Novel *P*-Stereogenic Bidentate Phosphorus Ligands for Asymmetric Catalysis

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M. Sc.

Nikolai Vinokurov

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Referent:	Prof. Dr. H. Butenschön
Korreferent:	Prof. Dr. H. Duddeck
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ZUSAMMENFASSUNG

Neue *P*-chirale zweizähnige Phosphanliganden für die Asymmetrische Katalyse

Heutzutage werden *P*-chirale Diphosphane für eine Vielzahl asymmetrischer Übergangsmetall-katalysierter Reaktionen wie Hydrierungen, Hydrosilylierungen, Alkylierungen, C-C-Kupplungsreaktionen und Isomerisierungen häufig angewandt. Die Synthesewege zu *P*-chiralen zweizähnigen Liganden beschränken sich jedoch auf nur wenige Beispiele, weil die Synthese *P*-chiraler Verbindungen oft als problematisch gilt.

Im Rahmen dieser Dissertation wurden neue Wege zu *P*-chiralen Diphosphanliganden beschrieben, um danach deren erste Anwendungen in der asymmetrischen Katalyse aufzuzeigen.

Die Ru-katalysierte Homo-Metathese von *P*-chiralem (*Sp*)-Methylphenylvinylphosphanoxid wurde in Gegenwart moderner Alkenmetathese-Katalysatoren durchgeführt. Anschließend wurde das *P*-chirale *trans*-1,2-Diphosphanyldioxid als Dienophil in einer asymmetrischen Diels-Alder-Reaktion mit Cyclopentadien und als Dipolarophil in einer asymmetrischen Huisgen-Cycloaddition mit acyclischen Nitronen eingesetzt, um die ersten *P*-chiralen Diphosphandioxide mit zwei asymmetrischen Phosphoratomen und einem starren Rückgrat zu erhalten.

Die Reduktion dieser neuen *P*-chiralen Diphosphandioxide durch die Umsetzung mit $Ti(O\textit{i}Pr)_4$/Polymethylhydrosiloxan (PMHS) in THF verläuft unter Erhalt der Konfiguration in hohen Ausbeuten. Die Synthese eines Rhodiumkomplexes mit den neuen *P*-chiralen Diphosphanen als Liganden konnte auch realisiert werden. Die asymmetrische Pd-katalysierte allylische Alkylierung von 1,3-Diphenyl-2-propenylacetat mit Dimethylmalonat lieferte ein erstes noch nicht optimiertes Ergebnis, indem das gewünschte Produkt in 97% Ausbeute und in einem Enantiomerenüberschuss von 81% vorlag.

Darüber hinaus ist es gelungen, einen neuen bimetallischen Ruthenium Präkatalysator für die Alken-Metathese herzustellen. Der Katalysator weist eine elektronenziehende Tricarbonylchromgruppe auf, welche am Benzylidenliganden koordiniert ist. Die katalytischen Eigenschaften dieses neuen Präkatalysators wurden in Ringschluss-, Enin-, Kreuz-, und Homo-Metathesen getestet. Aus den vorliegenden Ergebnissen ist zu schließen, dass der neue Katalysator eine vergleichbare Aktivität wie andere Alken-Metathesekatalysatoren besitzt und diese in manchen Fällen sogar übersteigt.

P-Chirale Vinylphosphanoxide · Homodimerisierung · Alken-Metathese · Ruthenium · Asymmetrische Cycloaddition · *P*-Chirale Diphosphane · Asymmetrische Katalyse · Rhodium

ABSTRACT

Novel *P*-Stereogenic Bidentate Phosphorus Ligands for Asymmetric Catalysis

Nowadays, *P*-stereogenic diphosphines are frequently employed in a variety of asymmetric transition metal catalyzed reactions such as hydrogenation, hydrosilylation, alkylation, C-C coupling reactions and isomerization. However, *P*-chiral diphosphine ligands were less investigated since the synthesis of highly enantiomerically enriched *P*-stereogenic phosphines often proves to be difficult.

This work is devoted to the synthesis of novel *P*-stereogenic diphosphines for asymmetric catalysis. The target of this project consists of the synthesis of new *P*-stereogenic diphosphines from *P*-chiral diphosphine dioxides and their first applications in asymmetric catalysis.

The *P*-chiral (*Sp*)-methylphenylvinylphosphine oxide was successfully homodimerized in the presence of modern olefin metathesis catalysts. After homo cross-coupling the *P*-chiral *trans*-1,2-diphosphinylethene dioxide was used as a dienophile for an asymmetric Diels-Alder cycloaddition with cyclopentadiene and as a dipolarophile for asymmetric Huisgen cycloaddition with acylic nitrones to access novel *P*-chiral diphosphine dioxides bearing two asymmetric phosphorus atoms located close to the rigid chiral backbone.

The novel *P*-stereogenic diphosphine dioxides were successfully reduced by the use of $Ti(O\textit{i}Pr)_4$/polymethylhydrosiloxane (PMHS) in THF with complete retention of configuration leading to diastereomerically pure *P*-chiral diphosphines in high yields. The rhodium complex of a new *P*-chiral diphosphine could also be synthesized.

The novel *P*-stereogenic diphosphine was employed in the enantioselective Pd-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethylmalonate leading as a first unoptimized result to 97 % yield and 81 % *ee* of the desired product

In addition, a new highly efficient bimetallic ruthenium precatalyst for alkene metathesis was synthesized, in which the benzylidene ligand has been coordinated to a highly electron withdrawing tricarbonylchromium moiety. Screening of the catalytic properties shows that the activity of the new catalyst in ring closing, enyne, cross, and homo-metathesis of alkenes is comparable to and in some cases better than that of known catalysts.

P-Chiral Vinylphosphine Oxides · Homodimerization · Alkene Metathesis · Ruthenium · Asymmetric Cycloaddition · *P*-Stereogenic Diphosphines · Asymmetric Catalysis · Rhodium

Die vorliegende Arbeit wurde unter der Leitung von Herrn Prof. Dr. Holger Butenschön in der Zeit von September 2003 bis Juli 2007 am Institut für Chemie der Leibniz Universität Hannover angefertigt.

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Bei meinen geliebten Eltern möchte ich mich für Ihre große Unterstützung bedanken!

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Посвящается Моим Дорогим Родителям - Валентине и Анатолию Винокуровым

ABBREVIATIONS

$[\alpha]^{D}_{20°C}$	Specific Rotation
Å	Angstrom
aq.	Aqueous
Ar	Ar
ATR	Attenuated Total Reflection
Bn	Benzyl
br	broad (NMR)
B. p.	Boiling Point
Bu	Butyl
t-Bu	*tert*-Butyl
c	Concentration
^{o}C	Degrees Celsius
calcd.	Calculated
cat.	Catalyst
CM	Cross-Metathesis
cm^{-1}	Wavenumber
^{13}C NMR	^{13} C Nuclear Magnetic Resonance
δ	Chemical Shift
d	Doublet
DBTA	Dibenzoyltartaric acid
dd	Doublet of Doublets
dr	Diastereomeric Ratio
de	Diastereomeric Excess
decomp.	Decomposition

ee	Enantiomeric Excess
EI	Electronic Impact (Mass Spectrometry)
equiv.	Equivalent(s)
Et	Ethyl
Fc	Ferrocene
g	gramm
GC	Gas Chromatography
h	hour (s)
^{1}H NMR	^{1}H Nuclear Magnetic Resonance
HRMS	High-resolution Mass Spectroscopy
Hz	Hertz
IR	Infrared
J	Coupling Costant (NMR Spectroscopy)
m	Multiplet
M	Molar
M^{+}	Parent Molecular Cation
Me	Methyl
Men	Menthyl
MHz	Megahertz
mL	Milliliter(s)
min	Minutes
mmol	Millimol
M. p.	Melting Point
MS	Mass Spectrometry
m /z	Mass-to-charge Ratio (Mass spectrometry)
NHC	*N*-heterocylic

NMR	Nuclear Magnetic Resonance
Nu	Nucleophile
PE	Petroleum Ether
Ph	Phenyl
Ppm	Part(s) per Million
i-Pr	Isopropyl
PMHS	Polymethylhexasiloxane
^{31}P NMR	^{31}P Nuclear Magnetic Resonance
rac	Racemic
RCM	Ring-Closing Metathesis
s	Singlet
TBME	*tert*-Butylmethyl Ether
THF	Tetrahydrofuran
t	Triplet
TLC	Thin-layer Chromatography

Table of Contents

1 Introduction

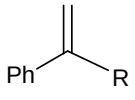
Chiral compounds play a key role in many areas of science including biologically active pharmaceuticals, agrochemicals, flavours and fragrances as well as advanced materials such as liquid crystals emphasize that life itself depends on chiral recognition. A pair of enantiomers will be differenced by biological systems as unlike substances, where one enantiomer may act as an effective therapeutic medicine whereas the other enantiomer is inactive or even causes adverse effects. Nowadays there are several methods to obtain substances in enantiomerically pure form, which include classical optical resolution via diastereomers, chemical kinetic resolution, enzymatic resolution, chromatographic separation and asymmetric catalysis. Among these type of asymmetric reaction, the most desirable and the most challenging is asymmetric catalysis, since one chiral molecule can create millions of chiral product molecules, just as enzymes do in biological systems. Asymmetric catalysis is defined as an enantioselective transformation effected by a small amount of a chiral catalyst with control over the absolute configuration of the desired product. A large number of asymmetric catalysts that have been developed are organometallic compounds, which are easily endowed with chemoselectivity, regioselectivity and both relative and absolute configuration. Consequently, the area of development of chiral catalysts for asymmetric synthesis has been extensively studied in many academic and industrial research laboratories and has become a mainstream chemical technology in the 20th century. [1]

1.1 Optically Active Phosphorus Ligands: A Historical Overview

There is no doubt that hydrogen is one of the powerful reducing agents and hydrogenation is arguably the most important catalytic method in synthetic organic chemistry both on the laboratory and the production scale. Molecular hydrogen is stable (bond energy: 104 kcal/mol) and does not react with organic compounds in the absence of a catalyst. Transition metal complexes can activate H_2 and hence hydrogen may be transferred from the metallic center to unsaturated organic molecules. Oxidative addition of hydrogen to metal complexes with optically active ligands affords chiral metal dihydride complexes, which are able to asymmetric hydrogenation. During the last three decades of the 20th century, significant attention was devoted to the discovery of new asymmetric catalysts, in which transition

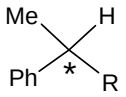
metals bound to chiral phosphorous ligands have emerged as preferential catalysts for asymmetric hydrogenation.[2]

The first homogeneous asymmetric hydrogenation using *P*-chiral phosphine ligands was found in 1968 and was independently reported by Horner and Knowles.[3] The Wilkinson complex $RhCl(PPh_3)_3$ was modified by replacing triphenylphosphine with optically active methylpropylphenyl phosphine (**1**) (69 % *ee*) or by *in situ* generation of the catalyst precursor from chloro(1,5-hexadiene)rhodium(I) dimer complex by its reaction with (*S*)-(+)-**1**. These rhodium(I) complexes were used for asymmetric hydrogenation of α-substituted styrenes or α-phenylacrylic acid derivates, albeit with poor enantioselectivity.



2

H_2 / L*



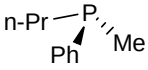
3

$[Rh(1,5\text{-hexadien})Cl_2]_2$ / L*

R = Et 8% *ee*
R = OMe 4 % *ee*

Horner 1968

L* =



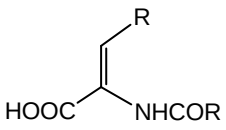
(*S*)-**1**

$RhCl(PPh_2L^*)$

R = Ph 8% *ee*
R = CH_2CO_2H 15% *ee*

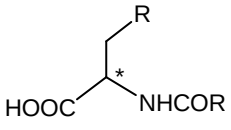
Knowles 1968

Further exploration by Knowles and Sabacky of monophosphines PAMP (**6**) and CAMP (**7**) provided noticeably improved *ee*'s in catalytic asymmetric hydrogenation of α-acylaminoacrylic acids.[4] A real breakthrough came when Kagan devised DIOP (**8**), a C_2-symmetrical chiral diphosphine obtained from tartaric acid. With DIOP as ligand α-acylaminoacrylic acids and esters can be hydrogenated to produce the corresponding amino acid derivatives in up to 80% *ee*.[5]



4

H_2, chiral Rh(I) complex



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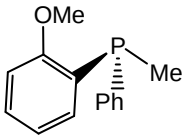
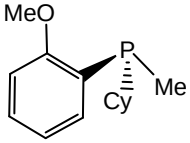


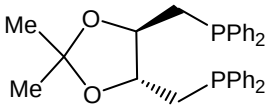
6

(*S*)-PAMP
58 - 60% *ee*



7

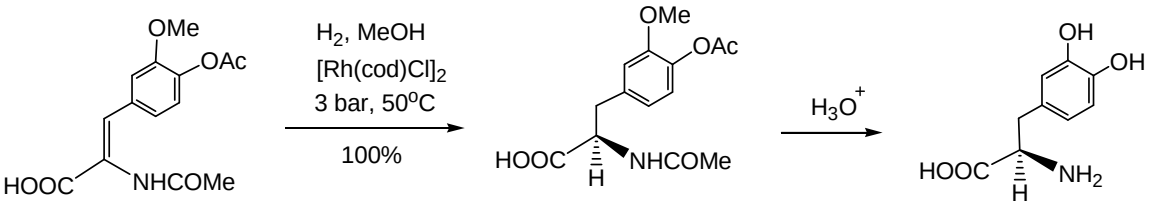
(*S*)-CAMP
80 - 88% *ee*



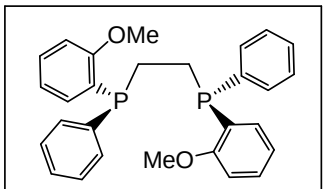
8

(*R,R*) -DIOP
68 - 80% *ee*

In 1975, Knowles made his significant discovery – the first *P*-chiral bidentate phosphine DIPAMP (**12**),[6] which simultaneously possesses C_2 symmetry and bears two chelating asymmetric phosphorus atoms, allowed the rhodium catalyzed hydrogenation of dehydroamino acids with up to 90 – 97.5 % *ee*. This methodology has become the basis for a commercial process for the amino acid, *L*-DOPA (**11**) (3,4-dihydroxyphenylalanine)**,** a drug used for treatment of Parkinson's disease.[7]

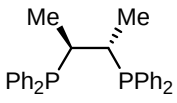


9 **10** 97.5 % ee **11** *L*-DOPA

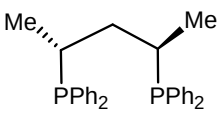


12
(*S,S*) - DIPAMP

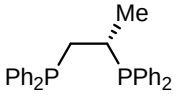
An intensive worldwide effort, in which literally hundreds of new optically active diphosphine ligands were synthesized, based on the Kagan model of backbone chirality in potentially chelating system (**13-19**. Scheme 1).[8] Most of these performed hydrogenation of aromatic dehydroamino acids with typically 75 – 95 % *ee* but it became obvious that rhodium asymmetric hydrogenation, despite its attractive specificity, is a reaction of limited scope. An extensive, systematic survey of the mechanism of this reaction revealed that double bond geometry and an α-amido function must be present for efficient enantioface differentiation.[9]



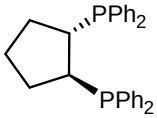
13
(*S,S*)-CHIRAPHOS



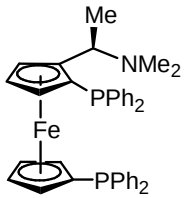
14
(*R,R*)-BDPP



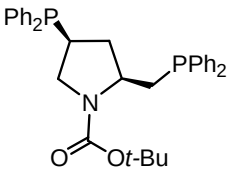
15
(*S*)-PROPHOS



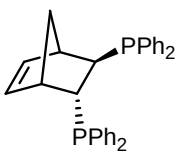
16
(*S,S*)-DPCP



17
(*R,S*)-BPPFA



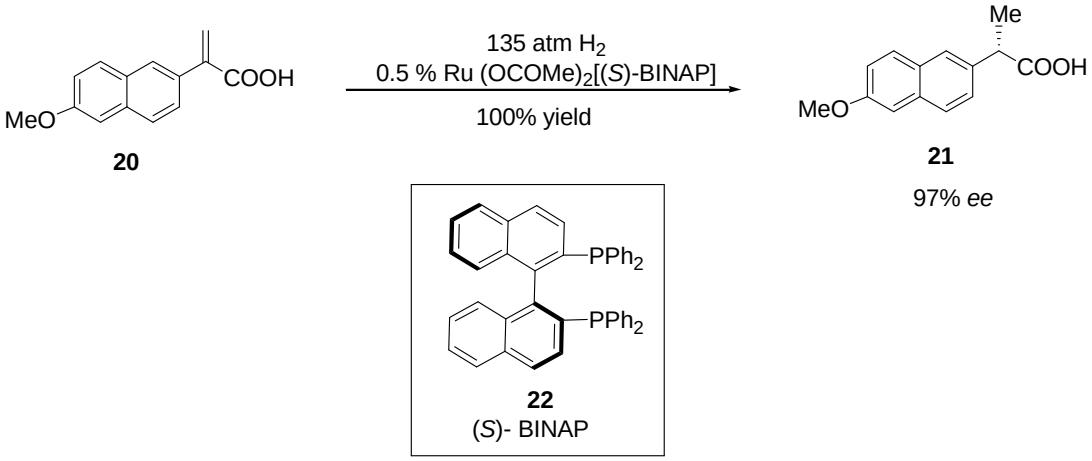
18
(*S,S*)-BPPM



19
(*R,R*)-NORPHOS

Scheme 1. Optically active diphosphine ligands (Kagan model)

The focus changed from rhodium to ruthenium, and in the 1980s, Noyori and Takaya reported an atropisomeric C_2-symmetric bisphosphine ligand, BINAP (**22**).[10] The discovery of the Ru(II) –BINAP system, could efficiently and selectively effect the asymmetric hydrogenation of various functionalized olefins, functionalized ketones, and unsaturated carboxylic acids.[2] An important application of Ru(II)-BINAP dicarboxylate complexes is the enantioselective synthesis of Naproxen® (**21**). This commercial antiinflammatory agent can be obtained in 97% *ee* under high hydrogen pressure.



20

21

97% *ee*

22

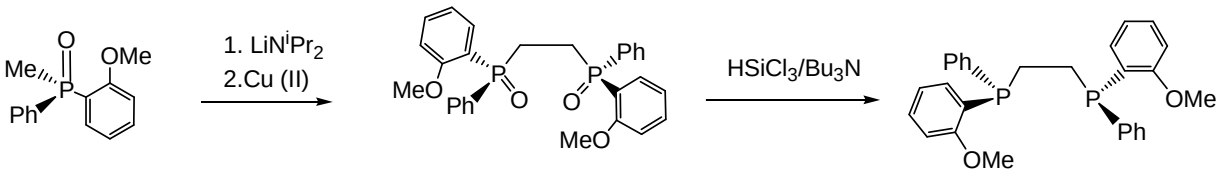
(*S*)- BINAP

For their significant achievements in field of asymmetric catalysis W. Knowles and R. Noyori with B. Sharpless were awarded the Nobel Prize in 2001.[11]

1.2 Synthesis of *P*-Chiral Diphosphine Ligands via Their Dioxides and Sulfides

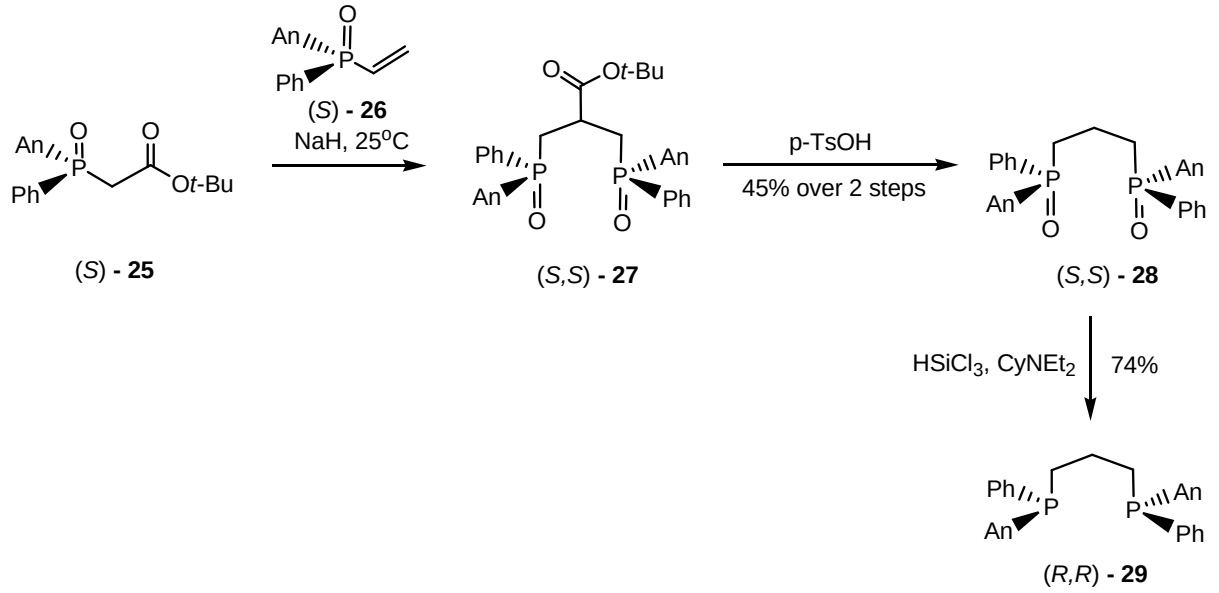
P-chiral phosphorus compounds were first introduced by Meisenheimer and Lichtenstadt in 1911 by partial resolution the ethylmethylphenylphosphine oxide into its enantiomers.[12] In the late of the 1960s Horner and Mislow developed synthetic methods for the formation of optically active phosphorus compounds and studied their stereochemistry. These methods include the reaction of quaternary benzyl phosphonium salts with (D)-benzoyl tartrate followed by separation of the respective diastereoisomers, hydrolysis and a cathodic reduction (Horner)[13] or the resolution of menthyl phosphinates into the diastereomeric forms followed by reaction with alkyl or aryl Grignard reagents leading to phosphine oxides in highly stereospecific manner (Mislow).[14]

First *P*-chiral diphosphine DIPAMP (**12**) was prepared by oxidative coupling of the (*R*p)-(*o*-methoxyphenyl)methylphenylphosphine oxide (**23**) in the presence of lithium diisopropylamide and Cu(II) chloride[15] to bisphosphine dioxide **24** which was stereoselectively converted to **12** by $HSiCl_3/Bu_3N$ reduction with double inversion at the phoshorus centers.[6]



(*R*) - **23** (*R,R*) - **24** (*R,R*) - **12**

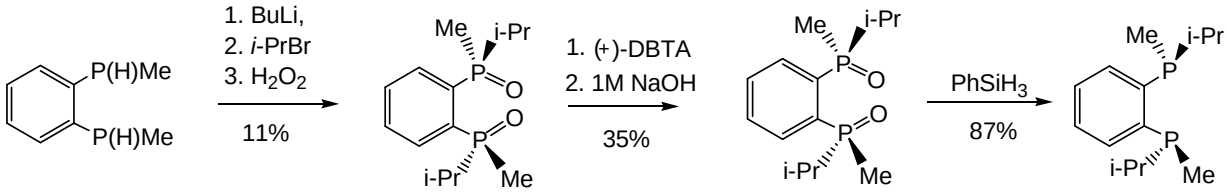
Imamoto used *P*-chiral vinylphosphine oxide (**26**) for the synthesis of bidentate phosphine ligands.[16] The addition to **25** in the presence of NaH proceeded at room temperature to yield **27**, which was converted to (*S,S*)-1,3-bis[(*o*-methoxyphenyl)phenylphosphinyl]propane dioxide (**28**), upon refluxing in xylene in the presence of *p*-TsOH. Bis(phosphine) oxide (**28**) was reduced to the phosphine by employing a combination of trichlorosilane and cyclohexyldiethylamine with inversion of configuration at the phosphorus atoms.[17] A rhodium complex of **29** was used for the asymmetric hydrogenation of several α-(acetamino)acrylic acids to give optical yields of 76-96%.



