^1H NMR. The results are shown in Table 4. The tube was placed at –20 °C. After 7 days, yellow crystals 6.3 mg (58%) were formed. ^1H NMR ($CDCl_3$, 500 MHz, 20 °C) δ 1.00–1.08 (m, 1H), 1.25–1.32 (m, 1H), 1.50–1.57 (m, 1H), 1.68–1.76 (m, 1H), 2.07–2.15 (m, 1H), 2.18–2.33 (m, 1H), 4.14 (m, 1H), 5.64 (brt, J = 6.8 Hz, 1H), 5.81 (brd, $J_{H\text{-}P}$= 5.4 Hz, 1H), 7.27–7.69 (m,15H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, 25 °C) δ 77.4 (C^3), 96.2 ($J_{C\text{–}P}$ = 29.9 Hz, C^1), 108.4 ($J_{C\text{–}P}$ = 5.3 Hz, C^2). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 202 MHz, 25 °C) δ 23.9. Anal. Calcd for $C_{24}H_{24}ClPPd$: C, 59.40; H, 4.99. Found: C, 59.45; H, 5.28.

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Chapter V

Regiocontrol in Palladium-Catalyzed Allylic Alkylation by Addition of Lithium Salts

Summary: Regioselectivity in the palladium-catalyzed allylic alkylation of 1-aryl-2-propenyl acetates ($ArCH(OAc)CH=CH_2$) or (*E*)-3-phenyl-2-propenyl acetate ($PhCH=CHCH_2OAc$) with sodium enolates of soft carbon nucleophiles is controlled by addition of a catalytic amount of lithium iodide to give linear products ((*E*)-$ArCH=CHCH_2Nu$) with 100% regioselectivity. Their branch isomers ($ArCH(Nu)CH=CH_2$) are not detected at all.

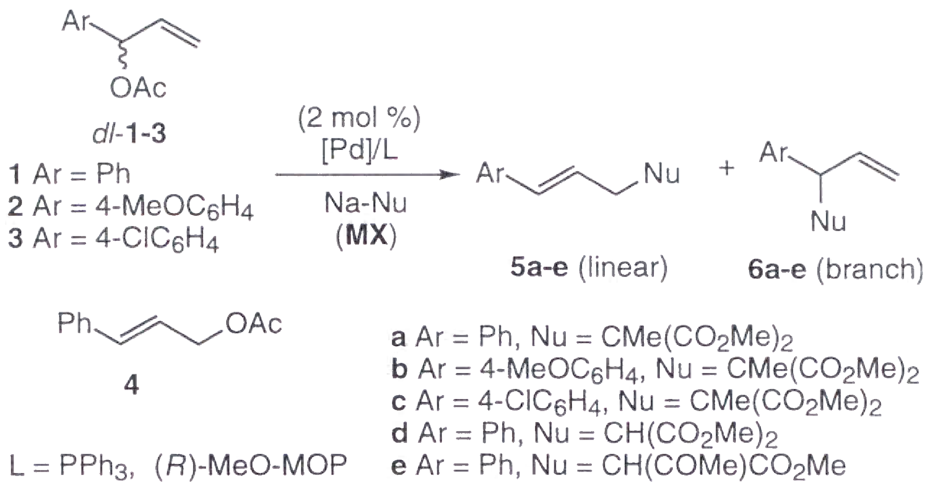
Introduction

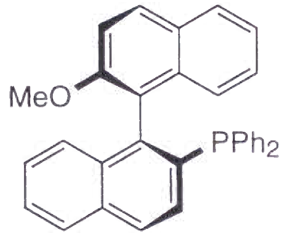
In synthetic organic chemistry, palladium-catalyzed allylic alkylation of allyl esters is a useful reaction for the formation of carbon-carbon bonds.[1] One of the challenging problems in the catalytic allylic alkylation is control of the regiochemistry in the reaction that proceeds through unsymmetrically substituted π-allylpalladium intermediates. For example, the π-allylpalladium containing one substituent at C-1 position usually produces both linear isomer and branch isomer, the ratio being dependent on the substituents, nucleophiles, and reaction conditions.[1,2,3] In Chapters III and IV, we reported that the allylic alkylation of 1-aryl-2-propenyl acetates catalyzed by palladium–PPh_3 gave linear products preferentially while the reaction catalyzed by palladium–(*R*)-MeO-MOP gave branch products, as major products, which are up to 87% ee. In this chapter, we wish to report the salt effects on the regio- and enantio-selectivity and exclusive formation of the linear isomers in the palladium-catalyzed allylic alkylation, which is realized by addition of a catalytic amount of lithium iodide.[4]

Results and discussion

In the presence of 2 mol % of palladium catalyst generated by mixing $[PdCl(\pi\text{-}C_3H_5)]_2$ with PPh_3 (2 equiv. to Pd), allyl acetates **1-4** were allowed to react with soft