(*S*) - **25** (*S,S*) - **27** (*S,S*) - **28** (*R,R*) - **29**

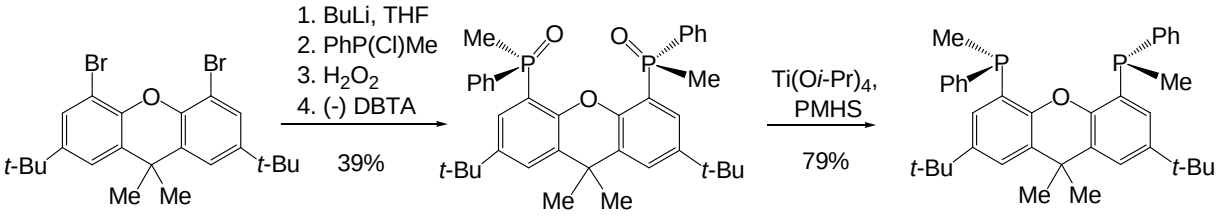
The enantiomerically pure *P*-chiral diphosphine ligand (*S,S*)-**32** was prepared by dilithiation of *rac*-**30** with BuLi followed by slow addition of 2-bromopropane leading to *rac*-**31** after

subsequent oxidation with hydrogen peroxide. Optical resolution of *rac*-**31** with dibenzoyl-*D*-tartaric acid (DBTA) in boiling ethyl acetate providing dioxide (*R,R*)-**31** with 99% *ee* in 35% yield. Reduction of (*R,R*)-**31** with phenylsilane afforded the chiral bidentate phosphine ligand (*S,S*)-**32** with 97% *ee* along with a small amount of the *meso* compound. High enantioselectivities 89-97 % *ee* were achieved in the asymmetric hydrogenation of dehydroamino acid methyl esters, using rhodium complex of **32** after recrystallization as the catalyst precursor.[18]



rac-**30** *rac*-**31** (*R,R*) **- 31** (*S,S*) **- 32**

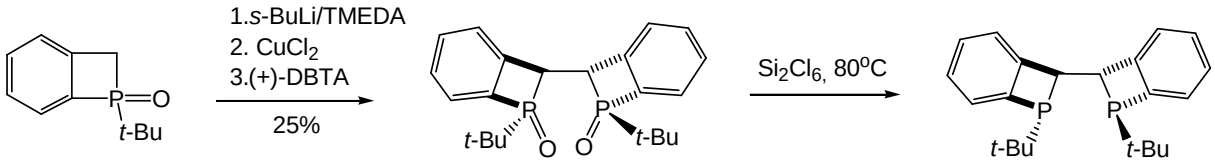
Commercially available dibromoxanthene derivate **33** was treated with BuLi and chloromethylphenylphosphine and subsequently with hydrogen peroxide. Resolution of the racemic intermediate was carried out by the diastereomeric salt formation with (–)-DBTA followed by hydrolysis with aqueous ammonia. The desired *P*-chiral diphosphine was obtained after reduction of the corresponding dioxide **34** with titanium tetra(isopropoxide) and polymethylhydrosiloxane (PMHS) with complete retention of configuration in high yield.[19] The utility of **35** was examined in the palladium catalyzed asymmetric allylic substitution reaction between 1,3-diphenyl-2-propenyl acetate and dimethyl malonate, and the enantiomeric excess was found to be 85%.[19]



33 (*R,R*) **- 34** (*S,S*) **- 35**

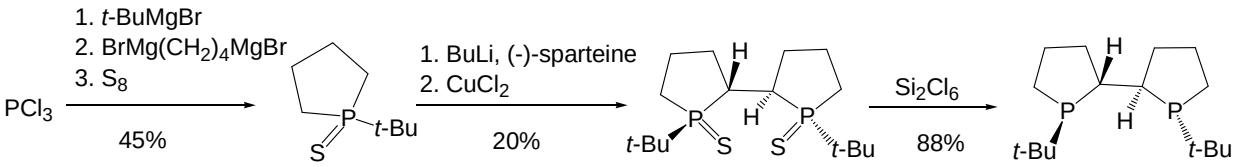
Imamoto and Crepy used the oxidative dimerization of *rac*-1-*tert*-butylbenzophosphete oxide *rac*-(**36)** to access enantiomerically pure diphosphine dioxides by treatment with the *s*-BuLi/$CuCl_2$ system, and subsequent resolution with (+) or (–)-DBTA. The difficulties with the reduction of **37** were overcome by use of hexachlorosilane as the reducing agent, presumably with retention of configuration. The diphosphine **38** is highly air-sensitive and

was hence converted to its rhodium complex directly after reduction. A markedly high *ee* (96%) was observed in hydrogenation of α-acetamidocinnamate.[20]



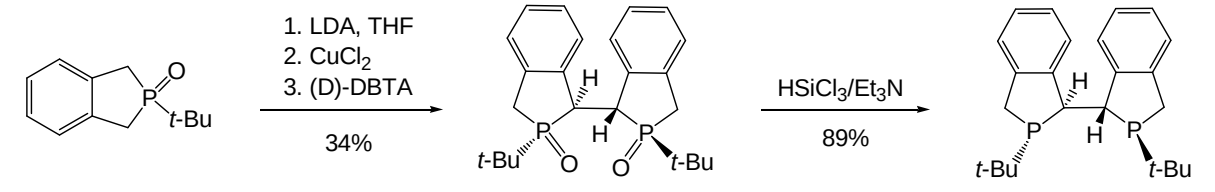
rac-**36** (*S,S*) **- 37** (*R,R*) **- 38**

Zhang et. al. developed a convenient method for the preparation of the *P*-chiral ligand TangPhos (**42**) based on phosphine sulfides as intermediates starting from commercially available phosphorus trichloride (**39**). Racemic phosphine sulfide **40** undergoes enantioselective deprotonation by BuLi/(–)sparteine followed by homo-coupling to generate **41**. After recrystallization disulfide **41** was obtained in only 20% yield. Desulfuration of C_2-symmetric diphosphine was found to proceed with inversion of configuration. TangPhos was used for highly efficient asymmetric hydrogenation of α-(acylamino)acrylic acids, β-(acylamino)acrylic acids, itaconic acid and enol acetate derivatives.[21]



39 *rac*-**40** (*R,R*) **- 41** (*S,S*) **- 42**

In addition, Zhang et. al. reported the highly efficient synthesis of the conformationally rigid chiral diphosphine DuanPhos (**45**) by copper mediated homo-coupling of *rac*-phosphine oxide **43** in the presence of LDA to diphosphine dioxide *rac*-**44**. A highly selective deprotonation directed by bulky *tert*-butyl group probably prevents the formation of the *meso* compound. Resolution was performed with inexpensive (+)-DBTA monohydrate affording desired enantiomer of **44** in 99 % *ee*. Reduction of **44** with chlorosilane and triethylamine gave *P*-chiral diphosphine **45** in high yield with inversion of the phosphorus atoms. The use of DuanPhos as a ligand in the rhodium catalyzed asymmetric hydrogenation of α-dehydroamino acids and α-arylenamides led to excellent enantiomeric excesses.[22]

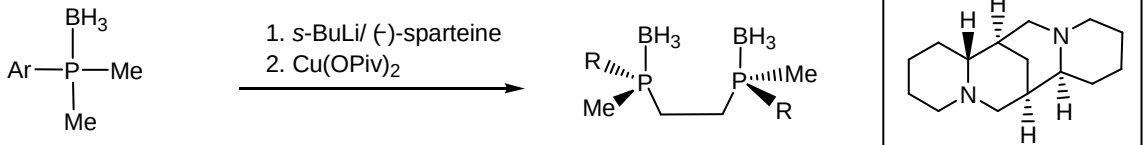


rac - **43** (*S,S*) **- 44** (*R,R*) **- 45**

1.3 Synthesis of *P*- Stereogenic Diphosphine Ligands From Phosphine-Boranes

Phosphine-boranes, adducts of phosphines and boranes, constitute a unique class of organophosphorus compounds. After first reports about phosphine-borane chemistry by Schmidbaur[23] at the end of 1970s, this field has attracted much attention and was extensively studied by Imamoto and others during last two decades.[24]

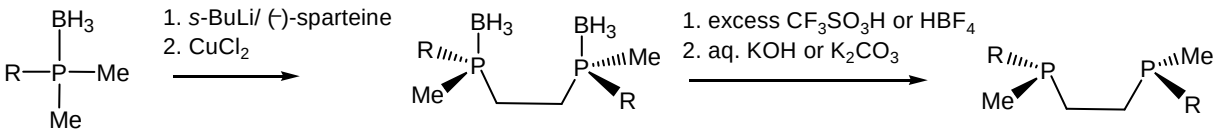
In 1995 D. Evans published an excellent method for asymmetric synthesis of C_2-symmetric *P*-chiral diphosphines based on the enantioselective deprotonation/oxidative coupling approach.[25] It was shown that prochiral dimethylarylphosphine boranes **46** may undergo enantiodifferentiating deprotonation of one methyl group using *s*-BuLi in the presence of (–)-sparteine[26] (**48**) as a chiral inductor. Addition of copper (II) pivalate to the lithiated species, which was generated after enantioselective metallation, led to formation of desired C_2-symmetric products **47** in moderate yields and 96-99% *ee* accompanied only by minor amounts of the *meso* forms.



46 **47** **48** (−)-Sparteine

Ar : Ph, *o*-An, *o*-Tol, 1-Np

Imamoto extended this methodology to some alkyldimethylphosphine boranes **49**. Enantiomerically pure C_2-symmetric bisphosphines BisP* **51** were obtained after direct recrystallization of the crude products followed by removal of the boranoto group by the Livinghouse method (CF_3SO_3H/KOH).[27] Cationic rhodium complexes of this novel family of bisphosphines were employed as catalyst precursors in asymmetric hydrogenation of α-(acylamino)acrylic derivatives as well as β-disubstituted ones and exhibited excellent enantioselectivities up to 99.9 % *ee*.[28]

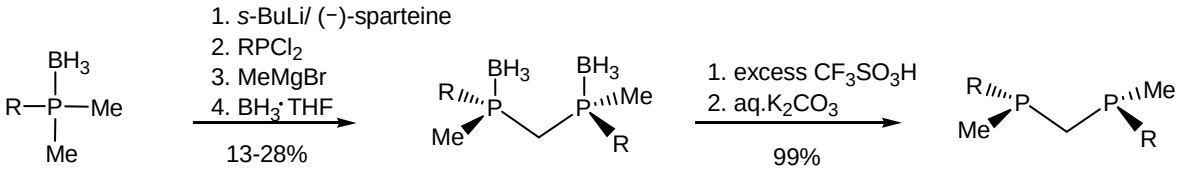


49 **50** **51**

R: *t*-Bu, Et_3C, Ad, Cp, Cy

Alkyldimethylboranes **49** are able to react with *s*-BuLi/(–)-sparteine followed by addition of various substituted alkyldichlorophosphines, methylmagnesium bromide and BH_3-THF to

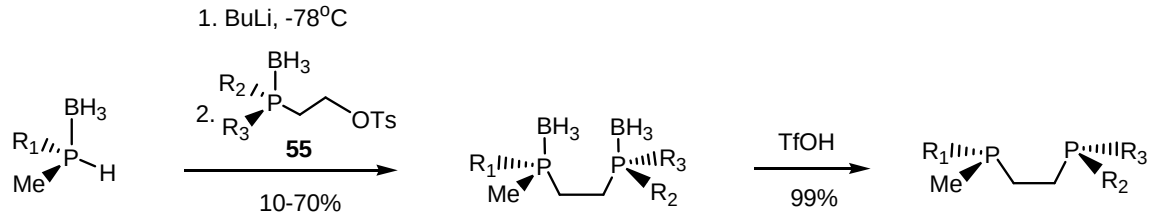
furnish optically active 1,1-diphosphine-borane **52**, albeit with contamination by its *meso* form, in ca. 1:1 ratio. After recrystallization from ethanol and deboronation with triflurometh anesulfonic acid, *P*-chiral diphosphines MiniPHOS **53** are accessible in almost quantitative yield. The C_2-symmetric environment of these ligands in combination with a bulky alkyl group and small methyl substituent is considered to be responsible for the high enantioselectivities in the hydrogenation of dehydroamino acids, hydrosilylation and copper catalyzed asymmetric Michael addition to α,β-unsaturated ketones.[29]



49 **52** **53**

R : *i*-Pr, Cy, *t*-Bu, Ph

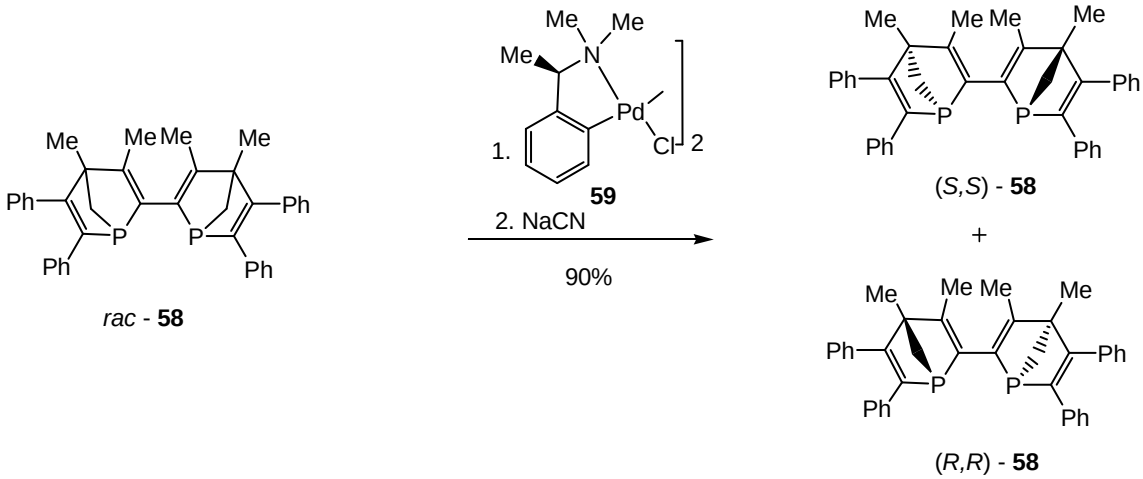
Unsymmetrical BisP* **57** were synthesized by lithiation of *P*-chiral secondary phosphine-boranes **54** followed by the nucleophilic substitution with *P*-chiral tosyl protected alcohols **55** derived from appropriate carboxylic acids. Removal of the boron moiety with triflurometh anesulfonic acid and *in situ* addition of bis(norbornadiene)rhodium(I) tetrafluoroborate afforded the desired catalyst precursors.[30] These unsymmetrical diphosphines were successfully applied for the asymmetric hydrogenation of dehydroamino acids and enamides to give up to 99.9% *ee*.



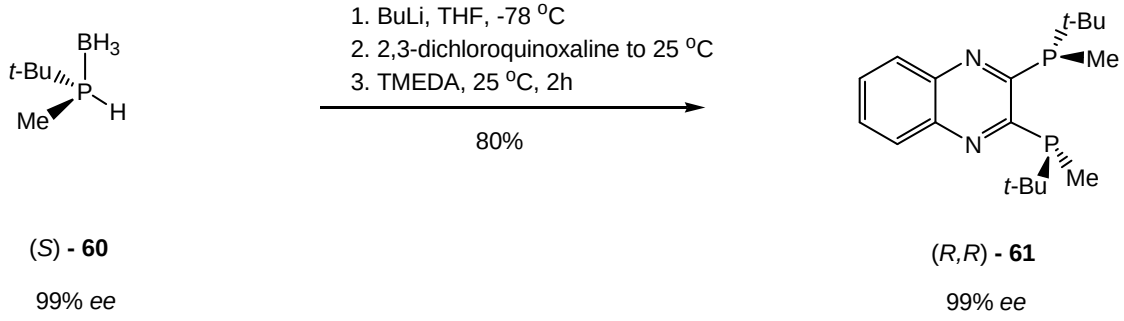
54 **56** **57**

R_1 : *i*-Pr, Cy, *t*-Bu, Ph, Ad, Cp

Racemic phosphine BIPNOR (**58**) was resolved by coordination of the optically active palladacycle **59**[31] to produce the corresponding diastereomeric complexes of **58**, which were separated by column chromatography and treated with sodium cyanide to furnish efficient ligands for asymmetric hydrogenation of various functional alkenes and ketones.[32] The phosphorus atoms are located at bridgehead positions of bicyclic systems, and therefore no racemization can occur.



P-chiral secondary phosphine-borane **60** was treated with BuLi to form a lithiated phosphine-borane species, which acts as a nucleophile towards 2,3-dichloroquinoxaline leading, after subsequent removal of borane by TMEDA, to the completely air-stable *P*-chiral ligand – QuinoxP (**61**). This ligand showed excellent enantioselectivities in Rh-asymmetric hydrogenation, 1,4-addition of arylboronic acids to α,β-unsaturated carbonyl compounds and also in Pd-catalyzed asymmetric alkylative ring-opening reactions.[33]



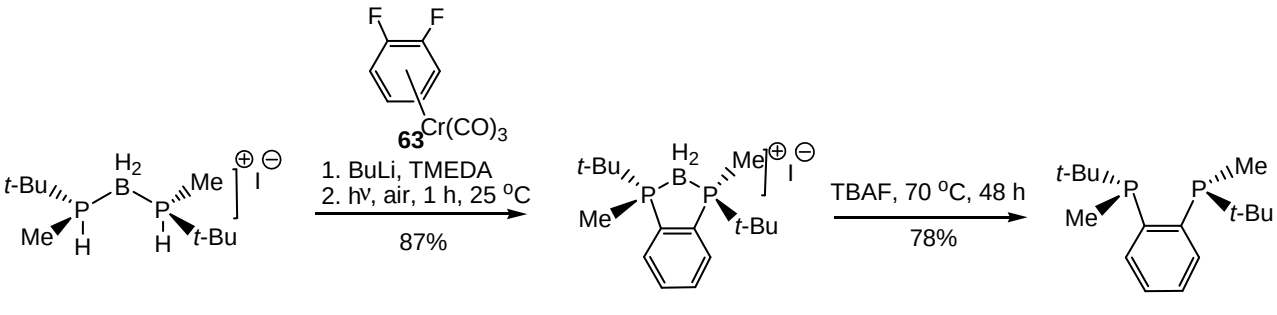
(*S*) **- 60**

99% *ee*

(*R*,*R*) **- 61**

99% *ee*

Quite recently, *P*-chiral sterically hindered *ortho*-phenylene-bridged diphosphine **65** was prepared in high optical yield (99% *ee*) by reaction of the *P*-chiral bis(phosphine)boronium salt **62** with tricarbonyl(difluorobenzene)chromium (**63**) and deboronation of **64** with TBAF in chlorobenzene.[34]

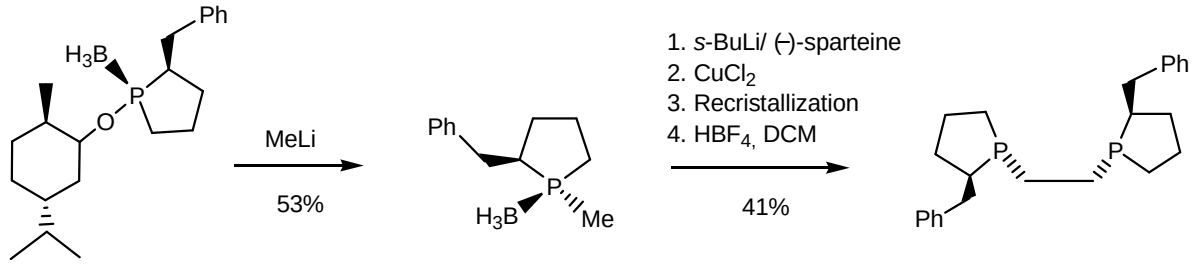


(*S*,*S*) - **62**
96% *de*

(*R*,*R*) - **64**
99% *ee*

(*R*,*R*) - **65**
99% *ee*

Enantiomerically enriched Mislow's menthyl phosphinate ester **66** was converted to methyl phospholane **67** with retention of configuration at phosphorus followed by Evans homo-coupling to afford *P*-chiral diphosphino-borane, which after recrystallization/deprotection with fluroboric acid gave a new *P*-chirogenic 1,2-bisphospholanoethane (*R*,*R*)-**68** in good yield. **68** was successfully employed in asymmetric hydrogenation for synthesis of pharmaceutical used CI-1008 (Pregabalin®).[35]



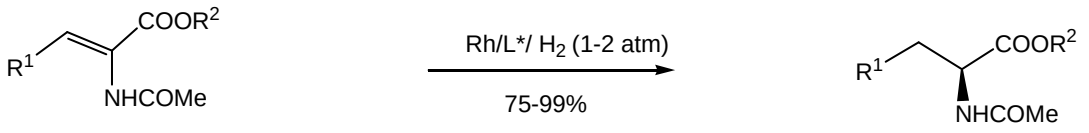
66
80% *de*

67
77 % *ee*

(*R*,*R*) - **68**
99% *ee*

1.4 Asymmetric Catalysis Involving *P*-Chiral Diphosphine Ligands

Nowadays, asymmetric synthesis using optically active phosphine ligands is an important field of synthetic organic chemistry. Hundreds of applications have been published including natural product synthesis, where an introduction of chirality plays a crucial role. Historically *P*-chiral diphosphines are frequently employed in asymmetric hydrogenation reactions of unsaturated bonds. Therefore, asymmetric hydrogenation of dehydroamino acids derivatives **69** has been become a common reaction to evaluate the efficiency of new synthesized chiral phosphorus ligands.[36]



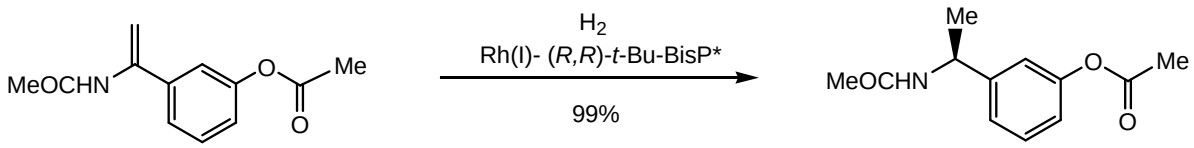
69

70

R^1 = Ph, Ar
R^2 = Me, H
R^3 = Me, Ph

L*	
t-Bu-BisP*	99.9% *ee*
t-Bu-MiniPHOS	99% *ee*
TangPHOS	99.9 % *ee*
BIPNOR	84% *ee*
QuinoxP	99.9 % *ee*

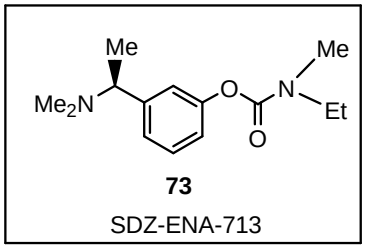
Asymmetric hydrogenation of 3-methoxy substituted enamide **71** was used as a key step to prepare acetylcholinesterase inhibitor SDZ-ENA-713 **73** catalyzed by rhodium complexes of BisP*.[36]



71

(*S*)**- 72**

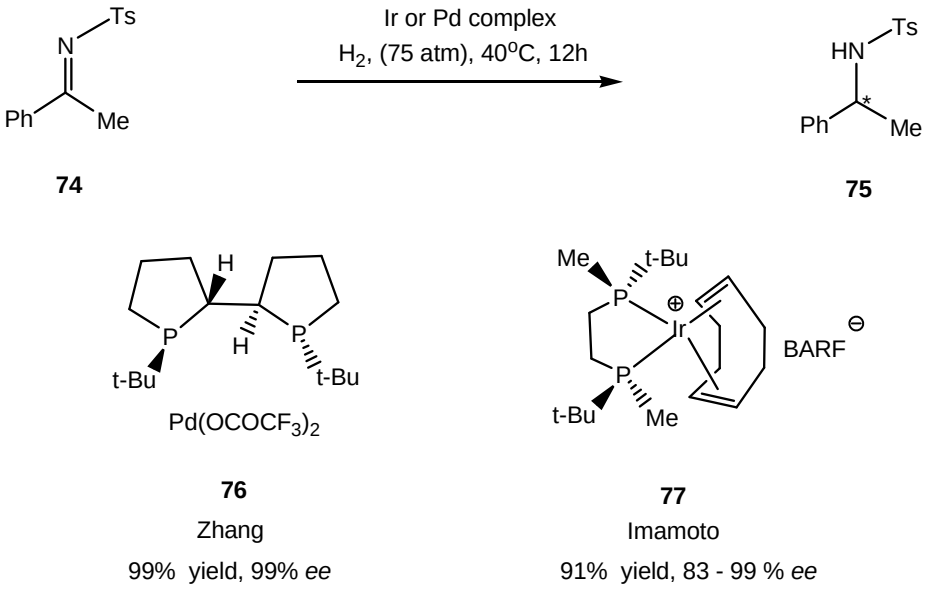
97% *ee*



73

SDZ-ENA-713

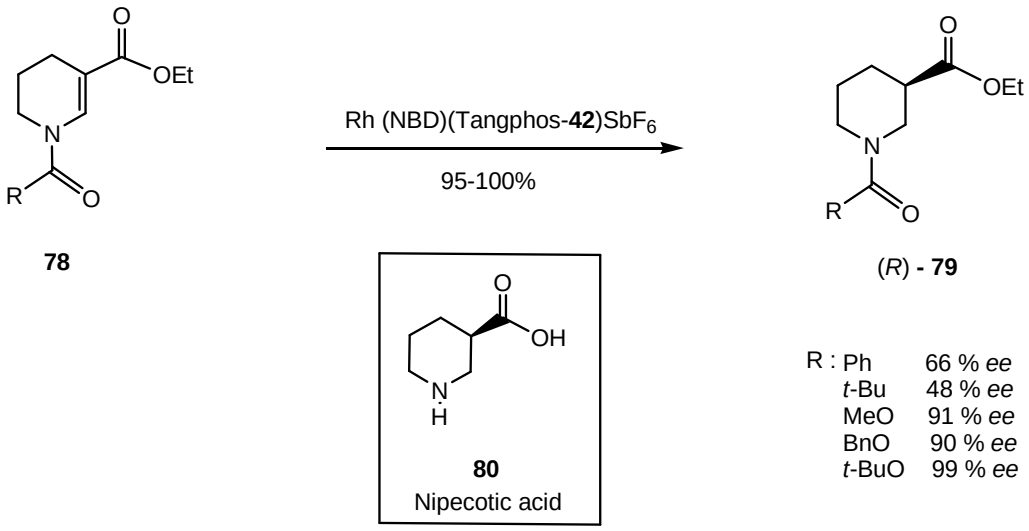
Zhang and Imamoto reported the palladium[37] **76** and iridium[38] **77** catalyzed asymmetric hydrogenations of acyclic imines, respectively, to give corresponding chiral amines in high yields and enantioselectivities up to 99% *ee*. Chiral amines are important intermediates in the synthesis of biologically active compounds.[39]



76
Zhang
99% yield, 99% *ee*

77
Imamoto
91% yield, 83 - 99 % *ee*

Zhang recently showed an application for asymmetric hydrogenation of vinylogous acyl amides **78** to give nipecotic acid derivatives **79** with moderate to high enantioselectivities. The enantiomeric excess was shown to be dependent on the nitrogen substituent. It is important to note that there is 100% chemoselectivity in hydrogenation of double bond while the carbonyl groups remained intact.[40]



78

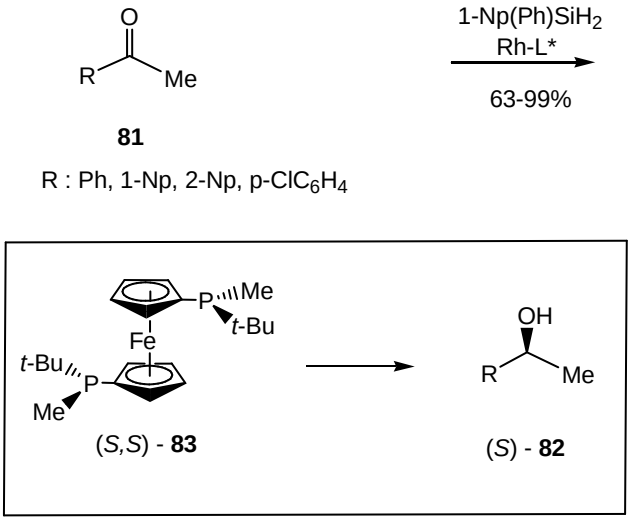
(*R*) **- 79**

80
Nipecotic acid

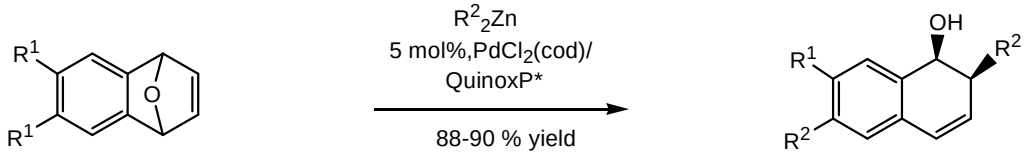
R : Ph 66 % *ee*
t-Bu 48 % *ee*
MeO 91 % *ee*
BnO 90 % *ee*
t-BuO 99 % *ee*

The asymmetric hydrogenation of ketones to generate chiral nonracemic secondary alcohols is an important transformation which has been extensively studied over two last decades.[40] Three chelating *P*-chiral diphosphines were tested for the highly enantioselective hydrogenation of various ketones **81** with α-naphtylphenylsilane as reducing agent.[42] Aryl methyl ketones, like dialkyl ones were hydrogenated with high level of enantioselectivity

leading to *R*-configurated secondary alcohols **82**. It is noteworthy that the chelating *P*-chiral diphosphine **83** showed excellent *ee*, but led to *S*-stereoisomers of **82**.[43]



Transition metal catalyzed enantioselective C-C bond formation is an important task in organic synthesis because of its impact on the synthesis of complicated natural products.[44] Imamoto reported a highly enantioselective alkylative ring opening of oxabenzonorbornadienes **84** with various dialkyl zinc derivatives catalyzed by palladium complex of QuinoxP* (**61**) leading to tetrahydronaphtalenes **85** in high yields.[33]