Scheme 1





(*R*)-MeO-MOP

carbon nucleophiles in THF at 0 °C (Scheme 1). The regioselectivity was found to be dramatically changed by the addition of lithium iodide. Thus, the reaction of 1-phenyl-2-propenyl acetate (**1**) with sodium salt of dimethyl methylmalonate in the absence of lithium iodide gave 96% yield of alkylation product consisting of linear isomer (*E*)-**5a** and branch isomer **6a** in a ratio of 77 to 23 (entry 1 in Table 1). On the other hand, the reaction carried out in the presence of 10 mol % of lithium iodide gave a quantitative yield of linear isomer **5a** with 100% regioselectivity (entry 2). The regioselectivity was not strongly affected by the addition of lithium salt of fluoride, chloride, or bromide, branch isomer **6a** being formed with about 20% regioselectivity (entries 3-5). The high linear selectivity was also observed in the reaction in the presence of sodium iodide (entry 6), indicating that iodide anion is important for the control of the regioselectivity. The amount of lithium iodide additive can be decreased to 2 mol %, which is the same amount as that of the palladium catalyst (entry 7). Use of palladium catalyst generated from $[PdI(\pi\text{-}C_3H_5)]_2$ instead of $[PdCl(\pi\text{-}C_3H_5)]_2$ showed the same linear selectivity in the absence of additional iodide anion (entry 8).

Table 1. Effects of Lithium Salts on Allylic Alkylation of Allyl Acetates **1-4** Catalyzed by Palladium–Phosphine Complexes[a]

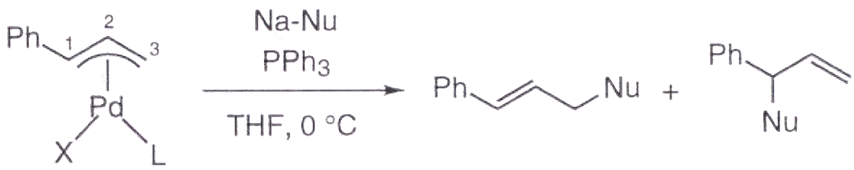
entry	allyl ester	MX (equiv)	phosphine ligand[b]	Nu	time (h)	yield (%)[c] **5 + 6**	ratio[d] **5 : 6**
1	**1**	none	PPh_3	$CMe(CO_2Me)_2$	12	96	77 : 23
2	**1**	LiI (0.1)	PPh_3	$CMe(CO_2Me)_2$	24	99	100 : 0
3	**1**	LiF (0.1)	PPh_3	$CMe(CO_2Me)_2$	24	89	78 : 22
4	**1**	LiCl (0.1)	PPh_3	$CMe(CO_2Me)_2$	24	96	82 : 18
5	**1**	LiBr (0.1)	PPh_3	$CMe(CO_2Me)_2$	24	90	80 : 20
6	**1**	NaI (0.1)	PPh_3	$CMe(CO_2Me)_2$	24	93	98 : 2
7	**1**	LiI (0.02)	PPh_3	$CMe(CO_2Me)_2$	24	97	100 : 0
8[e]	**1**	none	PPh_3	$CMe(CO_2Me)_2$	24	96	100 : 0
9	**2**	none	PPh_3	$CMe(CO_2Me)_2$	12	98	72 : 28
10	**2**	LiI (0.1)	PPh_3	$CMe(CO_2Me)_2$	24	92	100 : 0
11	**3**	none	PPh_3	$CMe(CO_2Me)_2$	12	96	86 : 14
12	**3**	LiI (0.1)	PPh_3	$CMe(CO_2Me)_2$	24	89	100 : 0
13[f]	**4**	LiI (0.1)	PPh_3	$CMe(CO_2Me)_2$	24	99	100 : 0
14	**1**	none	PPh_3	$CH(CO_2Me)_2$	12	94	83 : 17
15	**1**	LiI (0.1)	PPh_3	$CH(CO_2Me)_2$	12	91	100 : 0
16	**1**	none	PPh_3	$CH(COMe)CO_2Me$	12	95	92 : 8
17	**1**	LiI (0.1)	PPh_3	$CH(COMe)CO_2Me$	12	89	100 : 0
18[f]	**1**	none	dppe	$CMe(CO_2Me)_2$	12	92	89 : 11
19[f]	**1**	LiI (0.1)	dppe	$CMe(CO_2Me)_2$	12	61	89 : 11

[a] All reactions were carried out in THF under nitrogen: THF (1.0 mL), allylic acetate (0.20 mmol), NaNu (0.40 mmol), $[PdCl(\pi\text{-}C_3H_5)]_2$ (0.002 mmol), phosphine ligand and LiI (0.02 mmol) at 0 °C. [b] The ratio of Pd : Phosphine = 1 : 2. [c] Isolated yield by silica gel column chromatograpy. [d] The ratio was determined by ^1H NMR analysis of the products. [e] $[PdI(\pi\text{-}C_3H_5)]_2$ was used. $[PdI(\pi\text{-}C_3H_5)]_2$ was prepared by mixing $[PdCl(\pi\text{-}C_3H_5)]_2$ with LiI in THF. [f] Reactions were carried at 20 °C.

The perfect selectivity in forming linear isomer in the presence of lithium iodide was also observed in the reaction of 1-aryl-2-propenyl acetates **2** and **3** and 3-phenyl-2-propenyl acetate (**4**) with sodium salt of dimethyl methylmalonate (entries 9-13) and in the reaction with dimethyl malonate and methyl acetoacetate (entries 14-17).

It is noteworthy that the addition of lithium iodide is not effective for the reaction catalyzed by a palladium- bisphosphine complex. Thus, the reaction of **1** with dimethyl methylmalonate in the presence of a palladium catalyst prepared from $[PdCl(\pi\text{-}C_3H_5)]_2$ and 1,2-bis(diphenylphosphino)ethane (dppe) gave a mixture of **5a** and **5b** in a ratio of 89 to 11 irrespective of the addition of lithium iodide (entries 18-19). These results suggest that, in the reaction catalyzed by triphenylphosphine-palladium, the iodide coordinates to π-allylpalladium intermediate to form $PdI(\pi\text{-allyl})(PPh_3)$ and the iodide on palladium controls the regioselectivity of the nucleophilic attack.

Scheme 2



5a **6a**

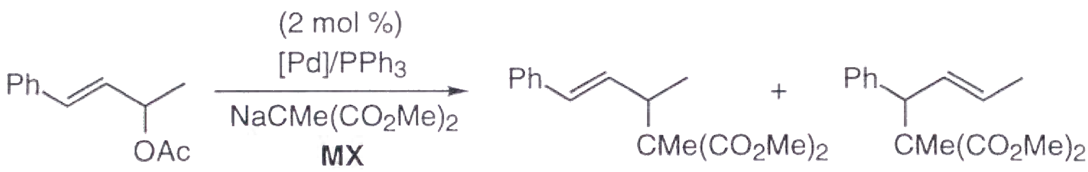
7: X = Cl — **7** (X = Cl) : **5a/6a** = 80/20

8: X = I — **8** (X = I) : **5a/6a** = 100/0

Palladium complex, $PdCl[\pi\text{-}(1\text{-phenyl})allyl](PPh_3)$ (**7**) and its analog **8** containing iodide in place of chloride, were prepared by mixing $[PdX[\pi\text{-}(1\text{-phenyl})allyl]]_2$ (X = Cl and I)[5] with 1 equiv. (to Pd) of PPh_3 and they were characterized by ^{31}P, ^{1}H and ^{13}C NMR spectra. Both of them have substituted carbon (C-1) of the π-allyl *trans* to the phosphorus atom of PPh_3 and the unsubstituted carbon (C-3) *cis* to phosphorus, which are determined by large coupling constants (J = 10.1 Hz in **7** and 10.5 Hz in **8**) between C-1 proton and phosphorus, and no couplings between C-3 protons and phosphorus. Stoichiometric reaction of chloride complex **7** with sodium enolate of dimethyl methylmalonate in THF at 0 °C gave **5a** and **6a** in a ratio of 80 to 20, while the reaction of iodide complex **8** gave **5a** with 100% regioselectivity (Scheme 2). These selectivities are in good agreement with those observed in the catalytic reactions, demonstrating that the iodide ligand bonded to π-allylpalladium intermediate controls the regioselectivity. Comparing ^{13}C NMR spectra of **7** and **8**, the chemical shift for C-3 of π-allyl group of **8** appears at lower field by 6.5 ppm than that for **7** and the chemical shift for C-1 of **8** appears at higher field by 3.1 ppm than that for **7**. It is probable that C-3 carbon of iodide complex **8** undergoes the nucleophilic attack more selectively than that of **7** giving linear isomer **5a**.[6]

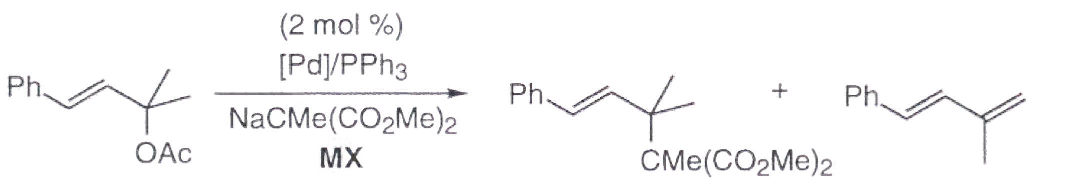
The high regioselectivity which is brought about by the addition of lithium iodide was also observed in the allylic alkylation that proceeds through unsymmetrically 1,3-disubstituted π-allylpalladium intermediates. Thus, the palladium-catalyzed reaction of 4-phenyl-3-buten-2-yl acetate (**9**) with sodium salt of dimethyl methylmalonate in the presence of lithium iodide at 20 °C gave 96% yield of dimethyl ((*E*)-1-methyl-3-phenyl-2-propenyl)methylmalonate (**10**) as a sole product. On the other hand, the reaction in the absence of lithium iodide gave a mixture of **10** and its regioisomer **11** in a ratio of 72 to 28. The alkylation of 1,1-dimethyl-3-phenyl-2-propenyl acetate (**12**) in the presence of lithium iodide proceeded smoothly to give dimethyl ((*E*)-1,1-dimethyl-3-phenyl-2-propenyl)methylmalonate (**13**) in 96% yield, while elimination reaction giving diene **14** was accompanied in the absence of lithium iodide. These results indicate that the lithium iodide control the reactivity as well as the regioselectivity in the palladium-catalyzed allylic alkylation.