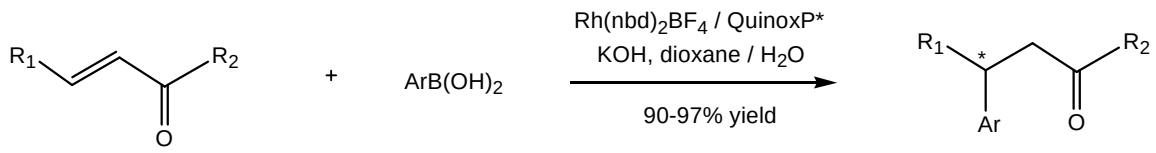
84

R^1 : H, F
R^2 : Me, Et

85

93.8-97.6 % *ee*

QuinoxP* (**61**) was also successfully employed in the Rh-catalyzed asymmetric 1,4-addition of arylboronic acids **87** into α,β-unsaturated carbonyls **86** to produce arylatated products **88** in high yields and with excellent *ee*, comparable with the BINAP system.[33]

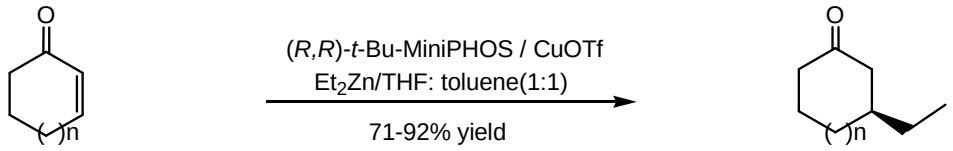


86 **87** **88**

Ar : Ph, 4-$MeOC_6H_4$

93.9-99.1 % *ee*

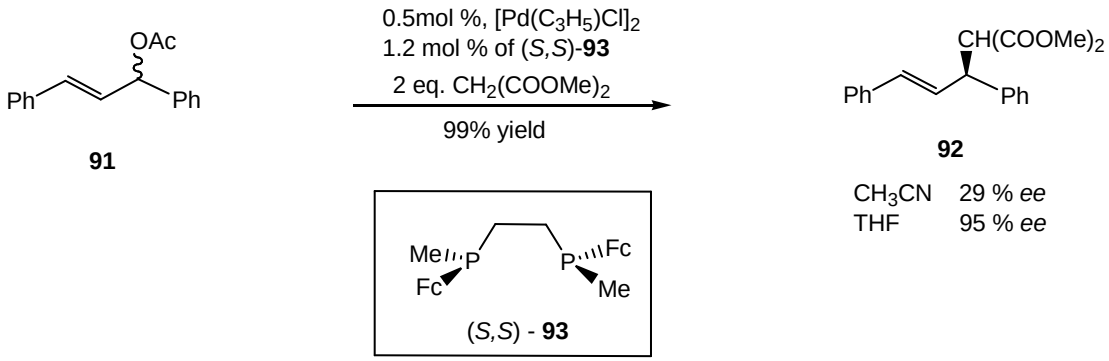
The copper-catalyzed asymmetric Michael addition of diethylzinc to α,β-unsaturated ketones **89** with MiniPHOS as ligand was performed by the Imamoto group. Corresponding addition products **90** were obtained in good yields and high enantioselectivities. No 1,2-addition was observed.[29]



89 **90**

n = 0, 43% *ee*
n = 1, 85% *ee*
n = 2, 75% *ee*

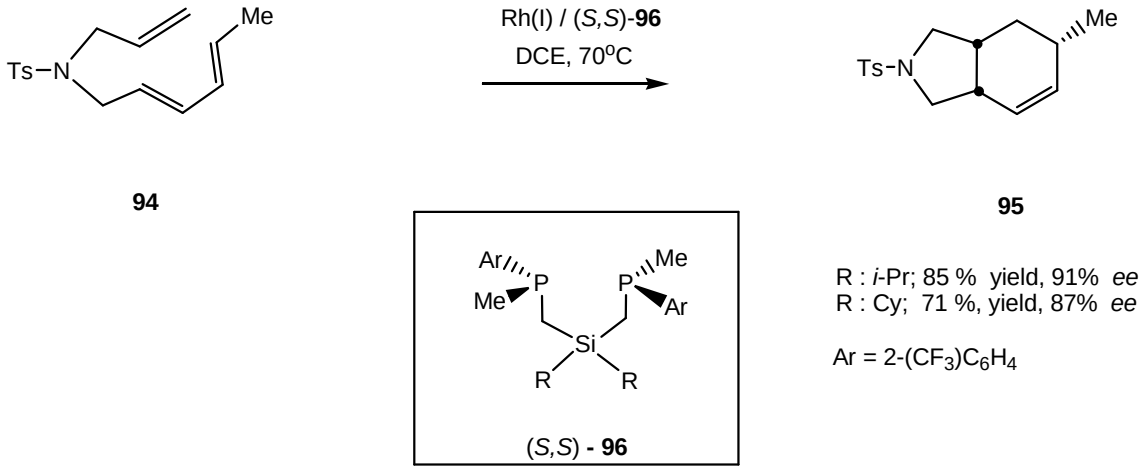
1,2-Bis(ferrocenylmethylphosphine)ethane [(*S*,*S*)-**93**] was employed in the palladium-catalyzed asymmetric alkylation of 1,3-diphenyl-2-propenyl acetate (**91**) and dimethyl malonate as nucleophile, which proceeded smoothly at room temperature in THF to give the substitution product **92** in quantitative yield with high enantioselectivity.[45]



91 **92**

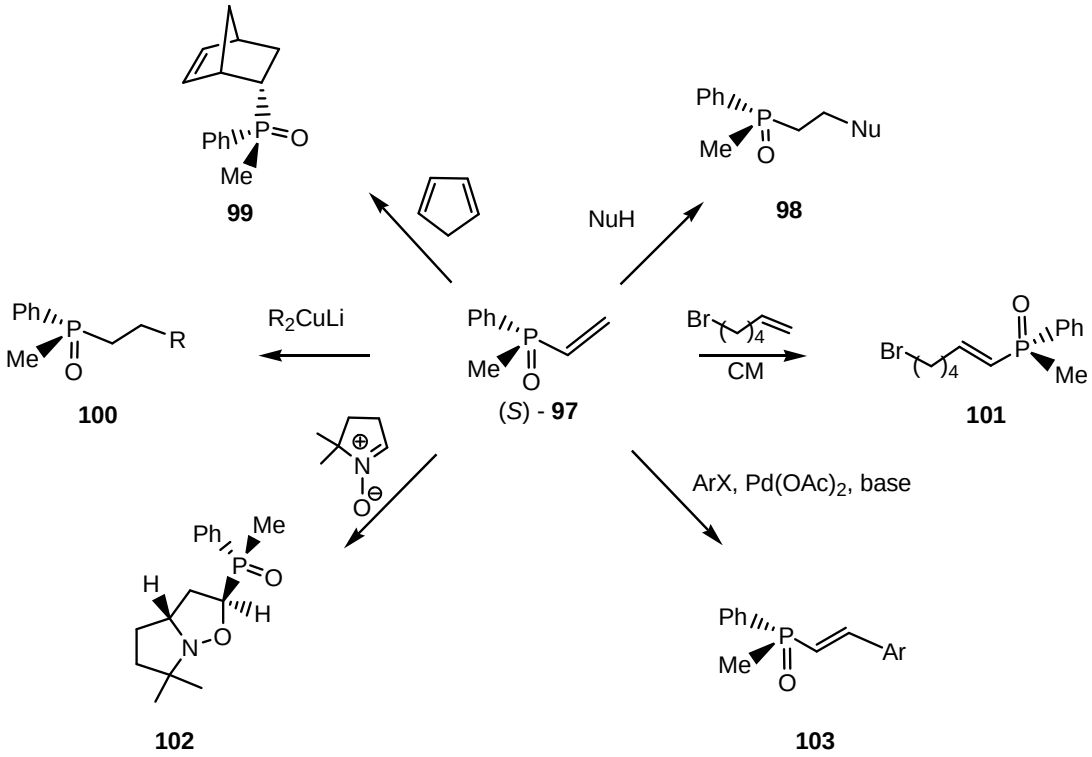
CH_3CN 29 % *ee*
THF 95 % *ee*

Asymmetric Diels-Alder cycloaddition of triene **94** and the hexahydroisoindole **95** in the presence of 2.5 mol % of the Rh(I)-complexes of *P*-chiral diphosphines **96** was reported by Livinghouse et. al. In all cases these cyclizations proceeded with excellent (>50:1) diastereoselectivities and respectable to very good *ee*'s.[46]



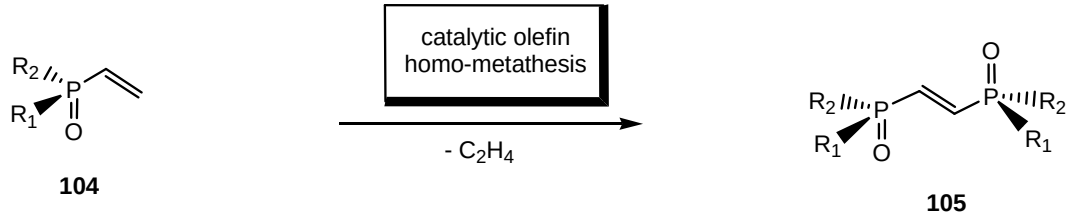
1.5 Novel *P*-Chiral Diphosphine Ligands for Asymmetric Synthesis

Enantiomerically pure vinylphosphine oxide **97** is a promising and versatile precursor to *P*-stereogenic ligands and can be used as a source of chirality in the P to C chirality transfer in conjugate addition reactions, Diels–Alder cycloaddition, [3+2]-cycloadditions, and coupling reactions (Scheme 2).[47]



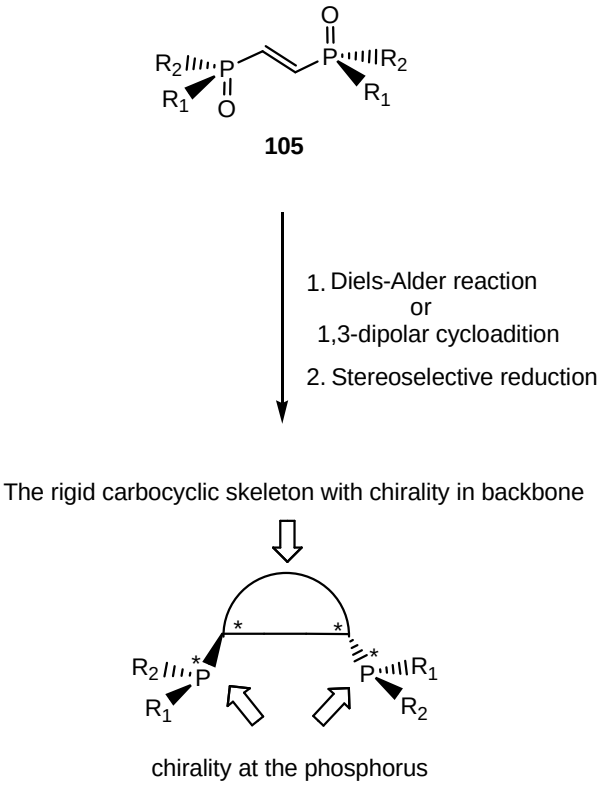
Scheme 2. Reactivity of *P*-stereognic vinyl phosphine oxide (*Sp*)-**97**

The availability of enantiomerically pure *P*-stereogenic vinylphosphine oxides **104** raises the question, in how far they may serve as substrates for catalytic olefin homometathesis presumably leading to enantiometrically pure *P*-stereogenic 1,2-diphosphanylethene dioxides **105**. (Scheme 3).



Scheme 3. Synthesis of *P*-stereogenic dienophiles **105**

Subsequently, the asymmetric cycloaddition reaction of *P*-chiral dienophiles **105** might lead to rigid carbocyclic systems bearing four centers of chirality simultaneously. A stereoselective reduction would afford a novel family of *P*-stereogenic diphosphines with two asymmetric phosphorus atoms standing *trans* one to another, which are close to chiral centers present in backbone of the ligand (Scheme 4).



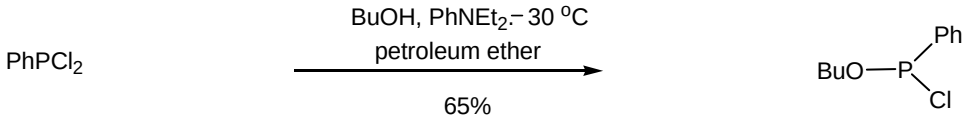
Scheme 4. Synthetic approach to to a novel family of *P*-stereogenic bidentate ligands

The transfer of both types of chirality should provide a more effective chiral environment at the site where enantioselectivity takes place. The aim of this project is the synthesis of new *P*-chiral bidentate phosphorus ligands and their first application in asymmetric catalysis.

2 Results and Discussion

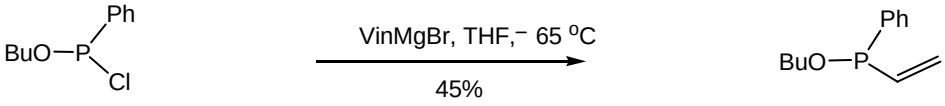
2.1 Synthetical Routes to *P*-Chiral (*Sp*)-Metyl(phenyl)vinylphosphine oxide (97)

The synthesis of *P*-chiral methyl(phenyl)vinylphosphine oxide (**97**) was accomplished in four steps starting from commercially available dichlorophenylphosphine (**106**). Firstly, selective nucleophilic displacement of one chlorine atom takes place by reaction of **106** with butanol in the presence of *N*,*N*-diethylaniline as HCl acceptor at –30 °C in dry petroleum ether to give *rac*-**107** in 65% yield.[48]



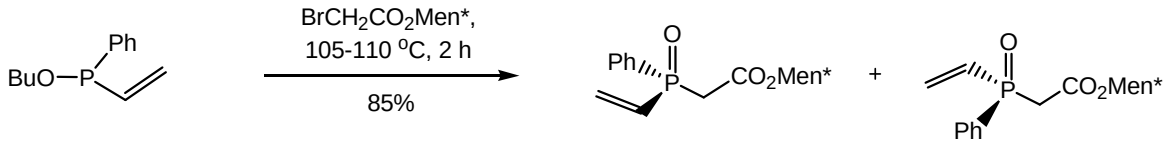
106 *rac*-**107**

The *rac*-butylchlorophenylphosphonite (**107**) must be used for the next step without purification (distillation), where it undergoes addition of Normant's reagent at – 65 °C to give the *rac*-butylphenylvinylphosphinite (**108**) in 45% yield. The reaction is highly dependent on the temperature and the rate of the addition of Grignard reagent.[49] Lower yields in this reaction can presumably be explained as the conjugate addition of organometallic reagent to double bond of desired *rac*-**108**.



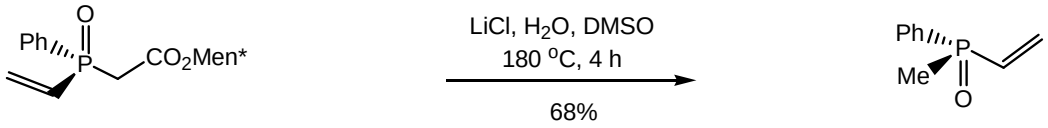
rac-**107** *rac*-**108**

The Michaelis-Arbuzov reaction[50] of *rac*-butylphenylvinylphosphinite (**108**) with (–) menthyl bromoacetate affords an equimolar mixture of the two diastreoisomeric menthyl (phenylvinylphosphinyl) acetates (*Sp*)-**109** and (*Rp*)-**109** in 85% yield. After washing the reaction mixture with cold benzene and several recristallizations until constant optical rotation value, (*Sp*)-**109** can be obtained in 100% diastereomeric and thus enantiomeric purity.[51]



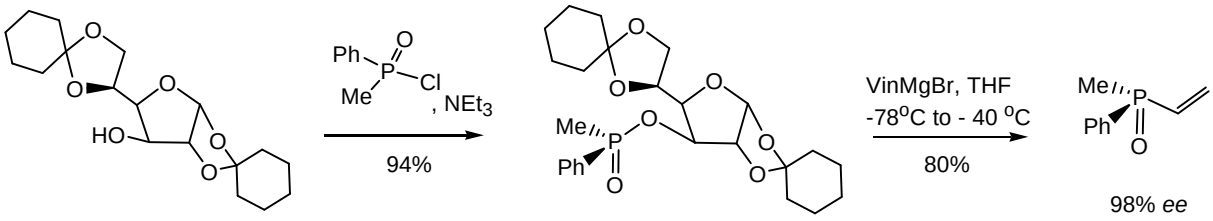
rac-**108** (*Sp*)-**109** 100% *de* (*Rp*)-**109**

The *P*-chiral **109** was submitted to the Krapcho decarboxylation with LiCl in wet DMSO to produce the desired enantiomerically pure (*Sp*)-methylphenylvinylphosphine oxide (**97**) in 68% yield.[52] The reaction proceeds smoothly in DMSO at 180 °C over 4 hours. Vacuum distillation of (*Sp*)-**97** is advised, since column chromatography proved to be insufficient.



(*Sp*)-**109** 100% *de* (*Sp*) **- 97** 98% *ee*

Recently, Hii et. al. reported the synthesis of *P*-chiral vinyl phosphine oxides by reaction of 1,2:5,6-di-*O*-cyclohexylidene-D-glucofuranose (DCG) (**110**) with substituted phosphinic acid chlorides followed by diastereomeric separation and reaction with vinyl magnesium bromide.[53] In the case of methylphenylphosphinic acid chloride and DCG two diastereomers were obtained as viscous crystalline material. Unfortunately, the separation of stereoisomers by column chromatography in relative large scale (up 2 g) provides difficulties. The reaction of (*Sp*)-(**111)** with vinyl magnesium bromide was conducted at – 78 °C to – 40 °C to give (*Rp*)-**97**. This reaction is accomplished by diluted conditions preventing a Michael addition of the Normant reagent to the double bond of formed vinyl phosphine oxide.



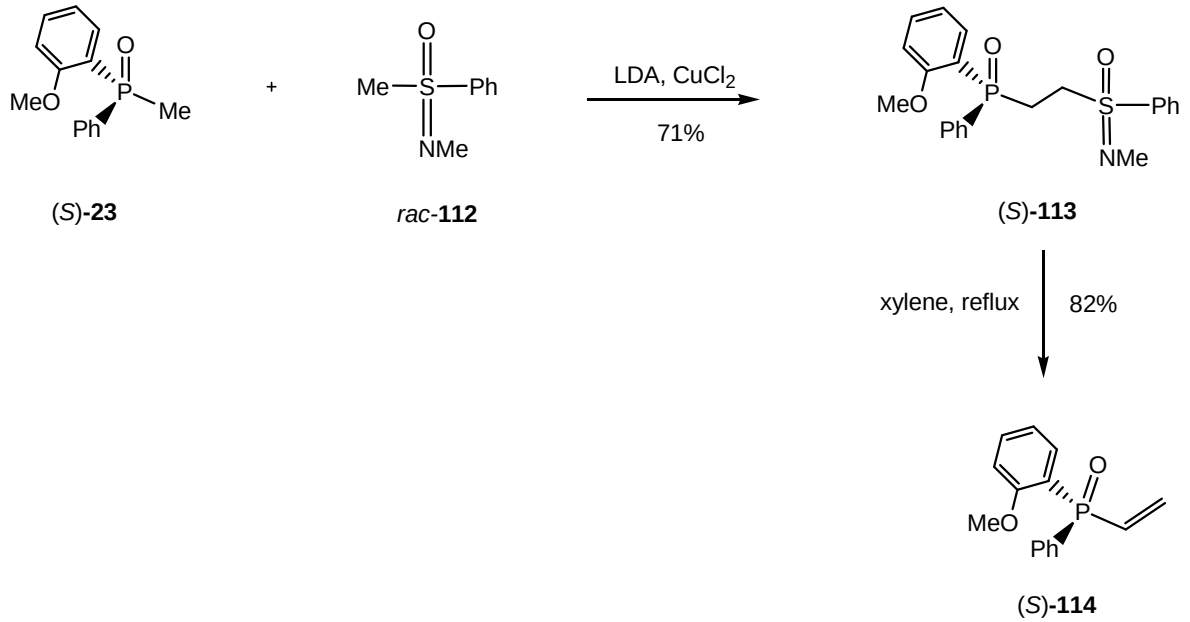
110 (*Sp*)-**111** 98% *ee* (*Rp*)-**97**

Both steps of this synthetic sequence provided several experimental difficulties. Therefore (*Sp*)-**97** was always obtained by Krapcho decarboxylation of the (*Sp*)-**109**.

2.2 A New Approach to *P*-chiral (S*p)*-metyl(phenyl)vinylphosphine oxide (97)

A very limited access to *P*-chiral vinylphosphine oxides in enantiomerically pure form led to development of a novel methodology using stable phosphine-boranes as intermediates.

The introduction of a vinyl group in organophosphorus compounds was recently applied by the Imamoto group. The *P*-chiral anisylphenylvinylphosphine oxide (*S*)-**114** was prepared by oxidative cross-coupling of (*Sp*)-(*o*-methoxyphenyl)methylphenylphosphine oxide (*S*)-**23** with racemic *N*,*S*-dimethyl-*S*-phenylsulfoximine (**112**) conducted by a modification of a Mislow procedure for the dimerization of phosphine oxides.[16] **113** was obtained as an inseparable mixture of diastereomers, which after heating to reflux furnished optically pure vinylphosphine oxide (*S*)-**114** as a stable crystalline solid.

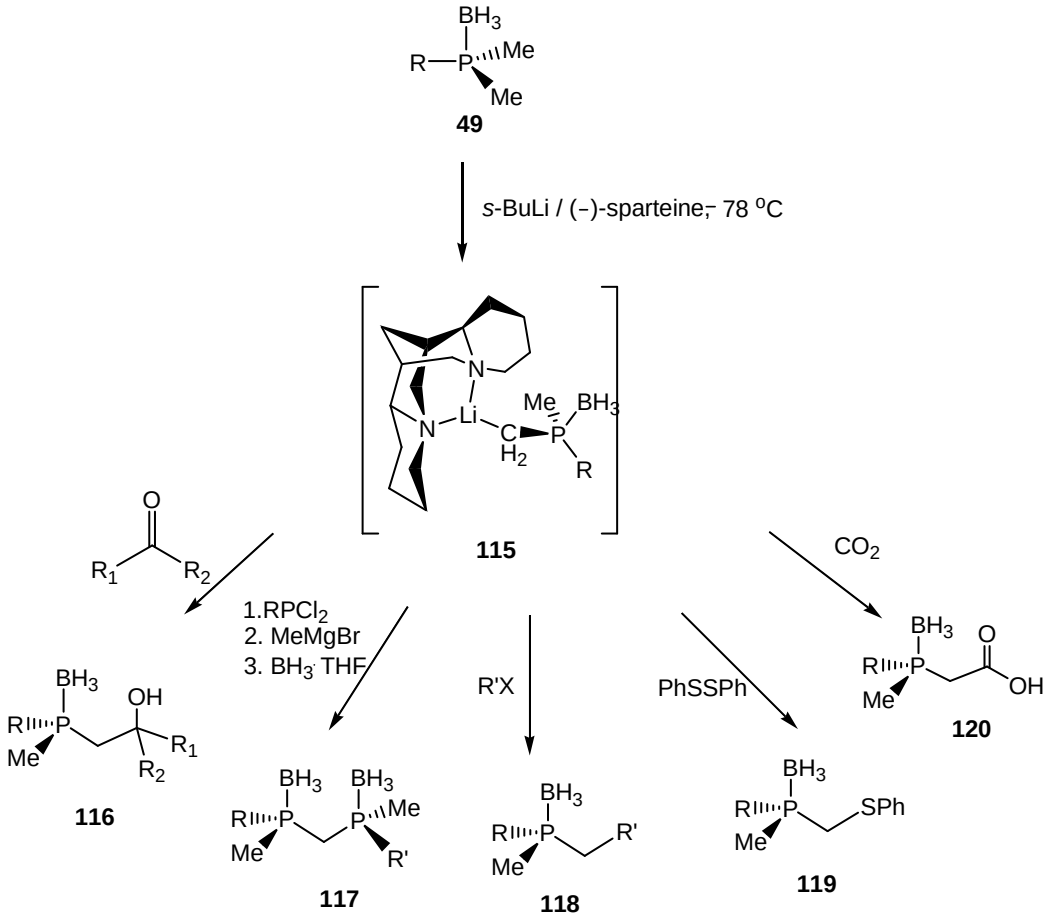


(*S*)-**23** *rac*-**112** (*S*)-**113** (*S*)-**114**

During the last decade, Imamoto et. al. also developed a versatile method for the preparation of a diverse set of achiral and chiral organophosphorus compounds starting from alkyl or aryl substituted dimethylphosphine boranes with the overall formula $RP(BH_3)Me_2$.[36] These can be easily synthesized from commercially available alkyl or arylphosphorus dichlorides ($RPCl_2$) by the reaction with MeMgI in diethyl ether or THF. Under mild conditions (– 78 ° C) by action of an appropriate lithium base, one of the methyl group in $RP(BH_3)Me_2$ is

deprotonated and the *C*-anionic nucleophile formed, reacts with alkylhalogenides, carbonyl compounds, phosphorus and sulfur electrophiles leading to a wide range of interesting phosphorus compounds. In the presence of (–)-sparteine as a chiral inductor an enantioselective deprotonation is possible, which allows formation of enantiomerically enriched or enantiomerically pure organophosphorus compounds by using the same deprotonation-alkylation sequence (Scheme 5).[24]

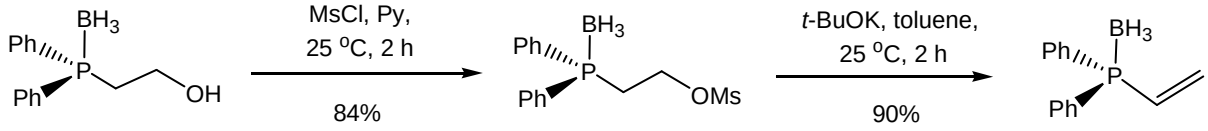
Previously, Imamoto reported that mesylated or tosylated alcohols derived from carboxylic acids **120** undergo nucleophilic displacement by reaction with lithiated secondary phosphine-boranes.[30] Presumably, a mesylate, which can be obtained from **120** undergoes elimination by action of a base under mild conditions leading to a vinylphosphine borane. Vinylphosphine boranes are not studied so far.*[55]



Scheme 5. Synthetic utility of prochiral phosphine-boranes **49**[36]

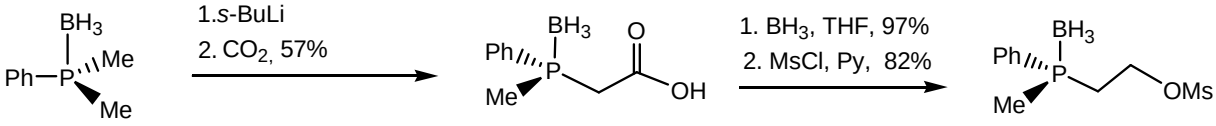
* Only one publication was found.

To test this suggestion, achiral diphenylphosphinoethanol borane (**121**) as a model substrate was reacted with mesyl chloride leading to appropriate mesylate in good yield. Surprisingly, mesylate **122** undergoes elimination within 2 hours at 25 °C to give diphenylvinylphosphine borane (**123**) in 90% yield. **123** was found to be unstable at 25 ºC. Obtained as a viscous liquid, it becomes a white solid on the standing. However, in a refrigerator at –25 ºC, it can be stored as a solution in dichloromethane for several months without decomposition.



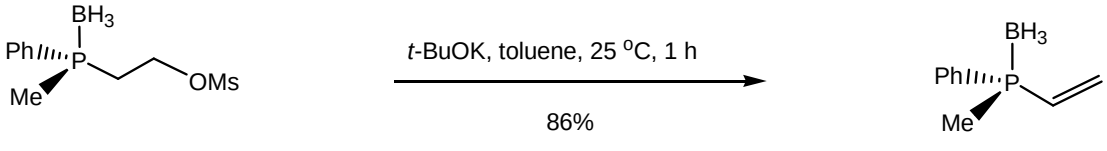
121 **122** **123**

To assess the previously unknown *rac*-methylphenylvinylphosphine borane, dimethylphenylphosphine borane (**124**) was deprotonated with *s*-BuLi following by reaction with carbon dioxide to give *P*-chiral carboxylic acid *rac*-**125** in 57% yield.[30] Reduction of carbonyl function in *rac*-**125** can be achieved by use of lithium aluminium hydride or borane THF complex at 25 °C. The desired alcohol was obtained in 97% yield and treated with mesyl chloride/pyridine leading to appropriate mesylate *rac*-**126** in 82% yield.



124 *rac*-**125** *rac*-**126**

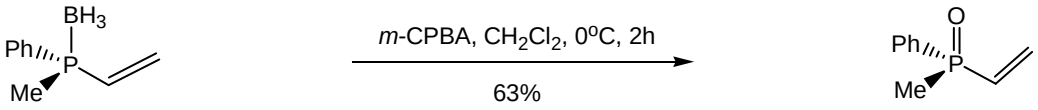
rac-**126** undergoes elimination within 1 hour at 25 °C by use of potassium *tert*-butoxide as the base to give *rac*-methylphenylvinyl phosphine borane (**127**) in 86% yield. This compound was found obviously more stable at 25 °C than **123**, but must still be stored as a solution in dichloromethane at –25 °C.



rac-**126** *rac*-**127**

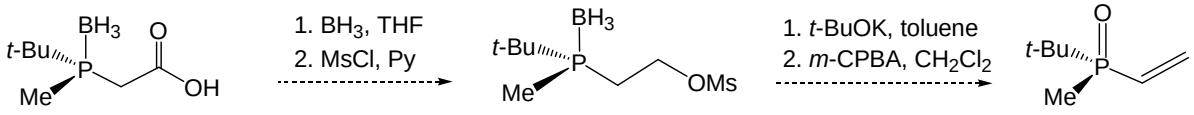
Recently, Imamoto et. al. published an excellent method for the synthesis of phosphine oxides by reaction of phosphine-boranes by the use of *m*-CPBA.[55] Some of *P*-chiral phosphine-boranes were oxidized with complete retention of configuration at phosphorus. Remarkably,

the *rac*-**127** reacts under these conditions leading to the desired racemic vinylphosphine oxide **97** in 63% yield. No oxidation of the double bond was detected.



rac-**127** *rac*-**97**

Since the combination of *tert*-butyl and methyl substituents at the asymmetric phosphorus atom plays a crucial role in the ligand design, this synthetic sequence can certainly be used for the synthesis of *P*-chiral vinyl phosphine oxide **130**, which would be an interesting precursor to new *P*-stereogenic diphosphines.



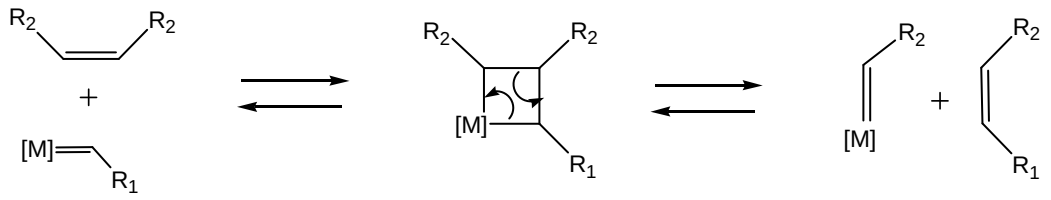
(S)-**128** *(S)*-**129** *(S)*-**130**

2.3 Olefin Metathesis

Although double-bond scrambling reactions were initially reported in the mid-1950s, it was not until several years later that Calderon and co-workers recognized that both ring-opening polymerization and the disproportionation of acyclic olefins constituted the same type of reaction. The term ”olefin-metathesis” was coined in 1967, which is currently understood as the metal-catalyzed redistribution of carbon-carbon double bonds.[56]

From the mid-1950 to the early 1980s, olefin metathesis was accomplished with poorly defined, multicomponent homogeneous and heterogeneous catalyst systems. Some of the classic combinations include WCl_6/Bu_4Sn, $WOCl_4/EtAlCl_2$, MoO_3/SiO_2 and Re_2O_7/Al_2O_3, among many others. The utility of these catalysts, however, was limited by the harsch reaction conditions and strong Lewis acids that they required making them incompatible with most functional groups. Ultimately, in 1971 Y. Chauvin postulated a mechanism of metathesis which was consistent with the experimental evidence at that time. According to

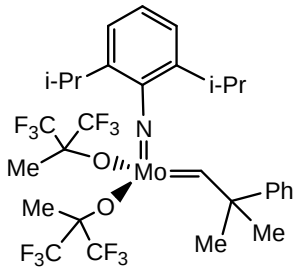
this mechanism metathesis proceeds by [2+2] cycloaddition between carbon-carbon double bond and metal carbene complex followed by cycloreversion remaining the generally accepted mechanism today (Scheme 6).[57]



Scheme 6. The mechanism of metathesis (Chauvin 1971)

This work on the mechanism initiated subsequent efforts to synthesize alkylidene and metallacylobutane complexes and led to the discovery of the first single component homogeneous catalysts for olefin metathesis until early 1980s. These new species included $(CO)_5W{=}CPh_2$, bis(cyclopentadienyl)titanacyclobutanes, tris(aryloxide)tantalacyclobutanes, various dihaloalkoxide –alkylidene complexes of tungsten[58] and titanocene derivates.[59]

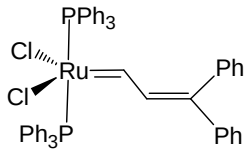
In the 1990 R. Schrock et. al. reported the synthesis of novel molybdenum imido alkylidene complexes and their reactivity towards acyclic olefins.[60] The alkylidene **131** was shown to be extremely active for synthesis oxygen and nitrogen heterocycles by ring-closing metathesis.[61] However, this catalyst and others based on the early transition metals are limited by the high oxophilicity of the metal centres, which renders them extremely sensitive to oxygen and moisture.



131

Schrock 1990

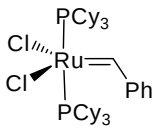
In 1992 R. Grubbs et. al. published the first ruthenium based olefin metathesis catalyst **132**, which was used for the polymerization of norbornene.[62] The discovery of **132** initiated a very fast progress in the development of new ruthenium alkylidene catalysts for alkene metathesis, which can tolerate many of common functionalities.[64]



132

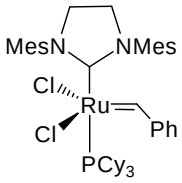
Grubbs 1992

In 1995 Grubbs et.al. reported the first highly active ruthenium catalyst **133**, the synthesis of which involved the reaction of $(Ph_3P)_3RuCl_2$ in an alkylidene transfer from phenyldiazomethane.[62] In 1999, Herrmann[63] and others[64] published the synthesis of a range of *N*-heterocyclic ruthenium complexes **134**, **135** by substitution reactions of the phosphine ruthenium benzylidene complex with imidazolin-2-ylidene groups. These nonlabile, sterically demanding ligands, which possess strong σ-donor and weak π-acceptor properties, stabilize both the 16-electron complexes and the highly electron deficient metathesis intermediates, resulting in pre-catalysts with increased metathesis activity as compared to the parent phosphine complexes.



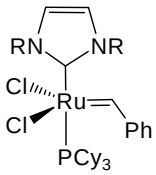
133

Grubbs 1995



134

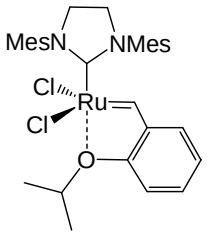
Grubbs 1999



135

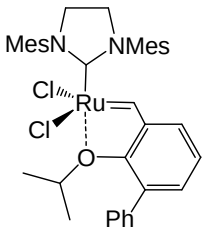
Herrmann, Nolan, Fürstner, Grubbs 1999

More recently, Hoveyda and Blechert introduced ruthenium complexes, **136**[65] and **137**[66], with chelating isopropoxybenzylidene ligands, which augment the catalyst stability and reactivity, and can be conveniently applied in a broad spectrum of metathesis reactions. In addition, Grela reported the nitro Hoveyda-Grubbs complex **138**.[67] These novel chelates are especially efficient in the cross-metathesis of olefins with electron-poor double bonds.



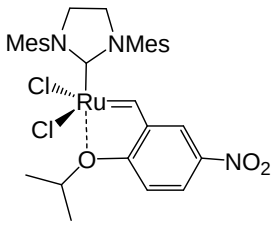
136

Hoveyda and Blechert 1999



137

Blechert 2002



138

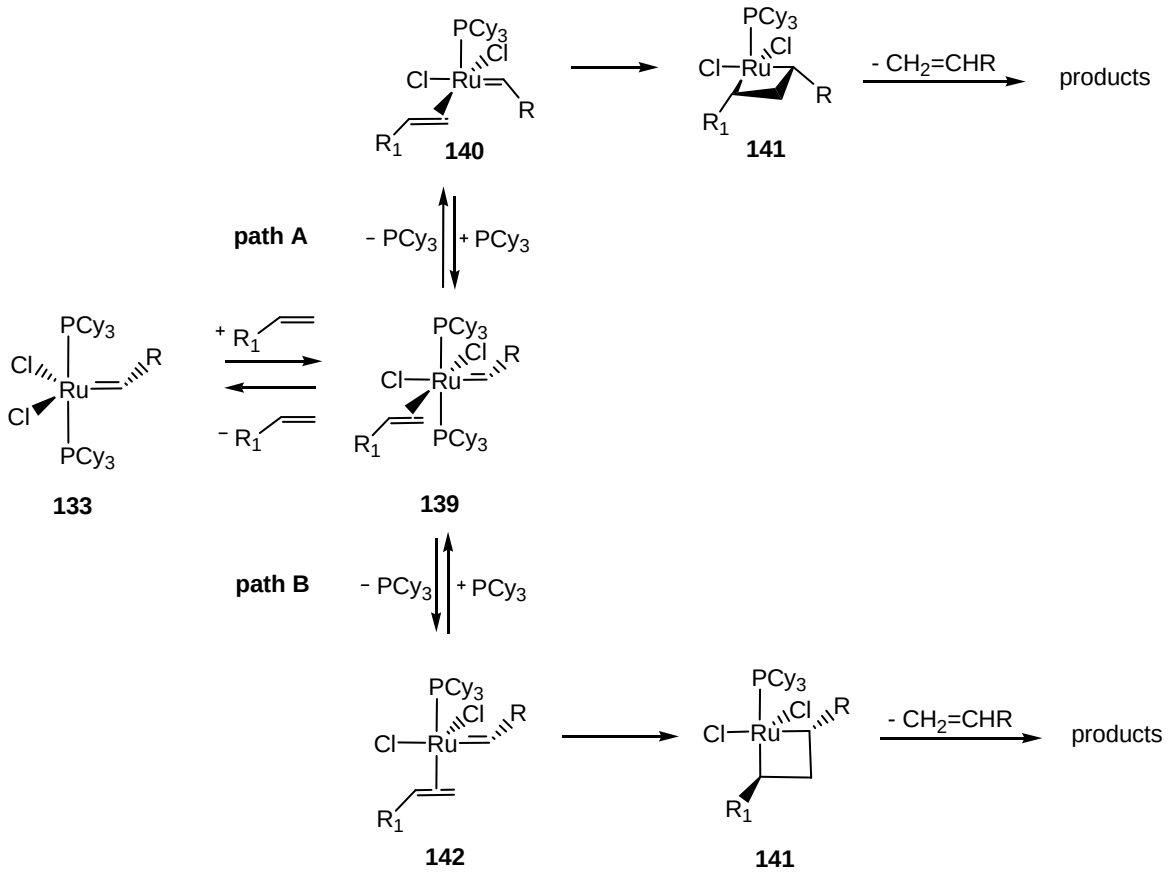
Grela 2002

For this significant developments in the field of homogeneous metathesis R.H. Grubbs, R. R. Schrock and Y. Chauvin were awarded Nobel Prize in 2005.[68]

Nowadays there are many kinds of alkene metathesis processes such as ring-closing metathesis (RCM),[69] enyne metathesis,[70] cross metathesis,[71] all of which are subject of current research and are frequently applied in the target-oriented synthesis of complicated organic compounds important for natural products synthesis,[72] materials science and other fields. Through these reactions, olefin metathesis provides a route to unsaturated organic molecules that are often challenging or impossible to prepare by other means.

2.4 Mechanism of Alkene Metathesis

During last two decades the Grubbs group[73] and some others[74] extensively studied the mechanism of alkene metathesis involving metal alkylidenes. Based on extensive kinetic studies and observed activity trends, it was proposed that the first step includes the coordination of the olefin to the metal center, presumably *cis* to the alkylidene. In one possible path (**A**), phosphine dissociation along with carbene rotation in order to generate 16-electron intermediate **140**, in which the olefin remains *cis* to the alkylidene. This intermediate has required geometry for metallacycle formation, then undergoes metallocyclobutane formation *cis* to the bound phosphine, followed by cycloreversion to release the metathesis products. An alternative path (**B**) involves phosphine dissociation and rearrangement of the olefin *trans* to the remaining phosphine. This intermediate **142** then undergoes metallocyclobutane formation *trans* to the phosphine. Although pathway (**B**) was initially disfavoured because of reversibility considerations, it is currently being reconsidered in more detail.[75]

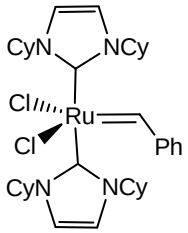


Scheme 7. Mechanism of alkene metathesis proposed by R.H. Grubbs

The activity of catalysts with overall formula $L_2X_2Ru=CHR$ is highly dependent on the identity of the X ligands. Whereas catalyst activity increases with larger and more electron-donating phosphines, it decreases with larger and more electron-donating halides. These trends can be rationalized with the proposed mechanism. One of the contributions of the phosphine ligands is *σ*-donation to the metal center, which promotes formation of the mono-(phosphine) olefin complex by facilitating phosphine dissociation and stabilizing the vacant trans site in **133**. Perhaps even more importantly, *σ*-donation helps stabilize the 14-electron metallacyclobutane intermediate. In these ways, catalyst activity is directly related to the electron-donating ability of the phosphine ligands. The steric bulk of the ligands may also contribute to phosphine dissociation by destabilizing the crowded bis(phosphine) olefin complex. In retrospect, the choice of PCy_3 was fortunate, because those phosphines that are more basic or bulkier than PCy_3 result in unstable complexes. In contrast to the trend for phosphines, the halide ligands correlate with decreasing activity as they become larger and more strongly electron donating, in the order Cl > Br >> I. Since the incoming olefin may initially bind *trans* to a halide, a more electron-donating halide should weaken the ruthenium-

olefin bond and disfavor olefin coordination. These small changes in the steric and electronic character of the X- and L-type ligands combine to influence olefin binding, phosphine dissociation, and the stability of intermediates, which results in large variations of catalyst activity.

It is well known that, compared to phosphines, *N*-heterocyclic carbene ligands[76] are stronger σ donors and much less labile. After the Herrmann report of the bis(substituted) complex **142** [77] it was found that the monosubstitution of one of PCy_3 ligand in **133** by unsaturated or saturated mesityl-substituted N-heterocyclic carbene provides more active catalysts.[63,64]

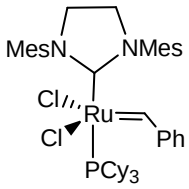
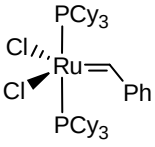
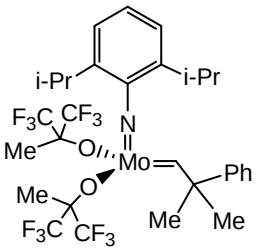


142

In the mixed-ligand complexes **134** and **135**, the more strongly electron-donating carbene ligand might enhance the dissociation of the more labile *trans* phosphine from the metal center. Then, by virtue of its steric bulk and electron-donating properties, the same ligand should more effectively stabilize the electron-deficient intermediates and promote olefin metathesis.

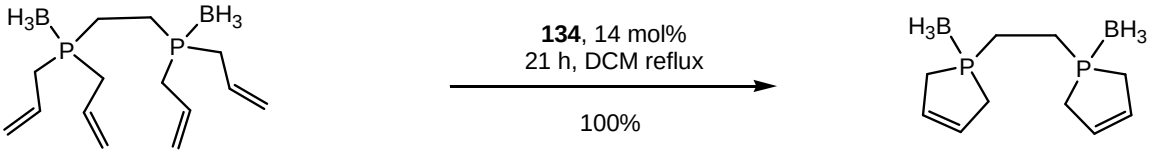
2.5 Olefin Cross-Metathesis

Olefin cross-metathesis (CM) is a convenient route to functionalized and higher olefins from simple alkene precursors. Recently, Grubbs published general classification of the reactivity terminal olefins in alkene cross-metathesis.[78]

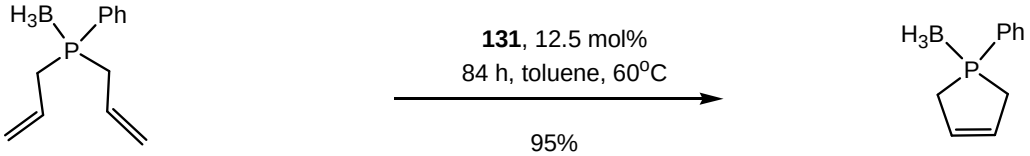
	 **134**	 **133**	 **131**
Type I **(fast homodimerization)**	terminal olefins, 1^{o} allylic alcohols, esters, allyl halides, allyl silanes, protected allyl amines, allyl boronotes	terminal olefins, 1^{o} allylic alcohols allyl boronates, allyl chlorides, ethers	terminal olefins, allyl silanes
Type II **(slow homodimerization)**	styrenes (large o-substit.), acrylates, acrylamides, vinyl ketones, unprotected allylic alcohols	styrene, 2^{o} allylic alcohols, vinyl boronates	styrene, allyl stannanes
Type III **(no homodimerization)**	1,1-disubstituted olefins, non-bulky trisub. olefins, vinyl phosphonates, phenylvinyl sulfone, 3^{o}allylic alcohols	vinyl siloxanes	acrylonitrile, 3^{o}allyl amines
Type IV **(spectators CM)**	vinyl nitro olefins, trisubstituted allyl alcohols (protected)	1,1-disubstituted olefins, disub.unsatureted carbonyls, 3-allyl amines(protected)	1,1-disubstituted olefins

Scheme 8. Classification of olefins by R.H. Grubbs, 2003.[78]

Although the second-generation Grubbs ruthenium complex **134** in general possesses a very good application profile the phosphine-free catalyst **136**, recently introduced by Hoveyda et al.[65] displays even higher reactivity toward electron-deficient substrates such as acrylonitrile, fluorinated olefins, and vinyl sulfones.[79] Recently, also some examples of metathesis of some phosphine oxides and phosphine boranes have been appeared in the literature.[80] The ring-closing metathesis of achiral bis-(alkenyl)phosphine boranes in the presence Ru-and Mo-based catalysts were applied for synthesis of unprotected and borane-protected cyclic phosphines **145** as possible precursors for the preparation of chiral phosphine ligands.[81] It is important to note that the cylization of unprotected diallylphenylphosphine (**146**) proceeded in 95% yield only with Schrock molybdenum catalyst **131**, whereas ruthenium catalysts were not suitable to achieve any conversion. This observation confirms the hypothesis by Grubbs that the presence of the free phosphine disfavours the equilibrium for olefin binding to the catalyst in the first step of the dissociative mechanism.

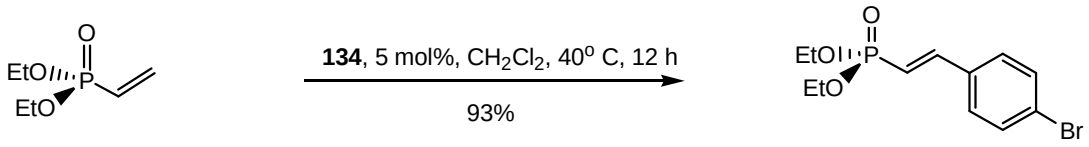


144 **145**



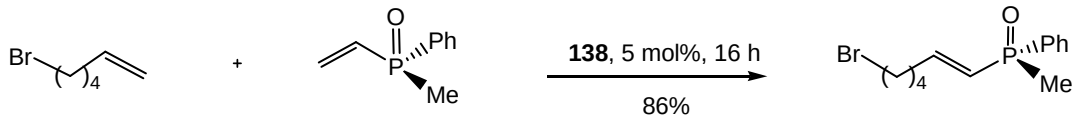
146 **147**

Grubbs reported that substituted styrenes can be coupled with diethylvinylphosphonate (**148**) to generate α,β–unsaturated phosphonates in excellent yield using catalyst **134**.[82] Importantly, no dimerization of the vinylphosphonate was detected by ^{1}HNMR allowing for selective CM.

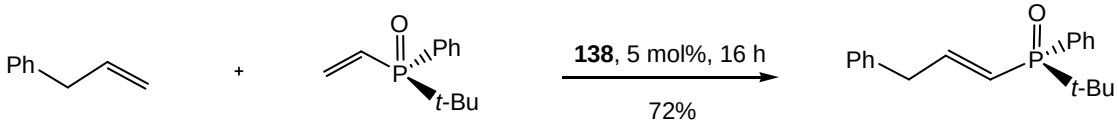


148 **149**

Grela and Pietrusiewicz reported that *P*-chiral vinylphosphine oxides (*Sp*)-**97** and (*Rp*)-**153** undergo olefin metathesis with terminal alkenes in high yields in presence of nitro-Hoveyda-Blechert precatalyst **138** exclusively leading to (*E*)-isomers without racemization at phosphorus.[83]

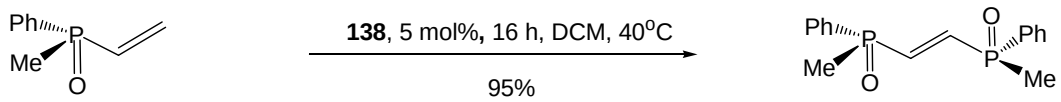


150 (*Sp*)-**97** (*Sp*)-**151**



152 (*Rp*)-**153** (*Rp*)-**154**

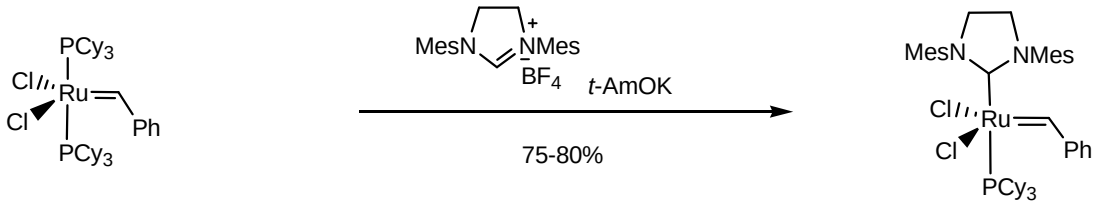
In addition, this paper mentioned that the *P*-chiral vinylphosphine oxide (*Sp*)-**97** undergoes homo-coupling without racemization at phosphorus in the presence of 5 mol% the nitro-catalyst **138** leading to homochiral 1,2-diphosphanylethylene dioxide (*Sp,Sp*)-**155** in 95 % yield.[83], which was curiously not reproducible.



(*Sp*)-**97** (*Sp,Sp*)-**155**

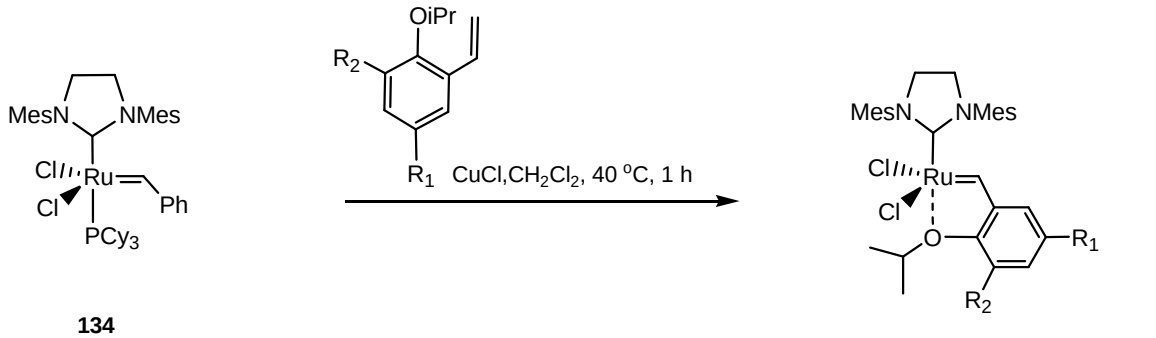
2.6 The Homo-Coupling of *P*-Chiral Vinylphosphine Oxide 97 via Catalytic Olefin Cross-Metathesis

To investigate homo-coupling of (*Sp*)-**97** in more detail with an emphasis on the choice of precatalyst and reaction conditions, some of the modern olefin precatalysts were synthesized by reported the literature procedures. Grubbs-II catalyst **134** was synthesized from commercially available Grubbs-I carbene **133**, by the use an improved method with *tert*-potassium amylate in hexane as base.[84] This reaction proceeds smoothly at 25 °C giving a high yield of **134**.



133 **134**

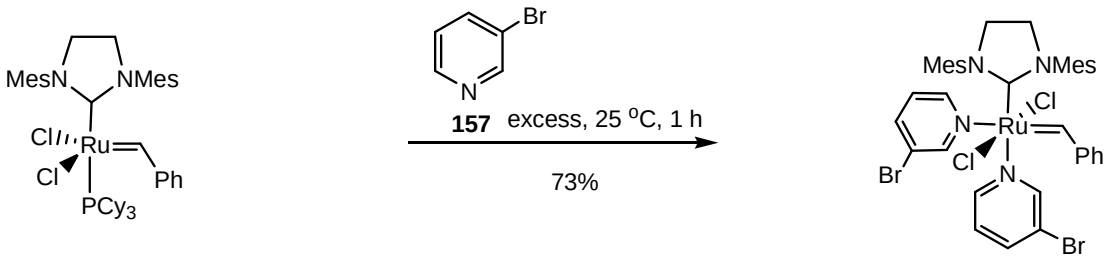
The catalysts **136-138**[65-67] and **156**[85] were obtained by mixing Grubbs-II catalyst with an appropriate substituted styrene derivative in dichloromethane in good yields.