Scheme 3



9 **10** **11**

MX = none **10/11** = 72/28
MX = LiI (0.5 equiv) **10/11** = 100/0



12 **13** **14**

MX = none **13/14** = 42/58
MX = LiI (0.5 equiv) **13/14** = 100/0

Table 2. Effects of Lithium Salts on Allylic Alkylation of Allyl Actates **1** and **2** Catalyzed by Palladium–(*R*)-MeO-MOP Complexes[a]

entry	allyl ester	ratio (P/Pd)	MX (equiv)	temp (°C)	time (h)	yield (%)[b] **5+6**	ratio[c] **5** : **6**	% ee of **6** (config.)
1	**2**	1/1	none	–30	2	96	10 : 90	87[d] (*S*)
2	**2**	1/1	LiI (0.5)	0	18	95	100 : 0	—
3	**2**	1/1	LiBr (0.5)	–30	24	90	85 : 15	61[d] (*S*)
4	**2**	1/1	LiCl (0.1)	–30	12	97	3 : 97	41[d] (*S*)
5	**2**	1/1	LiCl (2.0)	–30	12	94	7 : 93	87[d] (*S*)
6	**2**	2/1	none	–20	12	99	12 : 88	78[d] (*S*)
7	**2**	2/1	LiCl (2.0)	–20	12	97	11 : 89	90[d] (*S*)[e]
8	**1**	2/1	none	–20	6	99	21 : 79	68[f]
9	**1**	2/1	LiCl (2.0)	–20	12	93	25 : 75	82[f]

[a] All reactions were carried out in THF under nitrogen: THF (1.0 mL), allylic acetate (0.20 mmol), NaNu (0.40 mmol), $[PdCl(\pi\text{-}C_3H_5)]_2$ (0.002 mmol), (*R*)-MeO-MOP and LiI (0.02 mmol) at 0 °C. [b] Isolated yield by silica gel column chromatograpy. [c] The ratio was determined by ^{1}H-NMR analysis of the products. [d] Determined by HPLC analysis with Chiralpak AD (hexane/2-propanol = 9/1). [e] Specific rotation of **6b** (entry 7) was $[\alpha]_D^{20}$ +50.8 (*c* 0.8, $CHCl_3$). [f] Determined by GLC analysis with CP Cyclodex β236M after demethoxycarbonylation of one of the two methoxycarbonyl groups.

The effects of the addition of lithium salts were also examined in the alkylation of allyl acetates **1** and **2** catalyzed by palladium/(*R*)-MeO-MOP catalyst. The results are summarized in Table 2. The palladium-catalyzed reaction of **2** with the sodium salt of dimethyl methylmalonate in the presence of lithium iodide gave linear product **5b** exclusively (entry 2). This perfect linear selectivity is in contrast to the reaction in the absence of lithium salts which gives branch isomer **6b** with 90% selectivity (entry 1). Lithium bromide also showed the linear selectivity, though the selectivity was not so high as lithium iodide (entry 3). Interestingly, the addition of lithium chloride increased the branch selectivity and/or enantioselectivity depending on the amount of lithium chloride and the ratio of MeO-MOP ligand to palladium. The highest branch selectivity (97%) was observed in the reaction of **2** in the presence of 0.1 equiv. of lithium chloride and the palladium catalyst generated with 1 equiv. (to Pd) of MeO-MOP (entry 4). The enantioselectivity was increased to 90% ee by the addition of 2.0 equiv. of lithium chloride to the reaction catalyzed by palladium/MeO-MOP where the ratio of P/Pd is 2/1 (entry 7).

Experimental Section

General. All manipulations were carried out under a nitrogen atmosphere. Nitrogen gas was dried by passage through P_2O_5 (Merck, SICAPENT). NMR spectra were recorded on a JEOL JNM-EX270 spectrometer (270 MHz for ^1H and 109 MHz for ^{31}P), JEOL JNM-AL400 spectrometer (400 MHz for ^1H NMR), or JEOL JNM LA500 spectrometer (500 MHz for ^1H, 125 MHz for ^{13}C and 202 MHz for ^{31}P). Chemical shifts are reported in δ ppm referenced to an internal $SiMe_4$ standard for ^1H NMR, and to an external 85% H_3PO_4 standard for ^{31}P NMR. Residual chloroform (δ 77.0 for ^{13}C) was used as internal reference for ^{13}C NMR. ^1H, ^{13}C and ^{31}P NMR spectra were recorded in $CDCl_3$ at 25 °C unless otherwise noted. Preparative medium pressure liquid chromatography (MPLC) was performed with a silica gel prepacked column Si-10 (Kusano). HPLC analysis was performed on a Shimazu LC-6A liquid chromatograph system and a JASCO PU-980 liquid chromatograph system with chiral stationary phase column Daicel Co. Ltd., Chiralpak AD. GLC analysis was performed on a HEWLETT PACKARD HP 6890 series with a chiral stationary phase column, CP Cyclodex β-236M (50 m). Optical rotation were measured on a JASCO DIP-370 polarimeter.