134

136 R_1 = H R_2 = H 77%
137 R_1 = H R_2 = Ph 59%
138 R_1 = NO_2 R_2 = H 83%
156 R_1 = H R_2 = OMe 72%

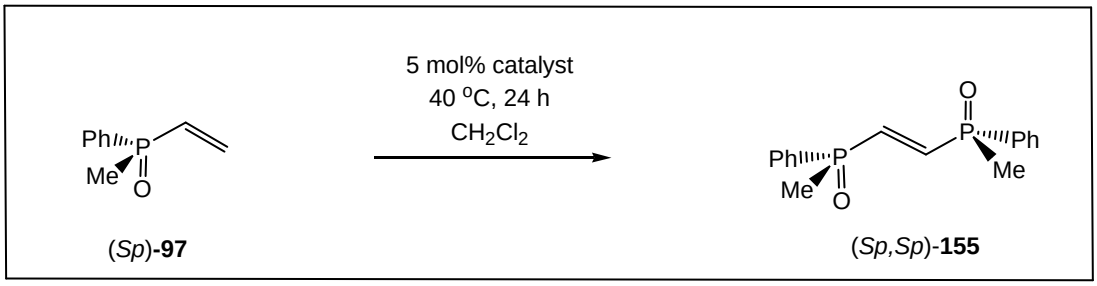
The Grubbs catalyst **158** was obtained by reaction of **134** with an excess of 3-bromopyridine (**157**) as a green solid in 73% yield after precipitation from hexane.[86]



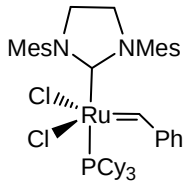
134

158

Homo-coupling of *P*-chiral vinyl phosphine oxide (*Sp*)-**97** was performed in dichloromethane at 40 °C under argon in the presence 5 mol% of the respective precatalyst. The results in Table 1 show, that, the homometathesis reactions are visibly dependent on the chosen ruthenium precatalyst. Electronically **138** and sterically **137**, **156** activated Hoveyda-Blechert carbenes showed increased catalytic activity, whereas second generation of Grubbs carbenes led only to moderate conversions.



(*Sp*)-**97** (*Sp,Sp*)-**155**



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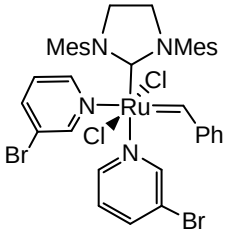

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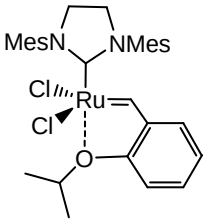

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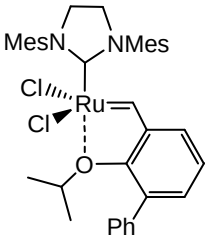

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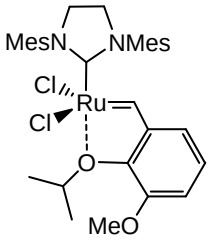
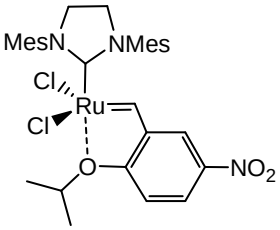


156



138

It is evident from the data compiled in Table 1, that the yield of (*Sp,Sp*)-**155** is highly responsive to the concentration of (*Sp*)-**155**.[87] For example, the reaction catalyzed by **138** at 0.020 M gave only 30% yield (entry 7), and decreasing the concentration further decreases the yield (entry 6). However, increasing the concentration increases the yield, and highest yields were obtained at 0.125-0.200 M (entries 8, 9). Because of the limited solubility of (*Sp*) - **97** in DCM, homo-dimerization was repeated at 0.4 M in chlorobenzene, however, without improving the conversion. The reaction of (*Sp*)-**97** catalyzed by **138** was then further refined using other solvents, including 1,2-dichloroethane and benzene, showing that the choice of dichloromethane was optimal. In striking contrast to previously reported CM reactions of vinylphosphine oxides with olefins,[80] the homo-metathesis of (*Sp*)-**97** has been found to be very dependent not only on the concentration but also on the scale and subtle experimental set-up. For example, homo-coupling reactions conducted under optimized conditions (0.100-0.125 M in dichloromethane, reflux) gave in the scale of 0.5 mmol the expected product in the 88-95% range of yield (two runs) while in 1.0-1.5 mmol scale reproducibly lower yields of (*Sp,Sp*)-**155** were obtained (63-80%, three runs).

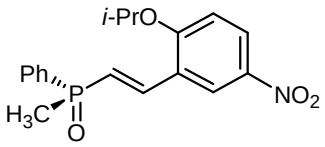
Table 1. Optimization results of homo-metathesis of (*Sp*)-**97**

Entry	Precatalyst	Concentration of (*Sp*)-**97** [M]	Yield of (*Sp,Sp*)-**155** [%][a]
1	**134**	0.020	(18)
2	**134**	0.125	(35)
3	**134**	0.200	(25)
4	**136**	0.125	(46)
5	**136**	0.200	(42)
6	**138**	0.005	(~5)
7	**138**	0.020	(30)
8	**138**	0.125	76
9	**138**	0.200	80
10	**156**	0.020	(30)
11	**156**	0.125	75
12	**156**	0.200	78
13	**137**	0.020	44
14	**137**	0.125	71
15	**137**	0.200	67
16	**158**	0.200	(10)

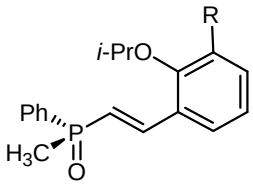
[a] Isolated yields of analytically pure products. In parentheses are conversions determined by ^{31}P NMR.

In line with the previous observation, the CM of (*Sp*)-**97** was in all cases highly stereoselective, as the (*Sp,Sp*)-**155** was the only isomer detected by ^{1}H and ^{31}P NMR. Careful spectroscopic inspection of the reaction mixture reveals that no racemization takes place during CM step and that the *ee* of the substrate (*ee* = 98%) and that of the product (*ee* = 98%) are identical.[88]

In some homo-dimerization reactions catalyzed by Hoveyda-Blechert complexes **137, 138** and **156** phosphane oxides **159**-**161** products of CM between and the corresponding precatalyst were isolated. These by-products, formed in theoretical yields (~5%), can be easily separated by flash chromatography because of their different polarity. The remainder of the mass balance was unreacted (*Sp*)-**97**, which can be easily isolated by flash chromatography and recycled.

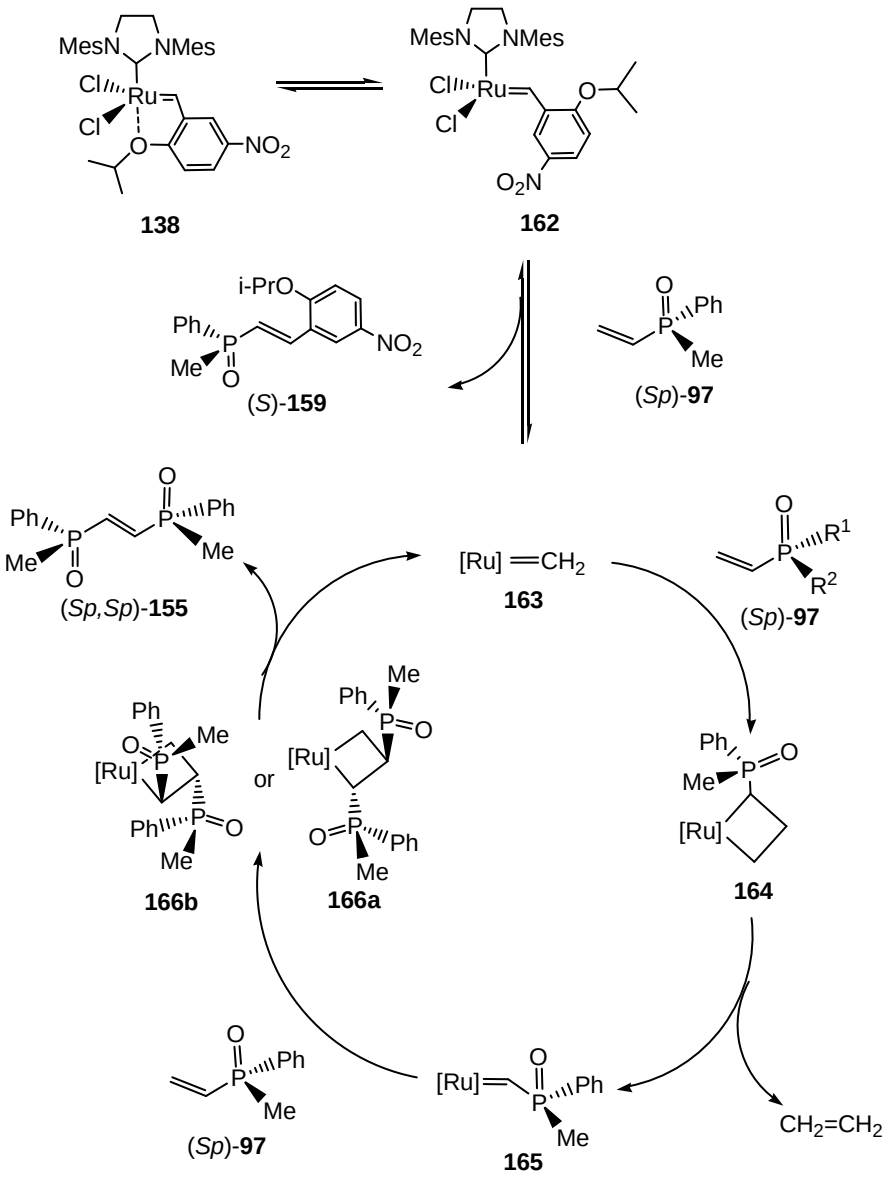


(*S*)-**159**



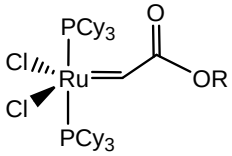
(*S*)-**160**: R = OCH_3
(*S*)-**161**: R = Ph

The mechanistical considerations suggest that the chelate Ru-O bond of the catalyst precursor decoordinates as a first step of the mechanism.[89] Vinyl phosphine oxide reacts with decoordinated catalyst to produce by-product (*S*)-**159** to liberate the active methylidene species **163**.[73,74] The methylidene **163** undergoes [2+2] cycloaddition with vinyl phosphine oxide (*Sp*)-**97** leading to enoic carbene complex **165**, through the formation of metallacyclobutane **164**.



Scheme 9. Plausible mechanism for the formation of (*Sp*,*Sp*)-**155**.

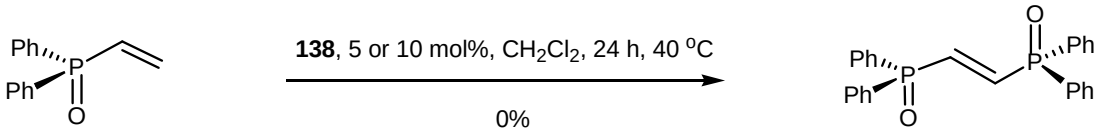
The formation of ruthenium carbene complexes **167** as intermediates in cross-metathesis has been recently postulated by Grubbs and Blechert.[90]



167

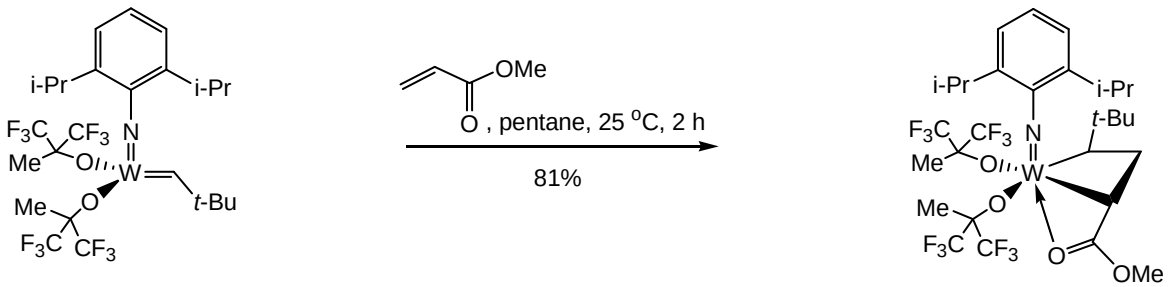
The carbene complex **164** reacts with a next molecule of vinyl phosphine oxide with formation of two diastereoisomeric metallacyclobutanes **166a** and **166b**, which are presumably in equilibrium. Formation of the product (*Sp,Sp*)-**155** liberates the methylidene **163**, which again enters the catalytic cycle.

In addition, homo-metathesis reaction of diphenylvinylphosphine oxide (**168**) was investigated. The reaction was performed in benzene in the presence 5 or 10 mol % of catalyst **138**.



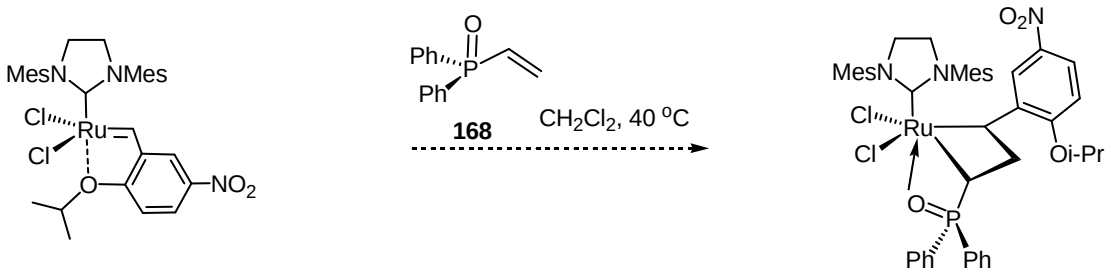
168 **169**

Unfortunately, no homodimer **169** and no by-product were observed. It is well established that the cross-metathesis of α,β-unsaturated substrates is very sensitive both to steric hindrance and electron density of the reacting C-C double bonds. One explanation is that double bond in **168** is more electron-deficient and therefore less reactive. From mechanistical point of view it is reasonable to conclude that diarylvinylphosphine oxides do not react with the catalyst precursor at all, because no by-products were observed during this metathesis experiments. Previously, R. Schrock et. al. reported that neopentylidene complexes of tungsten and molybdenum react with equimolar amounts of methyl acrylate to give metallacyclobutane complex **170**.[91]



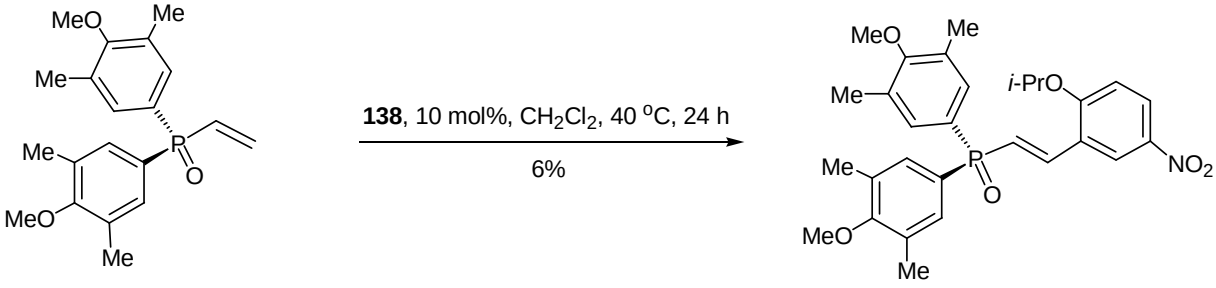
131 **170**

In the case of diphenylvinylphosphine oxide similarly treatment of the nitro Hoveyda catalyst **138** with equimolar amount of **168** would lead to metallacyclobutane complex **171**, which presumably should be stable:



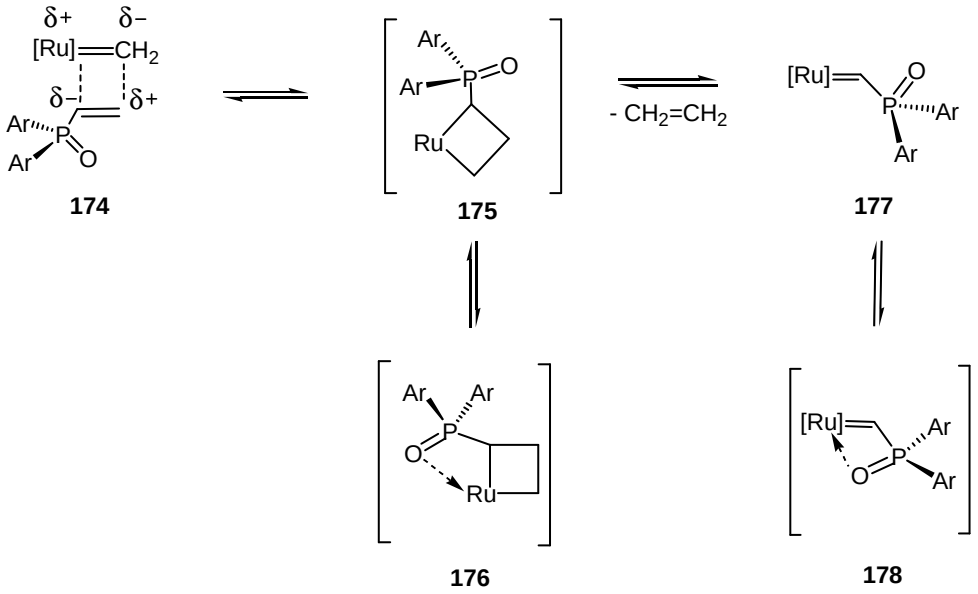
138 **171**

More interestingly, the attempted homometathesis of **172**, which possesses a more electron-rich double bond, led only to the formation of **173**.[92]



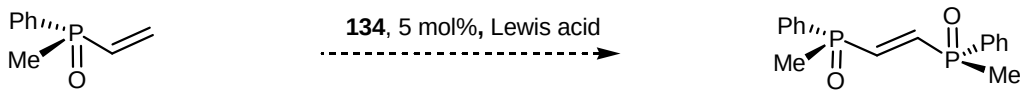
172 **173**

This observation clearly supports the formation of carbene complex **177** (Scheme 10), in which the phosphine oxide oxygen atom coordinates to ruthenium in an intramolecular fashion stabilizing the 14-electron enoic carbene **177** by the formation of the more favoured 16-electron chelate complex **178** or by the possibility of an intramolecular coordination in the metallacyclobutane **176** associated with same stabilization effect.



Scheme 10. Proposed formation of enoic-carbene complexes

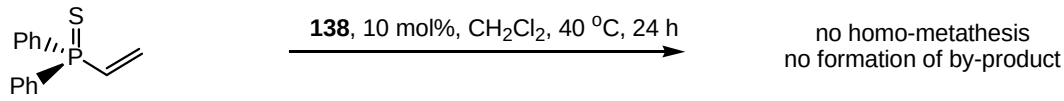
Blechert et. al. reported the efficient selective cross-metathesis of acrylonitrile using Grubbs II catalyst and copper(I) chloride as an additive to bind the liberated PCy_3.[93] This aspect was also established by Grubbs and Fürstner by using HCl or Ti(O*i*-Pr)$_4$ to remove dissociated tricyclohexylphosphine or to prevent the chelation of a carbonyl group to ruthenium.[94] It would be interesting to use a Lewis acid as a phosphine scavenger in the homo-coupling of (*S*)-**97**, expecting an increased yield of desired homodimer (*Sp*,*Sp*)-**155**.



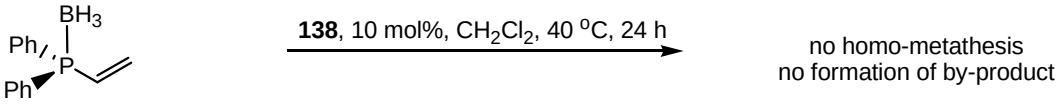
(*Sp*)-**97** (*Sp,Sp*)-**155**

2.7 The Homo-and Cross-Metathesis of Vinyl Phosphine Sulfides and Boranes

In order to investigate the influence of electronic effects on the homometathesis reaction, diphenylvinylphosphine sulfide (**179**) and diphenylvinylphosphine borane (**123**) were prepared. Disappointingly, no homo-metathesis or even no formation of by-product was observed with these substrates. Presumably, sulphur (soft-donor ligand) in **179** coordinates to ruthenium in order to prevent coordination of the double bond to the metal centre. However, it should be noted that cross-metathesis of vinyl sulfones, sulfides, disulfides and dithianes and even in the self-cross metathesis reaction of thiols has been previously reported.[95] Diphenylvinylphosphine borane (**123**) also did not react with catalyst.



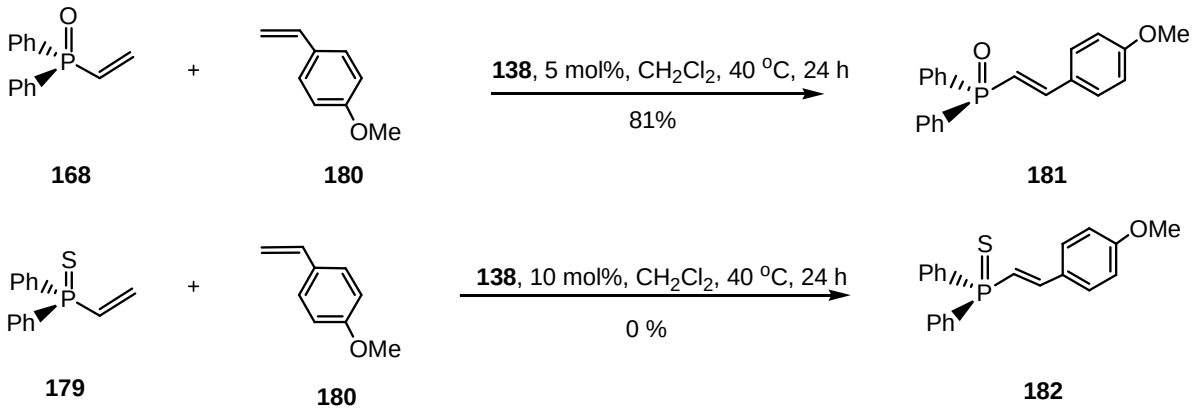
179



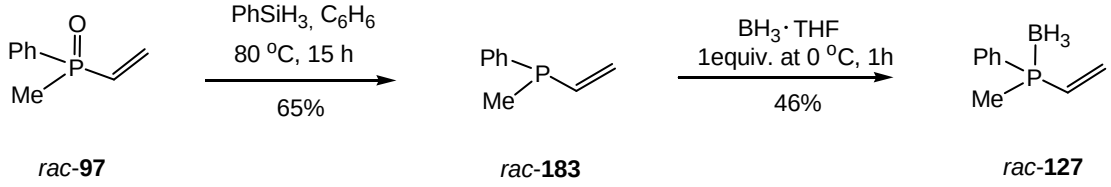
123

To confirm that sulfur interrupts the CM of **179**, the cross-metathesis between diphenylvinylphosphine sulfide and 4-methoxystyrene (**180**) has been performed. Under standard reaction conditions no reaction was observed. Instead, diphenylvinylphosphine oxide (**168**) smoothly reacts with **180** to give the expected product in 83 % yield. It led to the

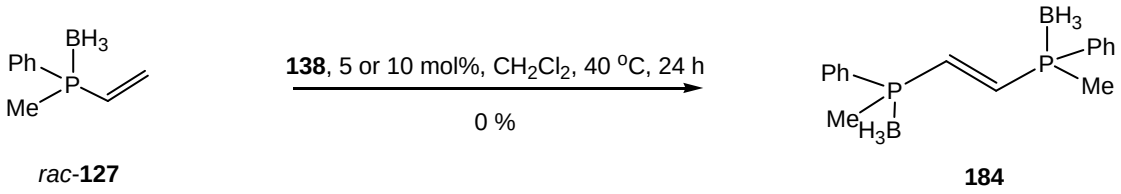
conclusion that only homometathesis of vinyl phosphine oxides can be used to achieve the desired homodimers.



rac-methylphenylvinylphosphine borane (**127**) was prepared by reaction of *rac*-methylphenylvinylphosphine (**183**) with BH_3·THF, indicating that formation of phosphorus boron bond is energetically favoured over a hydroboration of the double bond.



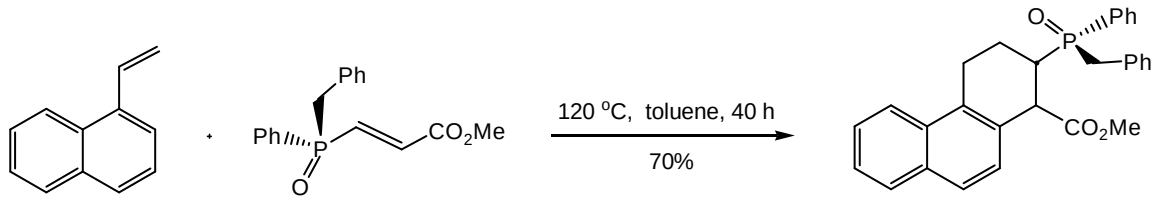
Attempted homo-metathesis of *rac*-**127** did not result in the formation of its homodimer **184** or reaction with the catalyst.