Materials. THF was dried over sodium benzophenone ketyl and distilled prior to use. $[PdCl(\pi\text{-}C_3H_5)]_2$,[7] (*R*)-MeO-MOP,[8] 1-aryl-2-propenyl acetates,[9,10] and 4-phenyl-3-buten-2-yl acetate[11] were prepared according to the reported procedures.

Palladium-Catalyzed Allylic Alkylation of 1, 2, 3 and 4. The reaction conditions and results are shown in Table 1. A typical procedure is given for the reaction of 1-phenyl-2-propenyl acetate (*dl*-**1**) in entry 2. To a solution of $[PdCl(\pi\text{-}C_3H_5)]_2$ (1.1 mg, 0.003 mmol), PPh_3 (3.1 mg, 0.012 mmol) and lithium iodide (4.1 mg, 0.031 mmol) in THF (0.1 mL) was added a solution of sodium salt of dimethyl methylmalonate (86 mg, 0.59 mmol) prepared from dimethyl methylmalonate and sodium hydride in THF (1.2 mL). Allyl acetate **1** (52 mg, 0.30 mmol) was added and the mixture was stirred at 20 °C for 24 h. The catalyst was removed by filtration through a short silica gel pad (Et_2O). The crude filtrate was chromatographed on silica gel (EtOAc/hexane = 1/5) to give 77 mg (99%) of dimethyl ((*E*)-3-phenyl-2-propenyl)methylmalonate (**5a**). ^1H NMR and analytical data for other allylic alkylation products **5** and **6** are shown below.

Dimethyl ((*E*)-3-Phenyl-2-propenyl)methylmalonate (5a): ^1H NMR ($CDCl_3$, 270 MHz) δ 1.46 (s, 3H), 2.77 (dd, *J* = 7.8, 1.0 Hz, 2H), 3.73 (s, 6H), 6.08 (dt, *J* = 15.6, 7.8 Hz, 1H), 6.45 (d, *J* = 15.6 Hz, 1H), 7.19–7.34 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.0, 39.5, 52.5, 54.0, 124.1, 126.2, 127.4, 128.5, 134.1, 137.1, 172.3. Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.55; H, 7.01. **Dimethyl (1-Phenyl-2-propenyl)methylmalonate (6a):** ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.43 (s, 3H), 3.62 (s, 3H), 3.72 (s, 3H), 4.10 (d, *J* = 8.6 Hz, 1H), 5.11 (d, *J* = 16.8 Hz, 1H), 5.12 (d, *J* = 10.0, 1H), 6.32 (ddd, *J* = 8.6, 10.0, 16.8 Hz, 1H), 7.18–7.34 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.4, 52.3, 52.4, 54.5, 58.9, 117.8, 127.1, 128.2, 129.5, 136.9, 139.1, 171.3, 171.5. Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.70; H, 6.95. **Dimethyl ((*E*)-3-(4-Methoxyphenyl)-2-propenyl)methylmalonate (5b):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.59 (s, 3H), 2.74 (dd, *J* = 7.8, 1.0 Hz, 2H), 3.73 (s, 6H), 3.80 (s, 3H), 5.93 (dt, *J* = 15.6, 7.8 Hz, 1H), 6.38 (d, *J* = 15.6 Hz, 1H), 6.82 (d, *J* = 6.4 Hz, 2H), 7.25 (d, *J* = 6.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.0, 39.5, 52.5, 54.0, 55.2, 111.0, 113.9, 121.8, 127.3, 133.5, 159.0, 172.4. Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.80; H, 7.11. **Dimethyl (1-(4-Methoxyphenyl)-2-propenyl)-methylmalonate (6b):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.51 (s, 3H), 3.71 (s, 3H), 3.79 (s, 3H), 3.87 (s, 3H), 4.19 (d, *J* = 8.3 Hz, 1H), 5.09 (d, *J* = 16.8 Hz, 1H), 5.14 (d, *J* = 11.3, 1H), 6.32 (ddd, *J* = 8.3, 11.3, 16.8 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.3, 52.3, 53.7, 55.1, 58.9, 113.5, 117.4, 130.5, 131.0, 137.1, 158.6, 171.3, 171.5. Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 66.00; H, 6.85. **Dimethyl ((*E*)-3-(4-Chlorophenyl)-2-propenyl)methylmalonate (5c):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.45 (s, 3H), 2.75 (d, *J* = 7.3 Hz, 2H), 3.73 (s, 6H), 6.07 (dt, *J* = 15.6, 7.3 Hz, 1H), 6.39 (d, *J* = 15.6 Hz, 1H), 7.25 (s, 4H). Anal. Calcd for $C_{15}H_{17}O_4Cl$: C, 60.71; H, 5.77. Found: C, 60.57; H, 5.93. **Dimethyl (1-(4-Chlorophenyl)-2-propenyl)methylmalonate (6c):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.42 (s, 3H), 3.63 (s, 3H), 3.70 (s, 3H), 4.11 (d, *J* = 8.8 Hz, 1H), 5.09 (d, *J* = 17.1 Hz, 1H), 5.15 (d, *J* = 10.3, 1H), 6.26 (ddd, *J* = 8.8, 10.3, 17.1 Hz, 1H), 7.22 (d, *J* = 8.7 Hz, 2H), 7.25 (d, *J* = 8.7 Hz, 2H). Anal. Calcd for $C_{15}H_{17}O_4Cl$: C, 60.71; H, 5.77. Found: C, 60.57; H, 5.89. **Dimethyl ((*E*)-3-Phenyl-2-propenyl)malonate (5d):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.81 (t, *J* = 7.3 Hz, 2H), 3.53 (t, *J* = 7.3 Hz, 1H), 3.75 (s 6H), 6.14 (dt, *J* = 15.8, 7.3 Hz,1H), 6.47 (d, *J* = 15.8 Hz, 1H), 7.20–7.33 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 32.2, 51.6, 52.4, 125.3, 126.1, 127.3, 128.4, 132.8, 136.9, 169.1. Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.88; H, 6.51. **Dimethyl (1-Phenyl-2-propenyl)malonate (6d):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.84 (d, *J* = 7.9 Hz, 1H), 3.14 (s, 6H), 4.11 (dd, *J* = 7.9, 10.3 Hz, 1H), 5.08 (d, *J* = 10.3 Hz, 1H), 5.12 (d, *J* = 17.1 Hz, 1H), 6.00 (dt, *J* = 10.3, 17.1 Hz, 1H), 7.22–7.34 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 49.7, 51.7, 52.5, 116.6, 126.2,