During our work Gouverneur et. al. published a paper describing the homometathesis and cross-metathesis of phosphine-borane tempelates with various alkenes. It was shown, that homometathesis of dialkylvinyl and diarylvinylphosphine boranes in presence of second generation Grubbs precatalyst is not possible.[96]

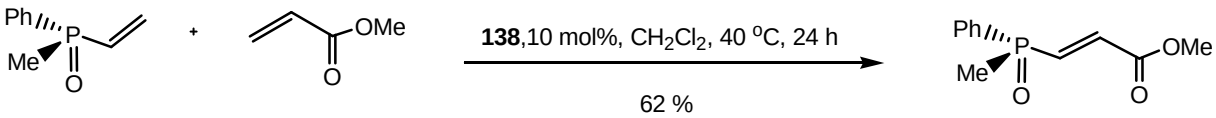
2.8 The Catalytic Olefin Cross-Metathesis between *P*-Chiral Vinylphosphine Oxide and Methyl Acrylate (188)

Previously, Pietrusiewicz et. al. reported that enantiomeric *trans*-benzylphenyl[*P*-(carbomethoxy)vinyl]phosphine oxide (*Sp*)-**186** undergoes regio- and stereoselective cycloaddition to 1-vinylnaphthalene (**185**) , providing two diastereomeric adducts **187**, which are further transformed into optically pure 17-phosphasteroid systems by intramolecular Dieckmann-type condensation.[97]



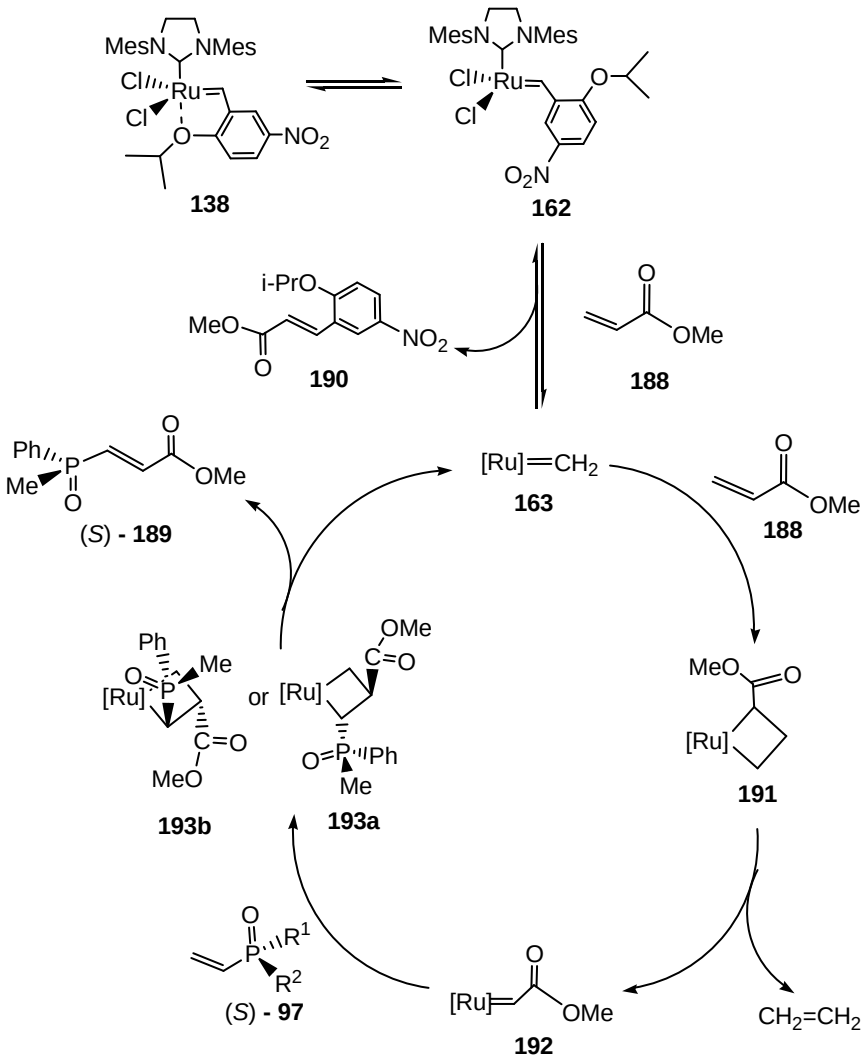
185 (*S*)-**186** (*S*)-**187**

To access other synthetically useful achiral and *P*-stereogenic phosphorus building blocks of such type, we attempted cross-coupling reactions of vinylphosphane oxide (*Sp*)-**97** with methyl acrylate (**188**). Initial experiments of cross-metathesis between (*Sp*)-**97** and **188** revealed that under standard conditions (2 equiv. of **188**, 5 mol% **138**, DCM, reflux) selectivity was low and homometathesis product (*Sp,Sp*)-**155** was formed in large amounts (12%). It was found that increasing the amount of methyl acrylate to 30 equiv. almost completely suppressed the undesired homometathesis of (*S*)-**97** and allowed for the formation of the desired cross metathesis product (*Sp*)-**189** in 47% (^{31}P NMR). Utilizing 10 mol % of **138** the yield was to increase the yield to 62%.



(*Sp*)-**97** **188** (*S*)-**189**

Varying amounts of dimethyl fumarate were detected in the crude reaction mixture by ^{1}H NMR. This by-product, formed in a homometathesis reaction of **188** could be easily separated by flash chromatography. In contrast to the above described homometathesis of vinylphosphane oxide (*Sp*)-**97**, changing the concentration of (*Sp*)-**97** from 0.02 M to 0.200 M did not result in a further improvement of the conversion.



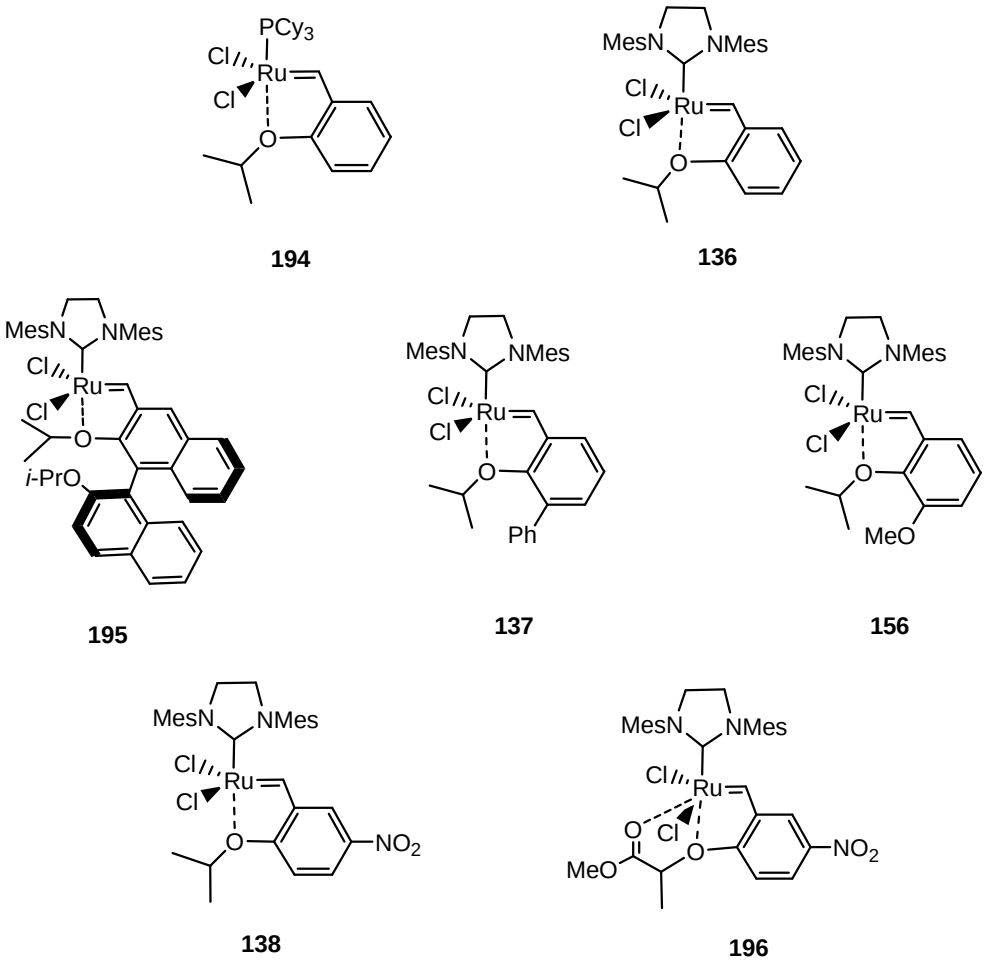
Scheme 11. Proposed mechanism fort he formation of (*S*)-**189**.

Interestingly, in the cross metathesis reaction of (*S*)-**97** with **188**, no by-product (*S*)-**159** was isolated after the reaction, or even detected by ^{31}P NMR. This observation suggests that **188** first reacts with Ru-carbene complex **162** to form Ru=CH-CO_2Me species, and that the vinylphosphane oxide (*S*)-**97** then enters the catalytic cycle (Scheme 11). Recently, Grubbs reported that electron-rich styrenes exchange faster with Grubbs I catalyst as electron-poor ones, forming stronger Ru-alkylidene, which are less reactive in metathesis.[98]

2.9 A New, Highly Active Hoveyda-Grubbs Precatalyst for Alkene Metathesis

The first observation by Hoveyda et. al. that certain styrenyl ethers could form stable carbene complexes with Grubbs-type systems in a bidentate fashion[99] followed with the subsequent report of the first isopropoxychelate complex **194**,[100] which showed good metathesis activity together with air- and moisture tolerance.

Since, in 2000, the groups of Hoveyda and Blechert simultaneously reported the phosphine free catalyst **136**[65] with enhanced catalytic activities especially towards electron-deficient alkenes, the development of catalysts with improved chelate isopropoxy ligands continues to be an important challenge.[101]

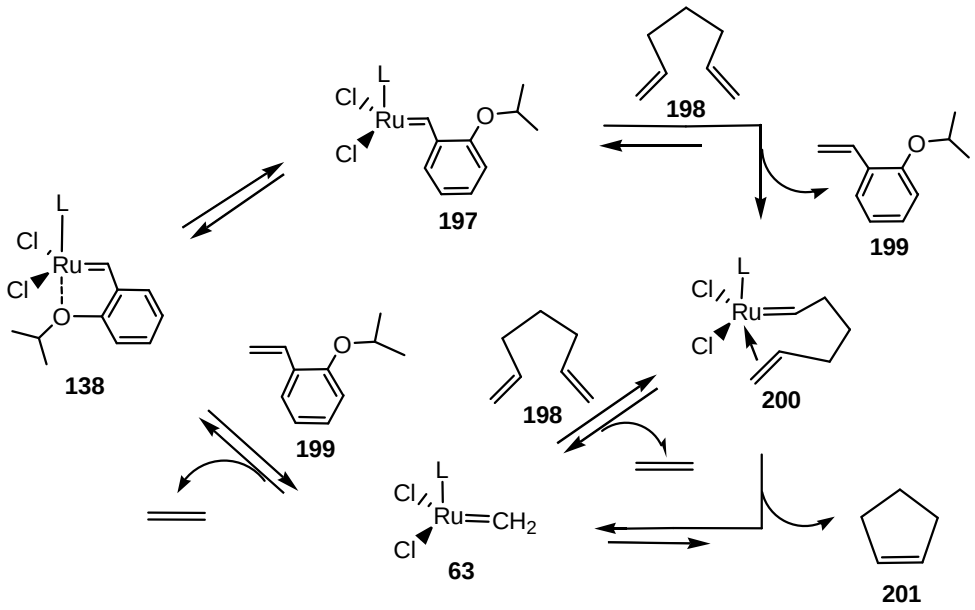


194 **136** **195** **137** **156** **138** **196**

Scheme 12. Modern precatalysts for alkene metathesis

The Blechert group has made several important contributions to this field, reporting that the activation of the catalyst **136** by increasing the steric bulk in the position *ortho* to the ligating O*i*-Pr group by a binaphthyl ring **195**, phenyl ring **137**, methoxy group **156** or others[66, 85] can significantly increase the catalytic activity of respective complexes. Presumably, steric

interactions between a substituent in the *ortho* position and O*i*-Pr group, which is coordinated to the ruthenium atom, facilitate decoordination and thus allow enhanced reaction rates. Recently, Grela et. al. developed the catalyst **138** showing that introduction of an electron-withdrawing nitro group in the position *para* to the isopropoxy substituent increased stability and activity of corresponding catalyst.[67] The effect of an electro-withdrawing (EWG) substituent on catalyst activity was then expanded by the same group and based on assumption that a decrease of electron density of the chelating oxygen atom allows to destabilize the adjacent five-membred ruthenacycle in the precatalyst to encourage initiation.[102] The mechanism of metathesis including this type of precatalysts was postulated by Hoveyda[89, 103] and appears to be still among debates (Scheme 13).[89]



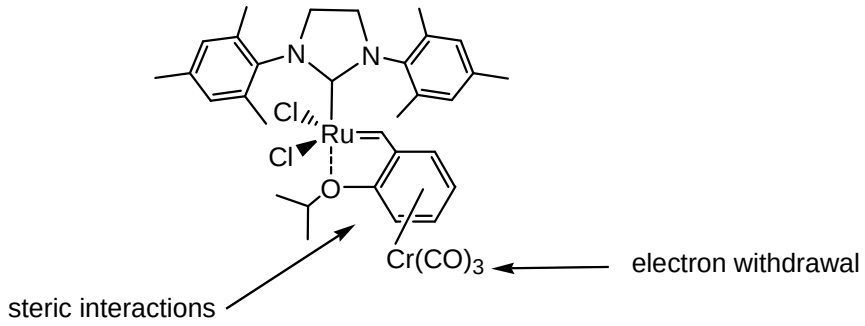
L = NHC

Sheme 13. Mechanism of metathesis including Hoveyda-Grubbs catalysts

In contrast to Grubbs second-generation precatalysts, which are likely to be activated by the loss of phosphine, bidentate carbene complexes such as **138**, are converted to the catalytically active 14-electron complex **197** through the dissociation of the Ru-O chelation. This is followed by olefin metathesis involving the substrate **198** and leading to the formation of isopropoxystyrene (**199**) (or a related derivative). The absence of released phosphine, which can intercept and deactivate certain ruthenium carbene complex is one of the key reasons for the unique reactivity profiles observed for this type of precatalysts. After initiating several catalytic olefin metathesis cycles (propagation), and upon complete consumption of the olefin, the active methylidene complex **63** encounters the initially released isopropoxystyrene (**199**) to regenerate the starting catalyst **138** (termination of the catalytic cycle). Obviously,

slight modifications of this ligating part in the precatalyst have a dramatic influence on the catalytic activity and stability of Ru-based metathesis precatalysts.[104]

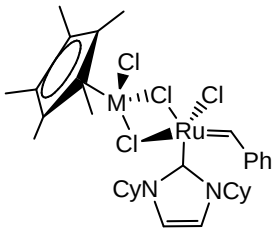
In order to reduce the electron density not only at the chelating oxygen atom but also at the benzylidene moiety, the novel bimetallic precatalyst **202** with a π-coordinated tricarbonylchromium group[105] at the benzylidene ligand has been envisaged (Scheme 14).



202

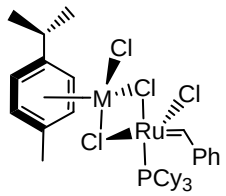
Scheme 14. Design of novel ruthenium precatlyst **202** for alkene metathesis

Recently, Herrmann and Grubbs reported some heterobimetallic olefin metathesis ruthenium complexes **203**[106] and **204**.[107] These complexes show a very high catalytic activity in ROMP of 1,5-cyclooctadiene and RCM of tetrasubstituted cycloalkenes[108]. The chloride bridged cymene and cyclopentadienyl ruthenium templates are prone to decoordination and thereby open the required vacant sites on the active species in solution.



203

M = Ir, Rh

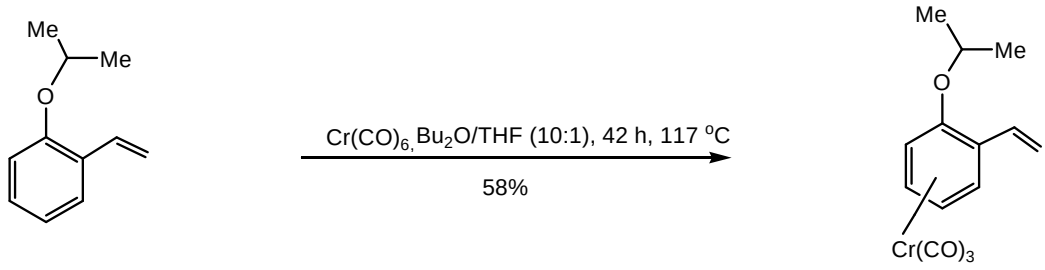


204

M = Ru, Os

In contrast to the nitro groups in **138** and **196** the sterically bulky, electron withdrawing tricarbonylchromium group in **202** is positioned comparatively near to the ruthenium atom and to the coordinated oxygen atom and might thus allow for some intramolecular interactions with Ru-O chelate bond possibly leading to a fast initiating and active precatalyst.

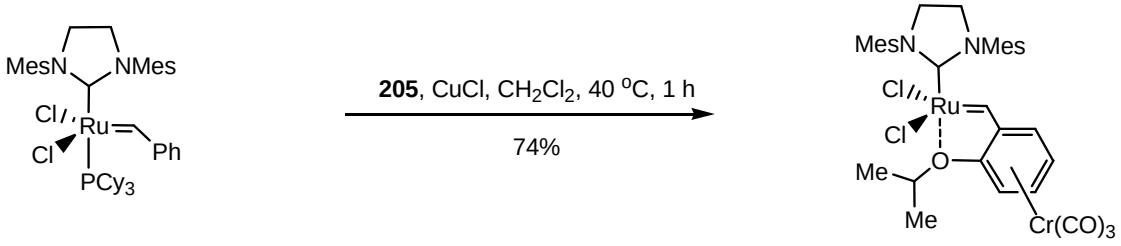
To access the bimetallic complex **202**, *ortho*-isopropoxystyrene (**199**) was treated with hexacarbonylchromium in dibutyl ether / THF (10:1)[105] affording the tricarbonyl(2-isopropoxystyrene)chromium (0) (**205**) in 58 % yield as an amorphous, moderately air stable yellow solid.



199 **205**

The presence of the tricarbonylchromium fragment at the aromatic ring of **205** can be confirmed from the ^{1}H, ^{13}C-NMR and IR-spectra. In ^{1}H NMR the signals of aromatic protons are shielded and appear between δ = 4.14 – 5.27 ppm. The methyl groups of O*i*-Pr substituent show the expected two doublets, in view of the fact that they are diastereotopic. ^{13}C NMR and IR allowed the assignment of the presence of $Cr(CO)_3$ moiety: δ = 230 ppm (^{13}C) and $\tilde{\nu}$ = 1970 cm $^{-1}$ (IR).

The ligand exchange, which was performed by treatment of **205** with **134** in the presence of CuCl as a PCy_3 scavenger, gave the desired bimetallic complex **202** in 74 % yield as a dark red powder. In the solution **202** proved to be highly sensitive to air, but surprisingly as a solid showed high stability during 2 months without a decomposition (^{1}H NMR).



134 **202**

202 was characterized spectroscopically. The ^{1}H NMR absorption of the benzylidene hydrogen atom is observed at δ = 15.49 ppm. This value compares to δ = 16.56 ppm for **136** and to δ = 16.42 ppm in **138**.[109] The signal assigned to the methine proton of the isopropoxy group is observed at δ = 4.62 ppm (**138**: 4.98 ppm, **136**: 4.89 ppm). Signals of protons at the aromatic ring, which bears tricarbonylchromium group, are shielded and resonate at δ = 4.14 – 5.27 ppm. These data clearly show that the coordination at a $Cr(CO)_3$ group has a much stronger electronic effect on the benzylidene moiety than the nitro substituent in **138**. In addition, it is remarkable that the mesityl CH protons give rise to *two* singlets at δ = 6.88 ppm and at δ = 7.00 ppm when measured in C_6D_6, whereas measurement in CD_2Cl_2 results in one broadened signal at δ = 7.03 ppm even at 500 MHz. The broadness of the signals in CD_2Cl_2, which belong to the methyl groups of the mesityl substituents, has also been detected.

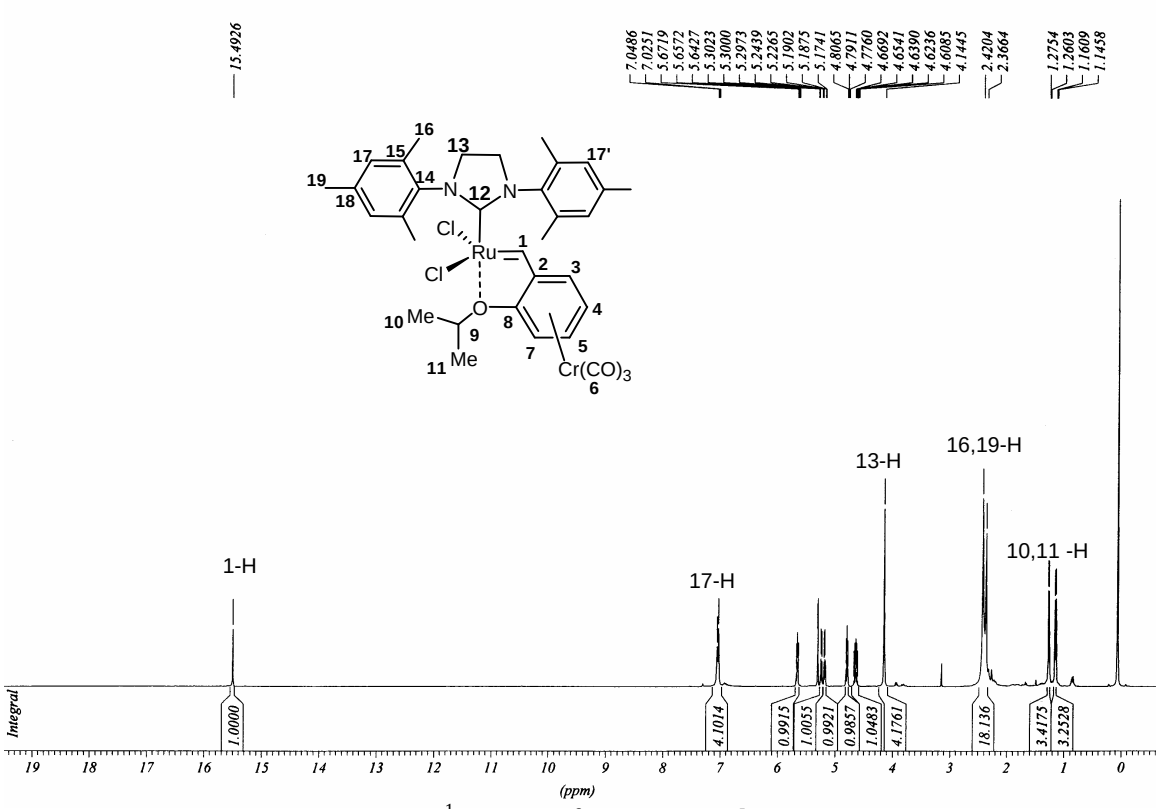


Fig. 1. ^{1}H NMR of **202** in CD_2Cl_2

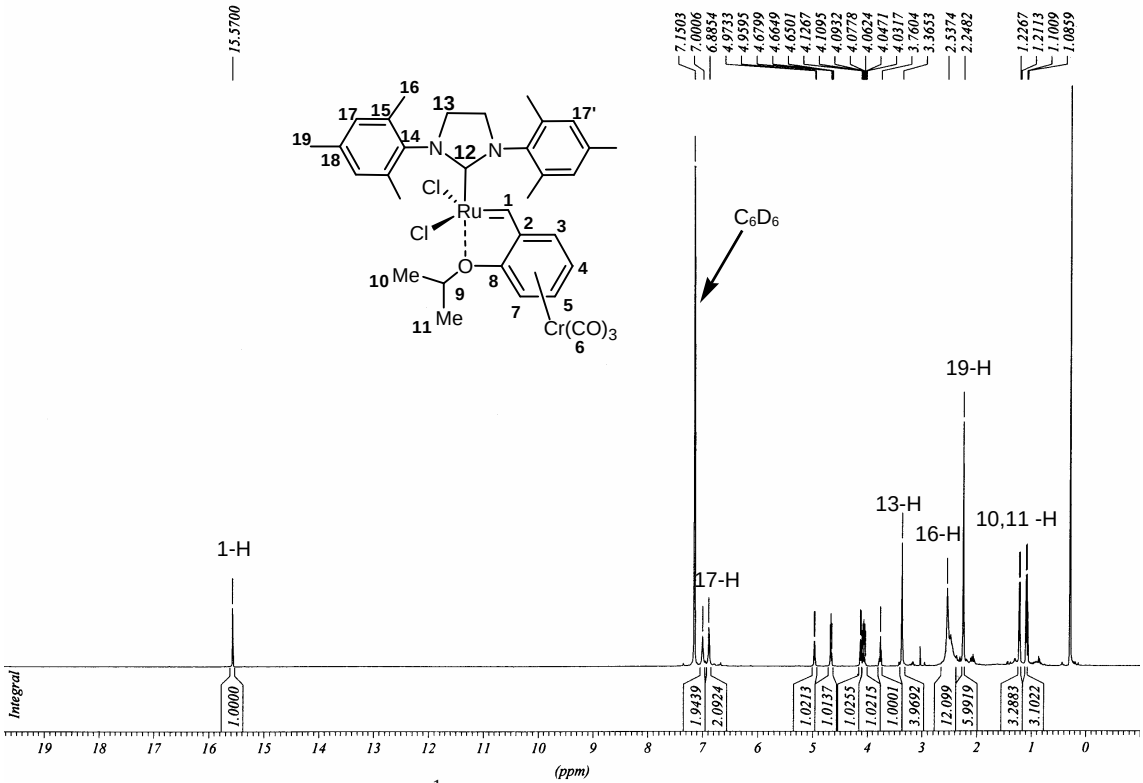


Fig. 2. ^{1}H NMR of **202** in C_6D_6

It reveals that the rotation of mesityl substituents around the C–N bond is hindered in C_6D_6. Such an observation has neither been reported for **136**[65] nor for **138**[67] and suggests that the

molecular dynamics is reduced in C_6D_6 as compared to CD_2Cl_2, a trend opposing reported by Fürstner[110a] and Grela.[110b]

The effect of the tricarbonylchromium group on the ^{13}C NMR chemical shift of the benzylidene carbon atom is also interesting: While catalyst **136** shows the signal at δ = 297.3 ppm, the signal for the nitro substituted complex **138** appears at δ = 289.1 ppm.[109] For **202** the signal is observed at even higher field and appears at δ = 285.4 ppm (Table 2).

Table 2. Selected ^1H NMR and ^{13}C NMR chemical shifts δ[ppm] of Ru-precatalysts[65,67, 113]

Precatalyst[a]	Ru=C***H***	Ru=***C***H	Ru=***C***NN	*i*-PrO-C***H***	*i*-PrO-***C***H
136[b]	16.56	297.3	211.1	4.89	74.9
138	16.42	289.1	208.2	4.98	78.2
202	15.49	285.4	208.8	4.62	77.7
202[c]	15.57	283.5	210.7	4.01	77.3

[a] All spectra were recorded in CD_2Cl_2. [b] In $CDCl_3$. [c] In C_6D_6.