127.8, 128.6, 132.9, 137.7, 169.2. Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.74; H, 6.69. **Methyl 2-((*E*)-3-Phenyl-2-propenyl)acetoacetate (5e):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.26 (s, 3H), 2.75 (t, *J* = 7.5 Hz, 2H), 3.62 (t, *J* = 7.5 Hz, 1H), 3.75 (s, 3H), 6.11 (dt, *J* = 15.5, 7.5 Hz, 1H), 6.45 (d, *J* = 15.5 Hz, 1H), 7.20–7.34 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 29.2, 31.5, 52.4, 59.3, 125.5, 126.1, 127.4, 128.5, 132.7, 136.9, 169.6, 202.2. Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.55; H, 7.10. **Methyl 2-(1-Phenyl-2-propenyl)acetoacetate (6e):** ^{1}H NMR ($CDCl_3$, 500 MHz) 2.27 (s, 3H), 3.10 (d, *J* = 5.9 Hz, 1H), 3.75 (s, 3H), 5.09 (d, *J* = 17.1 Hz, 1H), 5.10 (d, *J* = 10.3 Hz, 1H), 5.94 (ddd, *J* = 5.9, 10.3, 17.1 Hz, 1H), 7.21–7.34 (m, 5H). Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.33; H, 6.69.

Preparation of [PdI(π-C_3H_5)]$_2$ and [PdI(1-phenyl-π-allyl)]$_2$: A typical procedure is given for the preparation of [PdI(π-C_3H_5)]$_2$. To a solution of [PdCl(π-C_3H_5)]$_2$ (121.8 mg, 0.33 mmol) in THF (10 mL) was added of lithium iodide (91.3 mg, 0.68 mmol) at room temperature, and the mixture was stirred at room temperature for 12 h. The mixture was filtrated and evaporated gave 170 mg (94%) of orange powder. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.08 (d, *J* = 12.8 Hz, 2H), 4.38 (d, *J* = 6.7 Hz, 2H), 5.31 (tt, 6.7, 12.8 Hz, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 Hz) δ 67.6, 109.5. Anal. Calcd for $C_6H_{10}I_2Pd_2$: C, 13.13; H, 1.84. Found: C, 12.97; H, 1.69. ^{1}H NMR and analytical data for [PdI(1-phenyl-π-allyl)]$_2$ is shown below. **[PdI(1-phenyl-π-allyl)]$_2$:** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.05 (d, *J* = 12.2 Hz, 1H), 4.18 (d, *J* = 6.8 Hz, 1H), 4.87 (*J* = 11.7 Hz, 1H), 5.81 (ddd, *J* = 12.2, 11.7, 6.8 Hz, 1H), 7.29–7.48 (m, 5H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 Hz) δ 61.9, 88.6, 104.9, 128.1, 128.5, 128.9, 137.4. Anal. Calcd for $C_{18}H_{18}Pd_2I_2$: C, 30.84; H, 2.59. Found: C, 30.80; H, 2.62.

Stoichiometric Reaction of 7 and 8. The results are shown in Scheme 2. A typical procedure is given for the reaction of **8**. To a solution of [PdI(1-phenyl-π-allyl)]$_2$ (21.8 mg, 0.031 mmol) and PPh_3 (16.5 mg, 0.063 mmol) in THF (0.5 mL) was added a solution of sodium salt of dimethyl methylmalonate prepared from dimethyl methylmalonate (11.0 mg, 0.075 mmol) and sodium hydride in THF (0.15 mL) at 0 °C. The mixture was stirred at 0 °C for 3 h. The mixture was filtrated through a short silica gel pad (ether). The filtrate was evaporated and the residue was chromatographed on silica gel (hexane/EtOAc = 6/1) to give 14 mg (86%) of dimethyl (1-phenyl-2-propenyl)methylmalonate (**5a**).

NMR Study and Selected NMR Data of 7 and 8. A typical procedure is given for **8**. In an NMR sample tube were placed [PdI(1-phenyl-π-allyl)]$_2$ (7.3 mg, 0.010 mmol) and PPh_3 (5.1 mg, 0.019 mmol). The tube was filled with nitrogen, and CDCl3 (0.5 mL) was added. ^{1}H, ^{13}C and ^{31}P NMR spectra were measured at –40 °C.

Selected NMR data of **7** and **8**. **7**: ^{1}H NMR ($CDCl_3$ at –40 °C) δ 2.88 (d, J = 6.8 Hz, 1H, syn-H on C-3), 2.97 (d, J = 11.7 Hz, 1H, anti-H on C-3), 5.37 (dd, J_{H-H} = 13.2 Hz, J_{H-P} = 10.1 Hz, 1H, H on C-1), 6.08 (ddd, J = 6.8, 11.7, 13.2 Hz, 1H, H on C-2), 7.36-7.88 (m, 20H). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$ at –40 °C) δ 24.2 (s). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$ at –40 °C) δ 58.2 (C-3), 99.6 (J_{C-P} = 26.9 Hz, C-1), 111.4 (J_{C-P} = 5.2 Hz, C-2). **8**: ^{1}H NMR ($CDCl_3$ at –40 °C) δ 3.47 (d, J = 6.8 Hz,1H, syn-H on C-3), 3.14 (d, J = 12.2 Hz, 1H, anti-H on C-3), 5.21 (dd, J_{H-H} = 13.0 Hz, J_{H-P} = 10.5 Hz, 1H, H on C-1), 6.08 (ddd, J = 6.8, 12.2, 13.0 Hz, 1H, H on C-2), 7.26-7.63 (m, 20H). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$ at –40 °C) δ 27.9 (s). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$ at –40 °C) δ 64.7 (C-3), 96.5 (J_{C-P} = 29.0 Hz, C-1), 111.0 (J_{C-P} = 5.2 Hz, C-2).

Preparation of 1,1-Dimethyl-3-phenyl-2-propenyl Acetate (12): To a solution of methylmagnesium bromide (60 mL of 0.9 M, 54.0 mmol) in THF at 0 °C was added dropwise a solution of *trans*-4-phenyl-3-buten-2-one (7.0 g, 47.9 mmol) in THF (15 mL). The mixture was stirred at room temperature for 3 h. It was quenched with saturated ammonium chloride solution and extracted with ether. The ether extracts were washed with saturated sodium hydrogen carbonate solution, and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a crude allyl alcohol. To a solution of this crude alcohol, pyridine (5.8 mL, 71.8 mmol) and a catalytic amount of 4-dimethylaminopyridine in ether (50 mL) was added acetic anhydride (6.8 mL, 71.8 mmol). The mixture was stirred at room temperature for 12 h, quenched with water, and extracted with ether. The organic phase was washed with 10% $CuSO_4$ solution, water and brine, dried over anhydrous sodium sulfate and evaporated. The residue was chromatographed on alumina (hexane/Et_3N = 6/1) to give 6.5 g (67%) of 1,1-dimethyl-3-phenyl-2-propenyl acetate (**12**): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.66 (s, 6H), 2.03 (s, 3H), 6.55 (d, J = 3.9 Hz, 2H), 7.24 (d, J = 7.3 Hz, 1H), 7.32 (t, J = 7.3 Hz, 2H), 7.40 (d, J = 7.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.0, 26.6, 80.2, 126.3, 127.4, 127.8, 128.3, 133.8, 136.5, 169.7. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89. Found: C, 76.62; H, 8.17.