Crystallization by slow evaporation from a solvent mixture of hexane and TBME (2:1) afforded crystals suitable for a single-crystal X-ray structure analysis (Fig. 3). **202** has a strongly distorted trigonal bipyramidal coordination geometry at ruthenium with the isopropoxy ligand in an axial position and both chlorine atoms *trans* to one another and the equatorial position occupied by the Ru=C bond. One face of the benzylidene ligand moiety is efficiently blocked by the tricarbonylchromium group, which, for obvious steric reasons, adopts a staggered conformation with one carbonyl ligand pointing away from the chlororuthenium part of the complex. Compared to the Hoveyda-Grubbs catalyst **136**, a decreased Ru-C2 bond length in **202** is observed. As the heterocyclic carbene ligand is identical in both compounds its σ donor or π acceptor properties are unlikely to be the reason for the observed difference. Instead, the electron withdrawal of the tricarbonylchromium group seems to reduce the electron density at ruthenium by making the benzylidene ligand a much better π acceptorr thereby making the ruthenium atom a better σ acceptor with respect to the coordination of the heterocyclic carbene ligand. The Ru-O4 bond, which is decoordinated in metathesis catalysis, is slightly longer than in **136** [229.9(3) *vs*. 226.1(3) pm], possibly indicating a somewhat weaker bond in **202**. The distances between the chloro ligands and the *ortho*-methyl carbon atoms of the mesityl substituent at N2 are short (*ca.* 330

pm) and compare well with the sum of the van der Waals radii.[111] Another interesting observation is the short distance between the benzylidene proton and the center of the mesityl ring attached at N1 (253 pm) possibly indicating an interaction with the π system, which is in line with the differentiation of the mesityl groups by ^{1}H NMR. Interestingly to note, that the location of benzylidene proton directly below the mesityl ring in Hoveyda-Grubbs type precatalysts has previously been observed[112], but for **202** this distance is shorter, presumably because of the strong electron-withdrawing $Cr(CO)_3$ group attached to the ligating part. Recently, the precedent of a π-π stacking of the two perpendicularly arranged aromatic rings in Grubbs-type complexes has been documented.[110a]

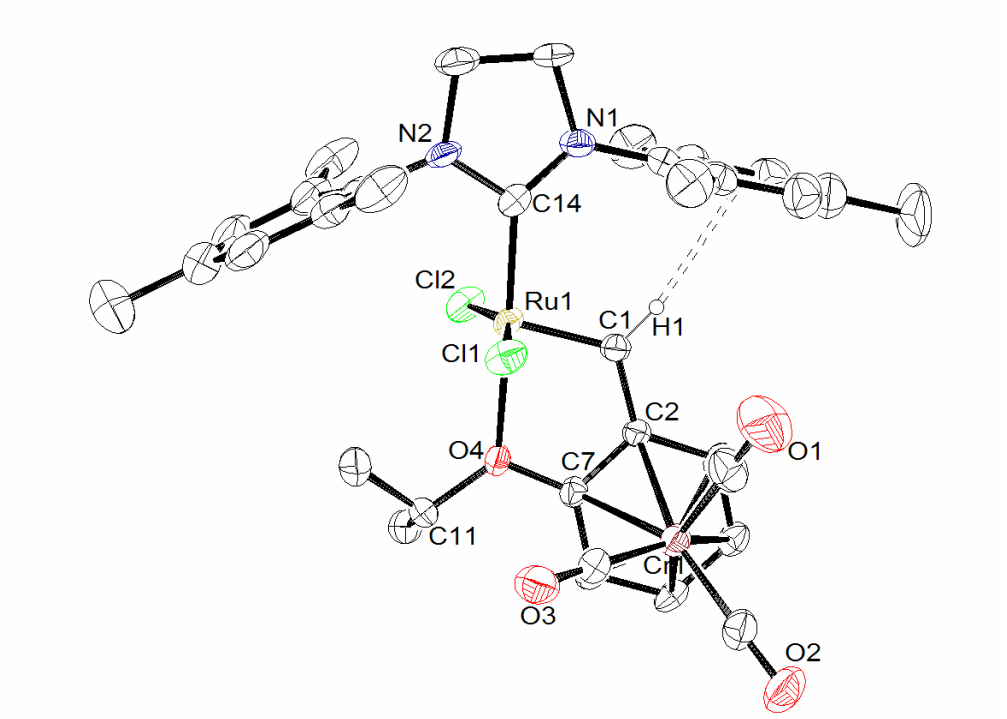
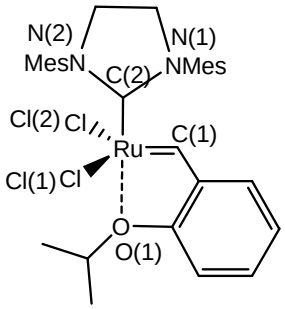


Fig.3. Structure of **202** in the crystal.[113] Selected bond lengths [pm], angles [°], and dihedral angles [°]: Ru-C1 180.6(5), Ru-C14 196.3(5), Ru-O4 229.9(3)**,** Ru-Cl1 231.9(2), Ru-Cl2 233.8(2), C14-N1 135.7(5), C14-N2 136.6(5), Cr-C2 225.2(5), Cr-C3 219.0(6), Cr-C4 219.4(6), Cr-C5 218.5(6), Cr-C6 222.4(5), Cr-C7 226.2(5); C1-Ru-O4 79.38(15), C1-Ru1-C14 102.0(2), C14-Ru-O4 178.39(16), Cl1-Ru-Cl2 160.07(6); N1-C14-Ru-C1 2.9(6), N2-C14-Ru-C1 –177.8(4), C14-Ru-C1-C2 –179.1(4).



Precatalyst	Ru-O(1)	Ru-C(1)	Ru-C(2)	Cl(1)-Ru-Cl(2)
136	226.1(3)	182.8(5)	198.1(5)	156.5(5)
202[a]	229.9(3)	181.0(5)	195.6(5)	160.1(7)

Scheme 15. Comparison of selected corresponding bond lengths [pm], angles [°] of **202** and **136**[65]

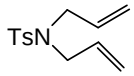
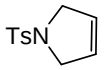
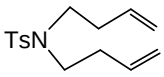
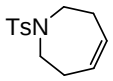
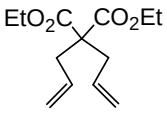
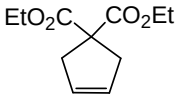
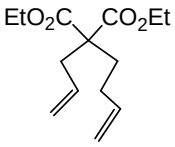
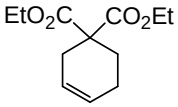
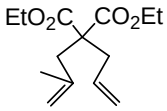
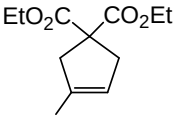
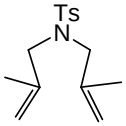
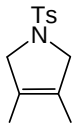
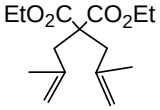
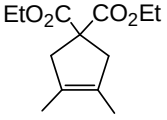
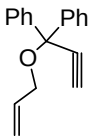
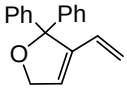
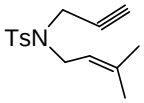
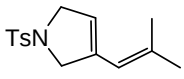
[a] In precatalyst **202** the bond lenghts Ru-O(1), Ru-C(2) correspond to Ru-O(4) and Ru-C(14), respectively depicted in Fig. 3

For the first time the catalytic activity of **202** was screened in ring closing metathesis (RCM), and enyne metathesis reactions (Table 3). Obtained results are compared with those using catalysts **137, 138** and **196**, which are among the most advanced catalysts known to date.

RCM (entries 1-4) was performed starting from dialkenes **206** - **209** with monosubstituted double bonds at 25 °C and at 0 °C with 1 mol% of catalyst **202** giving cyclic products **215** - **218** in very good yields. In addition, the **202** is stable in air at 25 °C for two months without significant loss of catalytic activity. Experiments with a tenfold reduced catalyst loading of 0.1 mol% of **202** showed that RCM works even at this low catalyst concentration, albeit with somewhat reduced yields as indicated by GC. RCM with more highly substituted alkenes (entries 5-6) was possible with substrates **210** and **211** giving **219** and **220** in 99 % and 49 % yield, respectively, which is again comparable to the efficiency of the best catalysts known today.[109] However, the experiment with **212** failed, and the known catalysts also gave very poor yields of RCM product **221**. **202** performed very well in enyne metatheses (entries 8-9), the reaction of enyne **213** afforded **222** in almost quantitative yield, and even with 0.1 mol% of catalyst 86 % yield were achieved. The reaction of enyne **214** to diene **223** showed a significantly higher activity of **202** as compared to the other catalysts[109, 110] as indicated by a much higher yield, lower catalyst loading and lower reaction temperature. When performed in benzene instead of dichloromethane as the solvent, the yield dramatically decreased to 8 %. Fürstner et. al. found that interactions of aromatic solvent molecules reduced the stabilizing effect of π–π stacking with benzylidene substituent in **135** making catalysis in toluene more effective than in dichloromethane. In the case of **202**, this effect is totally opposite. As a

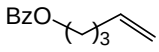
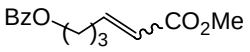
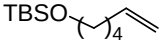
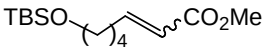
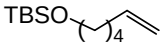
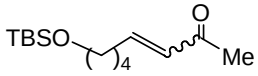
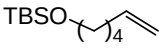
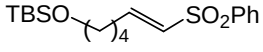
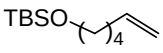
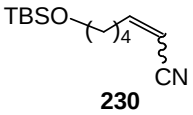
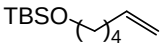
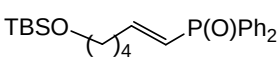
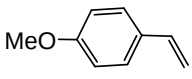
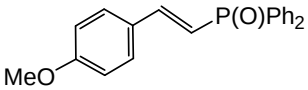
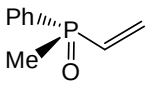
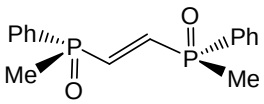
possible explanation we consider the reduced molecular dynamics in benzene as compared to dichloromethane, which has been indicated by NMR (*vide supra*). This might render conformations favorable for the metathesis catalysis less accessible.

Table 3. Ring-closing and enyne metathesis catalyzed by **202**[a].

Entry	Substrate	Product	mol % **202**	Temp (^{o}C)	Reaction time	Yield (%)
1	 **206**	 **215**	1	25	10 min	99
			1	0	2h	96
			0.1	25	2h	85[b]
2	 **207**	 **216**	1	25	8 min	99
			1	0	1h	98
			0.1	25	2h	85[b]
3	 **208**	 **217**	1	25	10 min	99
			1	0	5h	48[b]
4	 **209**	 **218**	1	25	12 min	99
5	 **210**	 **219**	1	25	50 min	99
			0.1	25	3h	59[b]
6	 **211**	 **220**	5	40	24h	49[b]
7	 **212**	 **221**	5	40	24h	0[b]
8	 **213**	 **222**	1	25	10 min	99
			1	0	1h	99
			0.1	25	2h	86[b]
9	 **214**	 **223**	1	25	20 min	99
			1	25	30 min	8[c]

[a] Solvent CH_2Cl_2. [b] yield determined by gas chromatography without product isolation. [c] Solvent C_6H_6

Table 4. CM catalyzed by **202**[a, b].

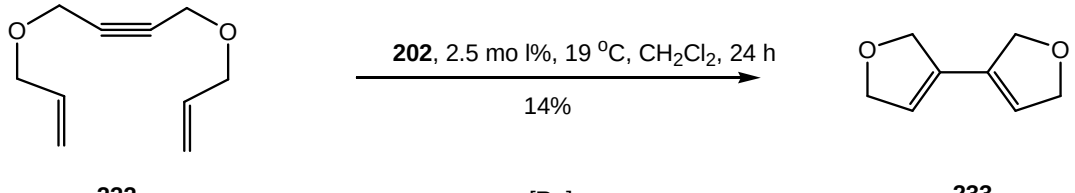
Entry	Substrate	Product	mol % **202**	Temp (^oC)	Reaction time	Yield (%) (*E*/*Z*)[c]
1	 **224**	 **226**	1	25	30 min	99 (9.7/1)
2	 **225**	 **227**	1	25	25 min	99 (3.7/1)
3	 **225**	 **228**	1	20	3h	93 (99/1)
4	 **225**	 **229**	1	20	16h	89
5	 **225**	 **230**	5	20	3h	76.5 (1/2.6)
6	 **225**	 **231**	5	40	16h	87
7	 **180**	 **181**	5	40	24h	83
8	 (*Sp*)-**97**	 (*Sp,Sp*)-**155**	5	40	24h	91

[a] Solvent CH_2Cl_2. [b] 2 equiv. of an electron poor-alkene were used in CM. [c] The *E*/*Z* ratio was determined by ^1H NMR, ^{13}C NMR.

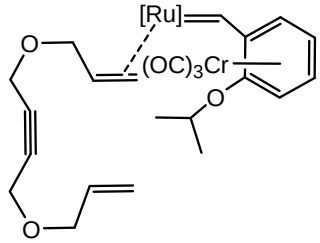
CM catalyses (entries 1-6) were performed with **202** using **224**, **225** as coupling partners for synthesis of α,β-unsaturated esters **226**, **227**, ketone **228**, sulfone **229**, nitrile **230**, and phosphane oxide **231**. The yields are very high and compare very well to those of the other advanced catalysts.[66, 109] The selectivity of cross-metathesis reactions with vinyl phosphane oxide and sulfone led exclusively to *E*-isomers, only experiments including methyl acrylate showed a tendency to an increased amount of the *Z*-isomer. **202** is active even over extended heating in dichloromethane as indicated by the reaction of **180** giving **181** in 83 % yield. The

(*Sp*)-**97** was homodimerized to give an improved yield of (*Sp,Sp*)-**155** in 91% yield, as compared to 80% with **138**.[92] Over all the experiments show that not only a nitro group as in catalyst **138** but also coordination at a tricarbonylchromium group gives a metathesis catalyst of good stability and extremely high catalytic activity.

Unfortunately, the enyne metathesis of **231** catalyzed by **202** using reported reaction conditions provided **233** only in 14% yield. For example, the use of the nitro-precatalyst **138** for this reaction resulted **233** in 71% yield.[109] Presumably, the bulky tricarbonylchromium fragment hindered the formation of the intermediate **234** making coordination to metal centre less accessible in view of a return of the decoordinated ligating part of precatalyst competing with a olefin coordination.

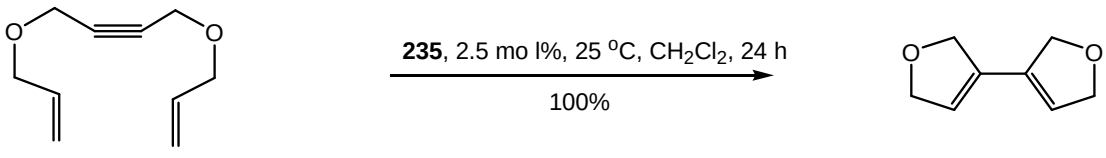


232 **233**

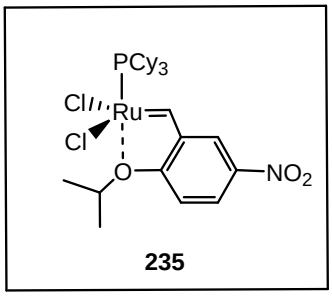


234

Recently, Grela et.al. showed that enyne metathesis of **232** is highly dependent on choice of precatalyst.[114] It was found, that use of first generation of Hoveyda-Grubbs precatalyst **235** referred to more active and allow a highly selective formation of **233**.

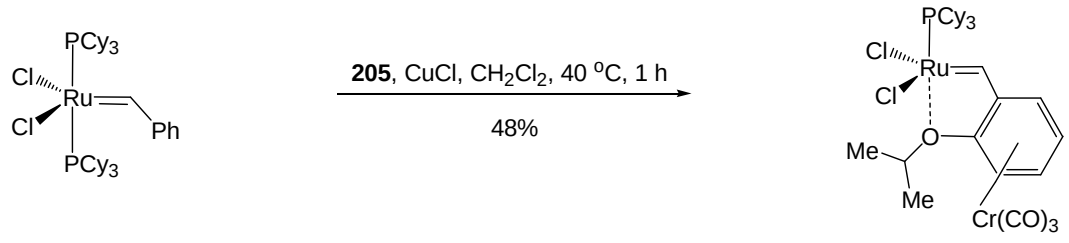


232 **233**



235

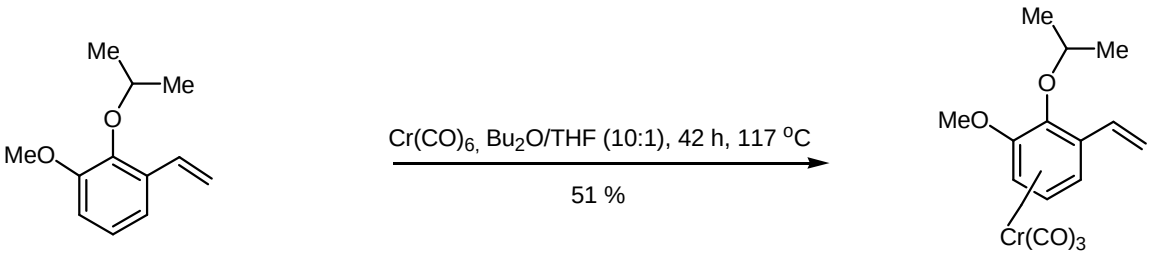
The precatalyst **236** was synthesized by the ligand exchange with **133** in dichloromethane in 48% yield. In contrast to **202**, this catalyst is much more sensitive to air in solution and therefore care must be taken to exclude oxygen during purification.



133 **236**

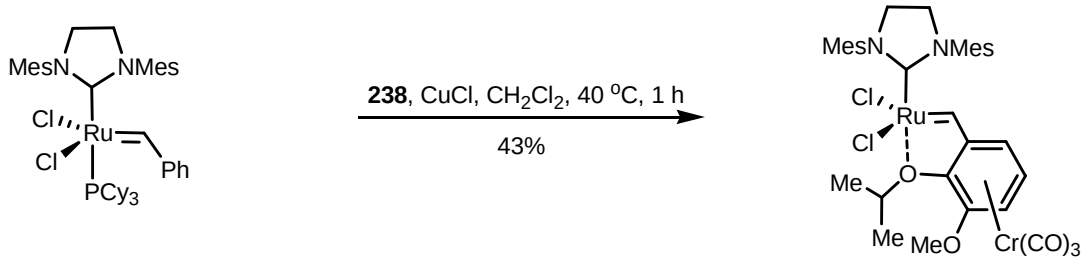
236 was characterized spectroscopically. The presence of coordinated PCy_3 was proved by the ^{31}P NMR where the respective signal is observed at δ = +64.1 ppm, which is in good agreement of previously reported data for such type of complexes.[100] Incontestable evidence for Ru-O chelation is the signal of the alkylidene proton, which results in an upfield shift of ~1 ppm from the parent complex **136** and appears at δ = 16.58 ppm as a doublet with J_{PH} = 4.22 Hz, indicating the formation of the five-membered chelate and coincident with a 90° rotation about the carbon-metal double bond.[100] Recently, Grubbs et. al. have suggested that a version of the vicinal Karplus correlation may be applicable in these Ru-based systems for the P-Ru-Cα-Hα dihedral angle.[115] In the ^{13}C NMR spectrum, the carbene carbon atom also resonates upfield at δ = 274.5 ppm in comparison to that δ = 297.3 ppm of **136**. The respective presence of $Cr(CO)_3$ was confirmed by shielding of the aromatic protons δ = 4.90 – 6.00 ppm and the corresponding CO signal in the ^{13}C NMR at δ = 232.6 ppm. The catalytic profile of **236** should be studied in the future, concerning of it potential higher activity in enyne metathesis of **232** and other related substrates.[114]

Next we became interested to prepare a bimetallic precatalyst, which would contain the methoxy substituent *ortho* to the ligating isopropoxy group and should be more reactive than **202**. The appropriate chromium(0) complex **238** was prepared in 51% yield as a light yellow solid by the treatment of hexacarbonylchromium in dibutyl ether / THF (10:1) and 2-isopropoxy-3-methoxystyrene (**237**).



237 **238**

The new bimetallic carbene complex **239** was isolated in 43% yield after tedious purification step and unfortunately decomposed very rapidly in dichloromethane during minutes, when it was submitted for a catalytic reaction.



134 **239**

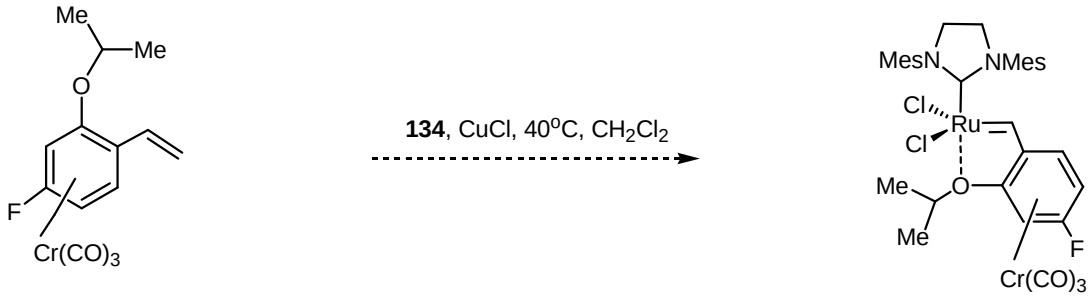
However, in the ^{1}H NMR of **239**, the signals of the decoordinated complex, which refer to **156**, are present. The corresponding benzylidene proton in **239** resonates upfield at δ = 15.72 ppm, whereas decoordinated **156** appears at δ = 16.74 ppm[85]. Presumably, the instability of **239** is the result of combination of both types of activation in one precatalyst: steric and electronic. Related findings were recently reported by Grela et. al. in the attempted double activation of **138** by introduction in *ortho* position to the chelating *i*-PrO the methoxy or phenyl substituent leading to very unstable complexes **240**.[109]

239 **240**

R = Ph, OMe or NO_2

Scheme 16. Attempted double activation of prectalysts **202**[113] and **138**.[109]

Since Blechert et. al. reported that the benzylidene electrophilicity is a crucial factor for precatalyst activity,[104] the synthesis of **242** via **241** is potentially of great interest, since this bimetallic complex would presumably have a more electrophilic benzylidene carbon and will thus be activated electronically by both substituents by fluorine and the tricarbonylchromium group.



241 **242**

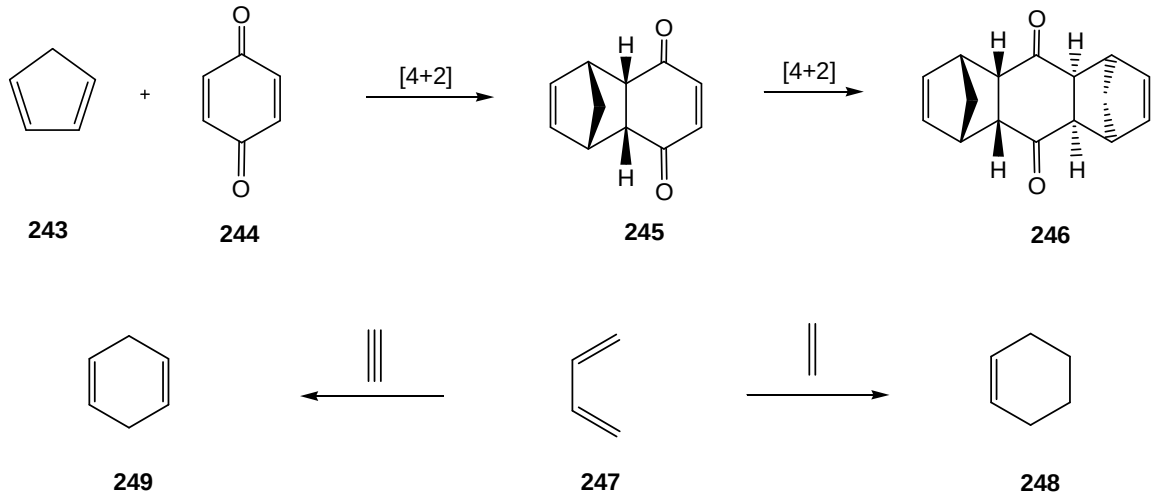
3 Synthesis of Novel Rigid *P*-Stereogenic Diphosphine Dioxides as Ligand Precursors via Asymmetric Cycloaddition

3.1 The Diels-Alder Reaction in Organic Synthesis

The Diels-Alder reaction is the best known organic reaction that is widely used to construct a six-membered ring with up to four stereogenic centers in a regio and stereo-controlled way.[116] Since its discovery in 1928 by O. Diels and K. Alder, where cyclopentadiene (**243**) was reacted with quinone (**244**) to give products **245** and **246**[117], more than 30.000 papers have been published concerning synthetic, mechanistic and theoretical aspects of the reaction and about half of these are appeared in the last decade.[118] In 1950 O. Diels and K. Alder

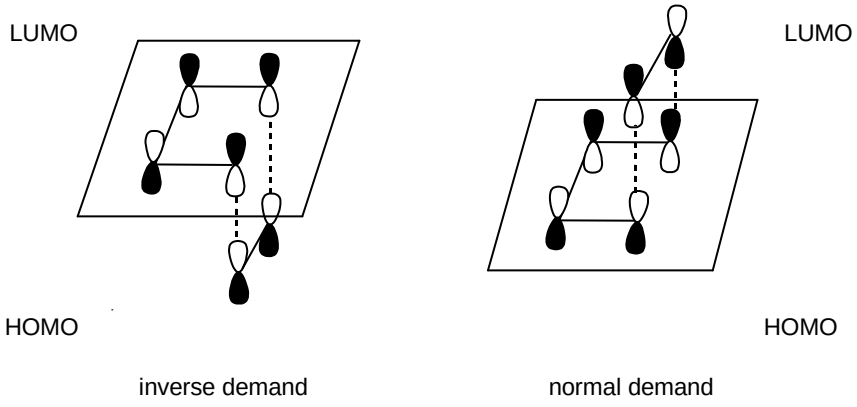
were awarded the Nobel Prize in chemistry for the discovery and development of this significant reaction.