Palladium-Catalyzed Allylic Alkylation of 9 and 12. The reaction conditions and results are shown in Scheme 3. A typical procedure is given for the reaction of 4-phenyl-3-buten-2-yl acetate (**9**). To a solution of $[PdCl(\pi\text{-}C_3H_5)]_2$ (0.93 mg, 0.0025 mmol) and PPh_3 (2.6 mg, 0.010 mmol) in THF (0.1 mL) was added a solution of sodium salt of dimethyl methylmalonate (73 mg, 0.50 mmol) prepared from dimethyl methylmalonate and sodium hydride in THF (1.0 mL). Allyl acetate **9** (47 mg, 0.25 mmol) was added and the mixture was stirred at 20 °C for 24 h. The catalyst was removed by filtration through a short silica gel pad (Et_2O). The crude filtrate was chromatographed on silica gel (EtOAc/hexane = 1/5) to give 65 mg (95%) of a mixture of dimethyl ((*E*)-1-methyl-3-phenyl-2-propenyl)methylmalonate (**10**) and dimethyl ((*E*)-3-methyl-1-phenyl-2-propenyl)methylmalonate (**11**). The ratio of **10** to **11** was determined to be 72 to 28 by ^{1}H NMR. Analytically pure samples of **10** and **11** were obtained by MPLC (hexane/EtOAc = 5/1). **Dimethyl ((*E*)-1-Methyl-3-phenyl-2-propenyl)methylmalonate (10):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.15 (d, *J* = 6.8 Hz, 3H), 1.42 (s, 3H), 3.15 (quintet, *J* = 6.8 Hz, 1H), 3.69 (s, 6H), 6.14 (dd, *J* = 6.8, 16.1 Hz, 1H), 6.43 (d, *J* = 16.1 Hz, 1H), 7.20–7.33 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.5, 20.3, 46.2, 52.4, 70.9, 72.1, 126.5, 127.9, 128.5 128.8, 131.7, 169.3. Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30. Found: C, 69.90; H, 7.33. **Dimethyl ((*E*)-3-Methyl-1-phenyl-2-propenyl)methylmalonate (11):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.66 (dd, *J* = 1.5, 6.4 Hz, 3H), 1.42 (s, 3H), 3.60 (s, 6H), 4.10 (d, *J* = 9.3 Hz, 1H), 5.55 (dq, *J* = 12.7, 6.3 Hz, 1H), 5.92 (ddd, *J* = 1.5, 9.3, 12.7 Hz, 1H), 7.20–7.33 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.1, 42.1, 52.3, 53.5, 59.0, 126.2, 128.0, 128.7, 129.4, 131.4, 139.8, 171.3. Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30. Found: C, 69.64; H, 7.49. ^{1}H and ^{13}C NMR and analytical data for **13** and **14** obtained for the reaction of **12** are shown below. **Dimethyl ((*E*)-1,1-Dimethyl-3-phenyl-2-propenyl)methylmalonate (13):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.33 (s, 6H), 1.47 (s, 3H), 3.70 (s, 6H), 6.34 (d, *J* = 16.1 Hz, 1H), 6.60 (d, *J* = 16.1 Hz, 1H), 7.19–7.37 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.9, 23.9, 41.1, 51.9, 60.2, 126.2, 127.0, 127.8, 128.4, 136.5, 137.7, 171.8. Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.33; H, 7.51. **3-Methyl-1-phenyl-1,3-butadiene (14):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.98 (s, 3H), 5.08 (s, 1H), 5.12 (s, 1H), 6.54 (d, *J* = 16.9 Hz, 1H), 6.88 (d, *J* = 16.9 Hz, 1H), 7.21–7.48 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.6, 117.3, 126.4, 127.4, 128.6, 128.7, 131.7, 137.5, 142.0. Anal. Calcd for $C_{11}H_{12}$: C, 91.61; H, 8.39. Found: C, 91.88; H, 8.12.

Palladium-Catalyzed Asymmetric Allylic Alkylation of 1 and 2. The reaction conditions and results are shown in Table 2. A typical procedure is given for the reaction of 1-(4-methoxyphenyl)-2-propenyl acetate (*dl*-**2**) in entry 7. To a solution of $[PdCl(\pi\text{-}C_3H_5)]_2$ (0.89 mg, 0.0024 mmol), (*R*)-MeO-MOP (2.4 mg, 0.0049 mmol) and lithium chloride (21.0 mg, 0.50 mmol) in THF (0.1 mL) was added a solution of sodium salt of dimethyl methylmalonate (71 mg, 0.49 mmol) prepared from dimethyl methylmalonate and sodium hydride in THF (1.0 mL). Allyl acetate **2** (50 mg, 0.24 mmol) was added and the mixture was stirred at 20 °C for 12 h. The catalyst was removed by filtration through a short silica gel pad (ether). The crude filtrate was chromatographed on silica gel (EtOAc/hexane = 1/6) to give 73 mg (99%) of a mixture of dimethyl ((*E*)-3-(4-methoxyphenyl)-2-propenyl)methylmalonate (**5b**) and dimethyl (1-(4-methoxyphenyl)-2-propenyl)methylmalonate (**6b**). The ratio of **5b** to **6b** was determined to be 11 to 89 by ^{1}H NMR. The regioisomers **5b** and **6b** were separated by MPLC (EtOAc/hexane = 1/6). **Dimethyl (1-(4-Methoxyphenyl)-2-propenyl)-methylmalonate (6b):** (90% ee) $[\alpha]_D^{20}$ +50.8 (*c* 0.8, $CHCl_3$).

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