The classical Diels-Alder reaction is a cycloaddition between a conjugated diene **247** and a second component, called dienophile, which has at least a π-bond can give rise to two different cycoadditions leading to **248** or **249** respectively.[119] When one or more heteroatoms are present in the diene or dienophile framework, the cycloaddition is called hetero-Diels-Alder reaction.[120]



Scheme 17. The classical Diels-Alder reaction

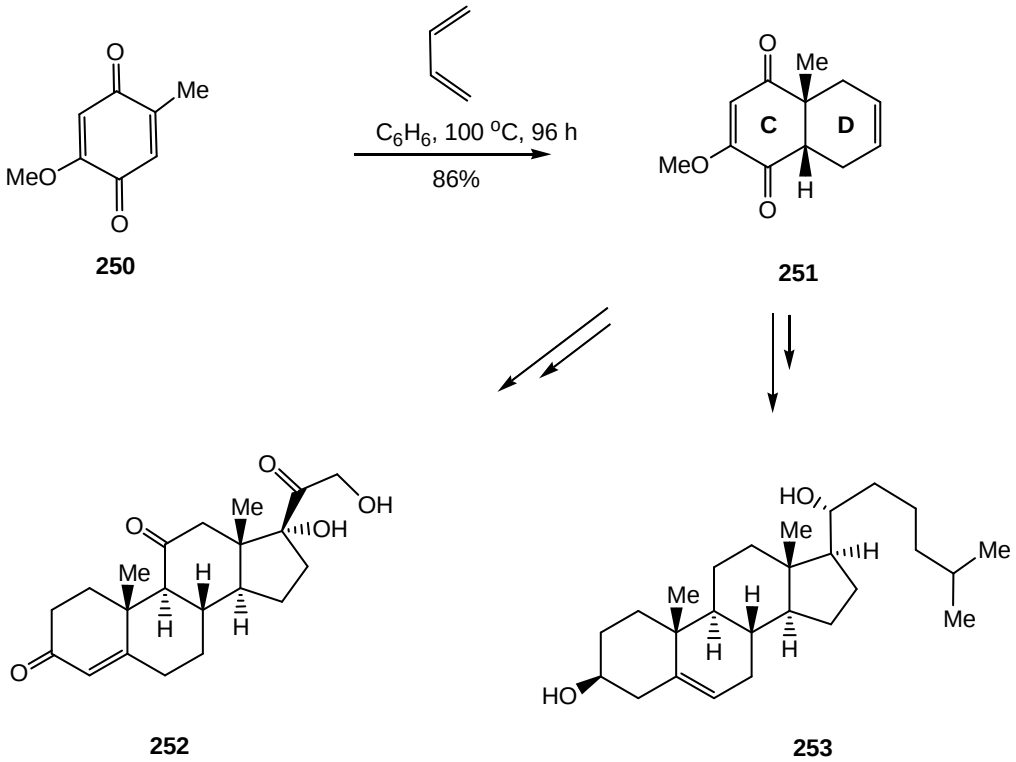
The reaction is classified as a [$_{\pi}4_s$ + $_{\pi}2_s$] cycloaddition, whreas 4 and 2 identify both the number of π electrons involved in the electronic rearrangement and the number of atoms originating the unsaturated six-membered ring.[121] According to frontier molecular orbital theory (FMO),[122] the reactivity, regioselectivity and stereochemistry of the Diels-Alder reaction are controlled by the suprafacial interaction of the highest occupied molecular orbital (HOMO) of one component and the lowest unoccupied molecular orbital (LUMO) of the other. The reactivity in a Diels-Alder depends on the HOMO-LUMO energy separation of components: the lower the energy difference, the lower is the transition state energy of the reaction. Electron-withdrawing substituents lower the energy of both HOMO and LUMO, while electron-donating groups increase their energies. HOMO diene-controlled Diels-Alder reactions are accelerated by electron-donating substituents in the diene and by electron-withdrawing substituents in the dienophile (normal electron-demand Diels-Alder reaction). LUMO diene-controlled Diels-Alder reactions are influenced by electronic effects of the substituents in the opposite way (inverse electron-demand).[123]



Scheme 18. Normal and inverse demands in the Diels-Alder reaction

Not only is a cyclohexene ring generated through the formation of two new σ-bonds, but up to four stereocenters are also simultaneously formed in the process. Fortunately, as a result of the regio and stereospecific nature of the Diels-Alder reaction and the diastereoselectivity of the union based on the Alder endo rule.[118]

The early total syntheses by Woodward illustrate the ability of the Diels-Alder reaction to create molecular complexity. A quinone-based Diels-Alder reaction was applied as the key step in synthesis of in the total synthesis of the steroid hormones cortisone (**252**) and cholesterol (**253**).[124]



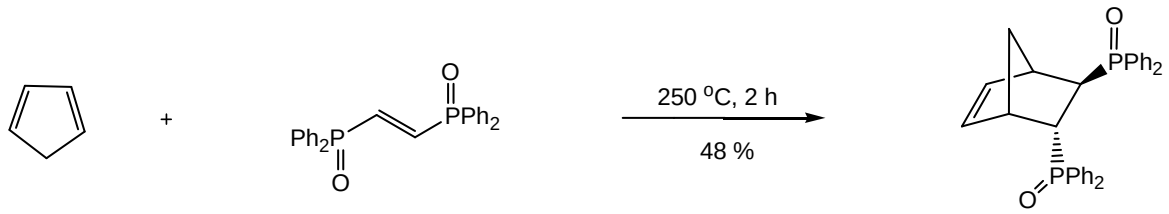
This work of Woodward initiated the employment of the Diels-Alder reaction in the total synthesis of naturally occurring substances.[125]

3.2 Asymmetric Diels-Alder Reaction of (*Sp,Sp*)-155 with Cyclopentadiene (243)

Organophosphorus compounds bearing a vinyl group are an interesting class of simple conjugated olefins, which has been used for as dienophiles in the Diels-Alder reaction.[47] Although in the conjugated system of vinylphosphine oxides, the phosphoryl group is analogous to the carbonyl group of α,β–unsaturated carbonyl compounds, the phosphorus atom of the phosphoryl group has a tetrahedral coordination, as opposed to the carbon atom of the carbonyl group with its flat configuration. Also, the multiple bond of the phosphoryl group is a d_{π}–p_{π}–π–bond, which is formed by 3d electrons of phosphorus and 2p electrons of oxygen, while the double bond of the carbonyl group produced by 2p electrons of both atoms.[126]

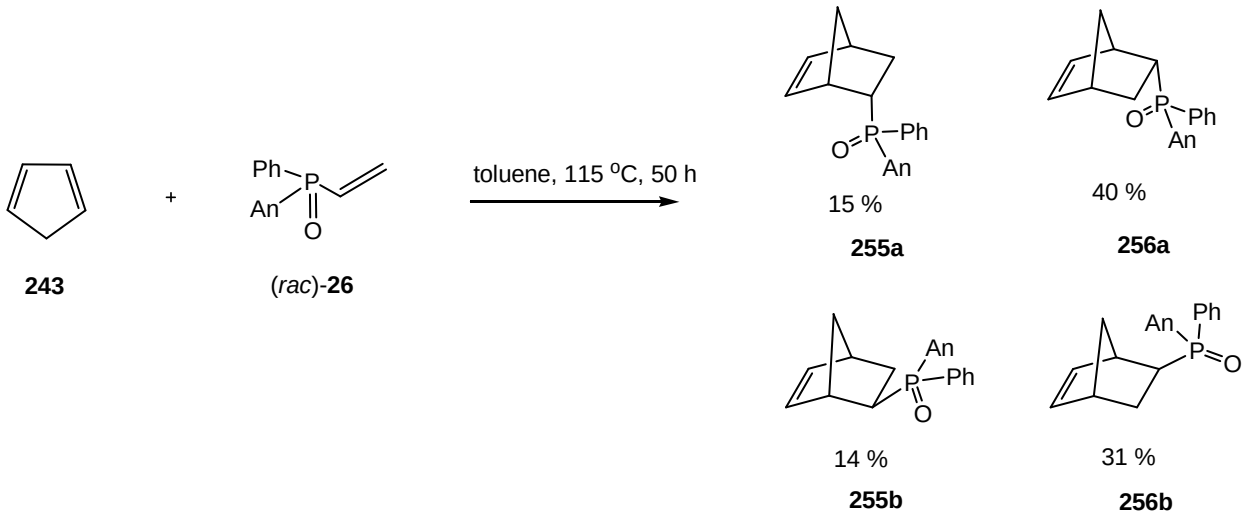
During last two decade organophosphorus dienophiles were less investigated and only several examples appeared in the literature. [52, 97, 127]

For example, Kabachnik[128] and some that later Brunner[129] showed that *trans*-1,2-bis(diphenylphosphoryl)ethylene (**169**) reacts with cyclopentadiene (**243**) at elevated temperature to give diphosphine dioxide NorphosO (**254**) in 48 % yield.



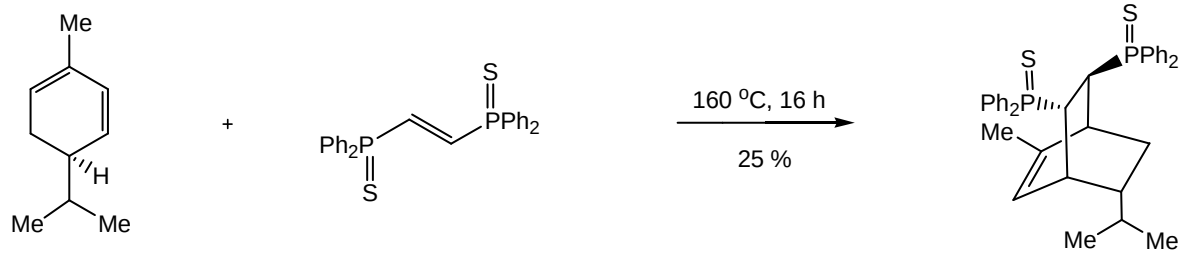
243 **169** **254**

Buono et. al. reported that *racemic* chiral anisyl(phenyl)vinylphosphine oxide (**26**) undergoes the Diels-Alder reaction with **243** to produce all diastereomeric cycloadducts, which are inseparable. Also, it was shown, that the *endo* / *exo* ratio of products **255** or **256** can be influenced by addition of various Lewis acids.[130]



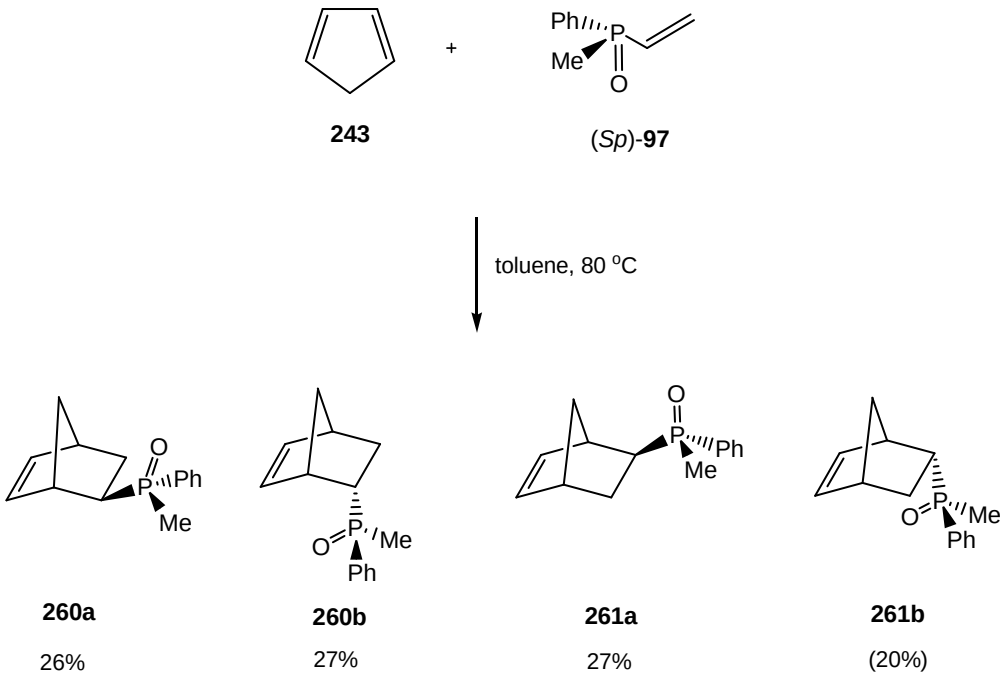
243 (*rac*)-**26** **255a** **256a** **255b** **256b**

Kagan et. al. used easily the available monoterpene α–phellandrene (**257**) as a chiral diene and *trans*-1,2-bis(diphenylthiophosphoryl)ethylene (**258**) for the synthesis of the disulfide **259**, which is a precursor to chiral diphosphine Phellanphos.[131]



257 **258** **259**

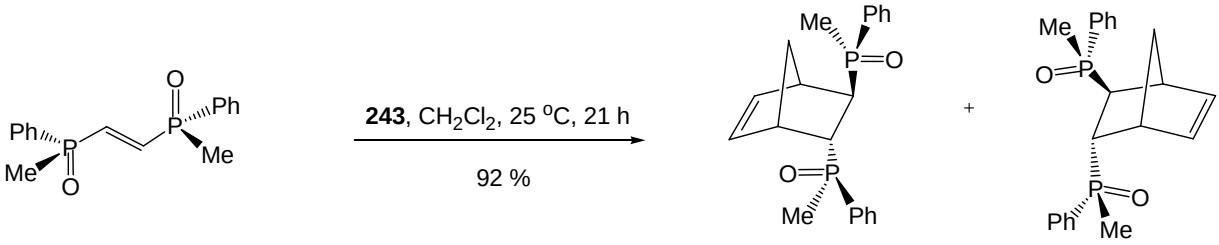
(Sp)-chiral vinylphosphine oxide (**97**) was used for the thermal Diels-Alder reaction with cyclopentadiene (**243**) to give four products **260**-**261**. The stereochemistry of the major *endo* adduct **260b** was analyzed by a single-crystal X-ray diffraction showing *S* configuration at C-2. Presumably, (*Sp*)-**97** prefers to react in the *s*-trans conformation.[132]



243 (*Sp*)-**97**

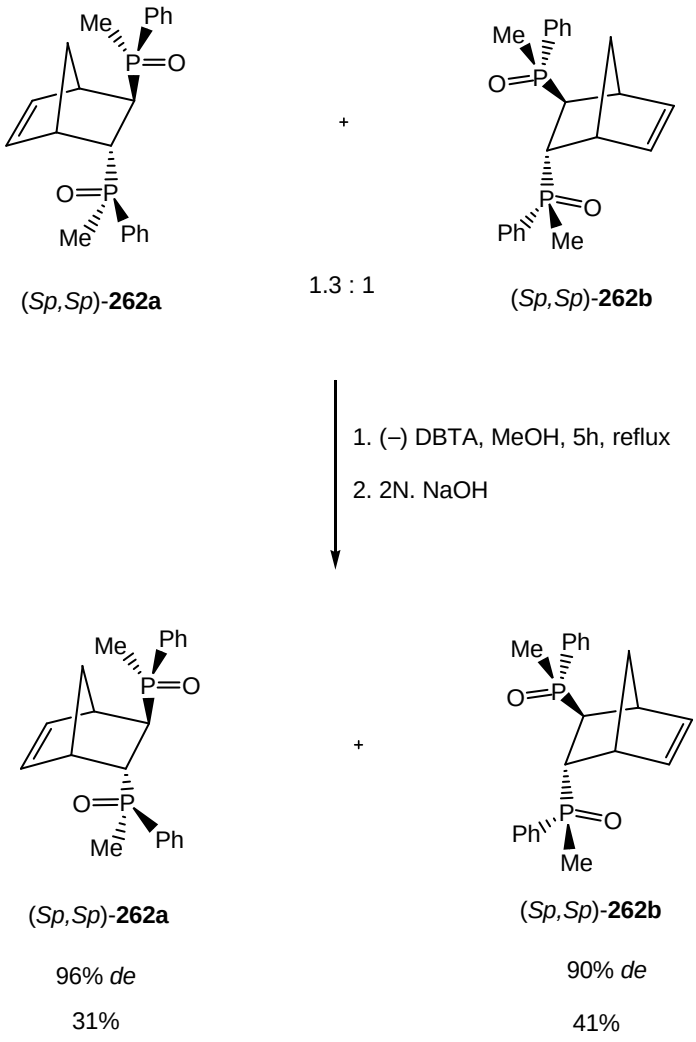
260a 26% **260b** 27% **261a** 27% **261b** (20%)

Thus, to access the rigid carbocyclic skeleton of a precursor for the novel *P*-chiral ligand system, the enantiomerically pure dienophile (*Sp,Sp*)-**155** was submitted to a Diels-Alder reaction with cyclopentadiene (**243**). Surprisingly, the reaction proceeds smoothly at 25 °C in CH_2Cl_2 to give two diastereomeric products (*Sp,Sp*)-**262a** and (*Sp,Sp*)-**262b** in a ratio (1.3 : 1- ^{31}P NMR, ^{1}H NMR) in 92%.



(*Sp,Sp*)-**155** (*Sp,Sp*)-**262a** 1.3 : 1 (*Sp,Sp*)-**262b**

Unfortunately, these two diastereoisomers were inseparable by column chromatography. To separate (*Sp,Sp*)-**262a** and (*Sp,Sp*)-**262b** a method developed by Brunner was applied.[133] By using (–)-di-*O*-benzoyltartaric acid monohydrate (DBTA) in boiling methanol cycloadducts were resolved affording after hydrolysis with 2N NaOH (*Sp,Sp*)-**262a** in 96% *de* and (*Sp,Sp*)-**262b** in 90% *de*. This resolution based on the different solubilty of diastereomeric adducts **262a** / (–) DBTA, which co-crystallization could be explained by the formation of a hydrogen bridge between a carboxy group of (–) DBTA and the P=O groups of **262a**.[133]



It should be mentioned that differentiation between (*Sp*,*Sp*)-**262a** and (*Sp*,*Sp*)-**262b** by ^{1}H NMR is not possible, because they differ only in the configuration at C-2 and C-3. Fortunately, the major diastreoisomer (*Sp*,*Sp*)-**262a** crystallized from the solvent mixture ($CHCl_3$ / MeOH 9:1) to give crystals suitable for the X-ray diffraction (Fig. 4). The absolute configuration of phosphorus atoms of the major diastreoisomer (*Sp*,*Sp*)-**262a** was found to be *S*. Both methyl(phenyl)phosphoryl groups are in *exo* and *endo* position standing *trans* one to another with absolute configuration *R* at C-2 and C-3 atoms. The phosphorus tetrahedron is deformed in the usual way showing increased O-P-C angles and decreased C-P-C angles with the corresponding values ranging from 114.1(5) to 109.6(4).

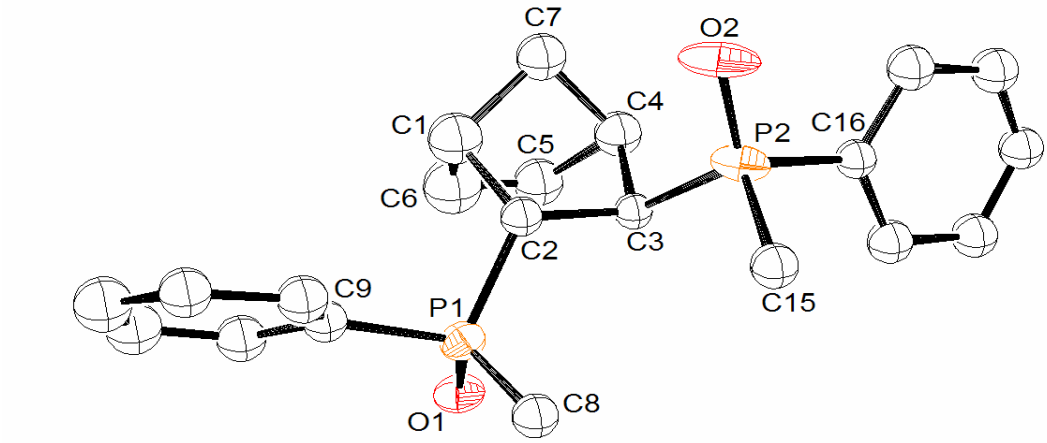
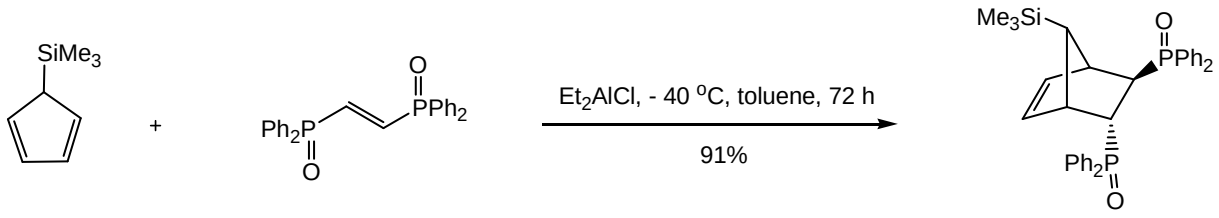


Fig. 4. Structure of (*Sp*,*Sp*)-**262a** in the crystal. Selected bond lengths [pm], angles [°], and dihedral angles [°]: P1-O1 153.9(6), P1-C9 180.0(10), P1-C8 180.5(7), P1-C2 181.6(9), P2-O2 149.5(7), P2-C15 181.6(8), P2-C16 182.0(9), P2-C3 182.9(9), C1-C6 139.0(2), C1-C7 157.8(13), C1-C2 162.7(13), C2-C3 154.2(9), C3-C4 161.1(12), C4-C5 145.5(13), C4-C7 158.8(12), C5-C6 126.4(14), C9-C14 137.1(11), C9-C10 142.9(11), O1-P1-C9 109.6(4), O1-P1-C8 113.1(4), C9-P1-C8 105.7(5), O1-P1-C2 114.3(4), C9-P1-C2 105.9(4), C8-P1-C2 107.7(4), O2-P2-C15 113.7(4), O2-P2-C16 110.6(5), C15-P2-C16 104.7(5), O2-P2-C3 114.1(5), C15-P2-C3 106.5(4), C6-P2-C3 106.5(4), P1-C2-C3-P2 116.9(1), C15-P2-C3-C2 72.9(1), C8-P1-C2-C3 71.4(1).

In addition, (*Sp*,*Sp*)-**262a** (96% *de*) was analyzed by ^{1}H, ^{13}C, ^{31}P NMR spectroscopy and correlated to its structure. In the ^{1}H NMR spectra the methyl groups at phosphorus resonate as two doublets, with a $^{2}J_{PH}$ = 12.7 Hz. The olefinic protons give two multiplets at 5.59 and 6.02 ppm. In addition, the ^{13}C NMR spectrum shows detailed information about coupling constants, for example, the methyl groups give again doublets at 9.2 and 13.2 ppm with $^{1}J_{PC}$ = 64.2 Hz and 65.3 Hz. C-2 and C-3 give doublets at 41.9 and 42.1 ppm with large coupling constants: $^{1}J_{PC}$ = 73.9 and 65.2 Hz. The bridgehead carbon atom C4 gives a quartet, whereas C1 provides a doublet with $^{2}J_{PC}$ = 4.4 Hz. Since both asymmetric phosphorus atoms are *trans* and therefore chemically not equivalent, there are two doublets appearing in ^{31}P NMR at δ = + 38.6 and + 39.8 ppm, respectively, with a coupling constant J_{PP} = 8.9 Hz.

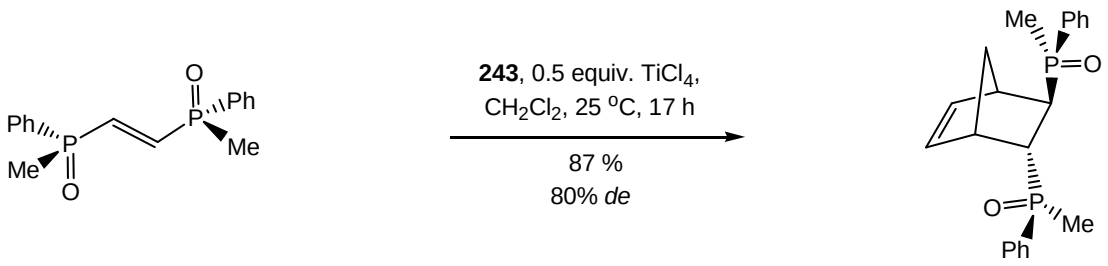
A classical method to enhance diastereoselectivity is based on the use of Lewis acid catalysts.[134] Upon complexation of such species to the dienophile, the normal demand Diels-Alder reaction is accelerated since the energy gap between the lowest unoccupied molecular orbital (LUMO) of the dienophile and the highest occupied molecular orbital (HOMO) of the diene is reduced, thus decreasing the activation energy required to achieve the cycloaddition.[134]

Recently, a Diels-Alder reaction of trimethylsilylcyclopentadiene (**263**) and *trans*-1,2-bis(diphenylphosphoryl)ethene (**169**) catalyzed by Et_2AlCl at –40 °C led to 7-*anti*-trimethylsilylnorbornene (**264**) in 91 %.[135]



263 **169** **264**

To increase diastereoselectivity of the Diels-Alder reaction between (*Sp*,*Sp*)-**155** and cyclopentadiene (**243**), several Lewis acids were tested. After some screening reactions it was found that titanium(IV) chloride can be successfully used to improve the diastereomeric ratio of desired cycloadducts (*Sp*,*Sp*)-**262a** and (*Sp*,*Sp*)-**262b**. (Table 5).



(*Sp*,*Sp*)-**155** (*Sp*,*Sp*)-**262a**

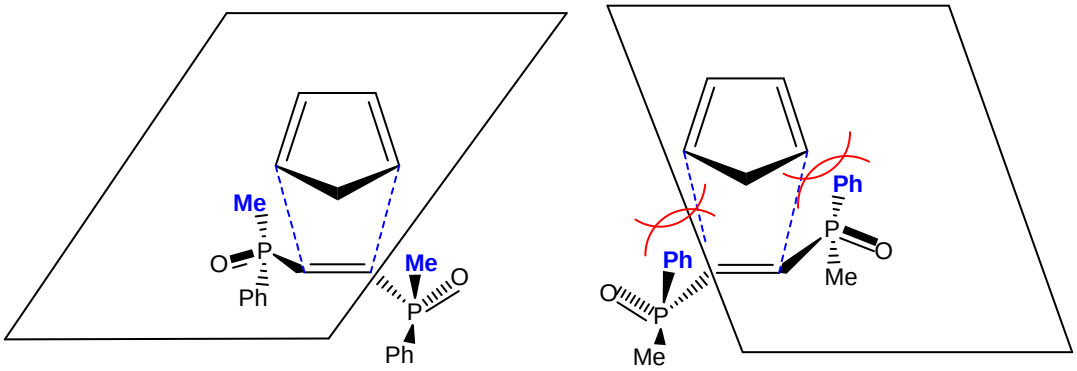
Addition of only 0.5 equiv. of $TiCl_4$ significantly increased the ratio of diastereoisomers as by addition of 1.0 and 1.5 equiv., which decreased the diastereoselectivity. (Table 5)

Table 5. The asymmetric Diels-Alder cycloaddition of (*Sp*,*Sp*)-**155** with cyclopentadiene (**243**)

$TiCl_4$ (equiv.)	solvent/ T °C	t, h	**262a** : **262b** [a]	yield, %
–	Toluene /110	18	1,3:1	95
–	CH_2Cl_2 / 20	21	1,3:1	90
0.5	CH_2Cl_2 / 20	17	9:1	87
1.0	CH_2Cl_2 / 20	19	7:1	85
1.5	CH_2Cl_2 / 20	24	5:1	82
2.0	CH_2Cl_2 / 20	48	3:1	70

[a] The diastereomeric ratio was determined by ^{31}P NMR

Formation of the two diastereomeric adducts (*Sp*,*Sp*)-**262a** and (*Sp*,*Sp*)-**262b** in unequal amounts indicates on an asymmetric induction. Recent stereochemical studies concerning asymmetric cycloaddition reactions involving conjugated olefins with strongly activating groups revealed that under thermal reaction conditions the reactive conformations of the conjugated systems reflect the conformation in the corresponding ground states, and that for majority of the systems studied they are *s*-cis.[136] However, for the Diels-Alder reaction the reactive *s*-*trans* conformation of the organophosphorus dienophiles (*Sp*)-**97** and (*Sp*)-**187** was proposed.[97, 132] Taking into the account, that (*Sp*,*Sp*)-**155** reacts in the *s*-*trans* conformation, two transition states for the uncatalyzed Diels-Alder reaction might be reasonable to discuss (Scheme 19):



(*Sp*,*Sp*)- **262a** **major**

MODEL **A**

(*Sp*,*Sp*)- **262b** **minor**

MODEL **B**

Scheme 19. Diastereoselection in the asymmetric Diels-Alder reaction

If in the reactive conformation of the dienophile (*Sp*,*Sp*)-**155**, the conjugated C=C and P=O groups are assumed to be *s*-*trans* coplanar, the configurations of the two newly created

centers of asymmetry, C-2 and C-3, should be controlled mainly by steric interactions between the phosphorus substituents and the diene coming in *endo* with respect to the methyl group (model **A**). In the (model **B**) the formation of (*Sp,Sp*)-**262b** will disfavour the diene approach by steric repulsions with the phenyl substituent of the phosphoryl group.

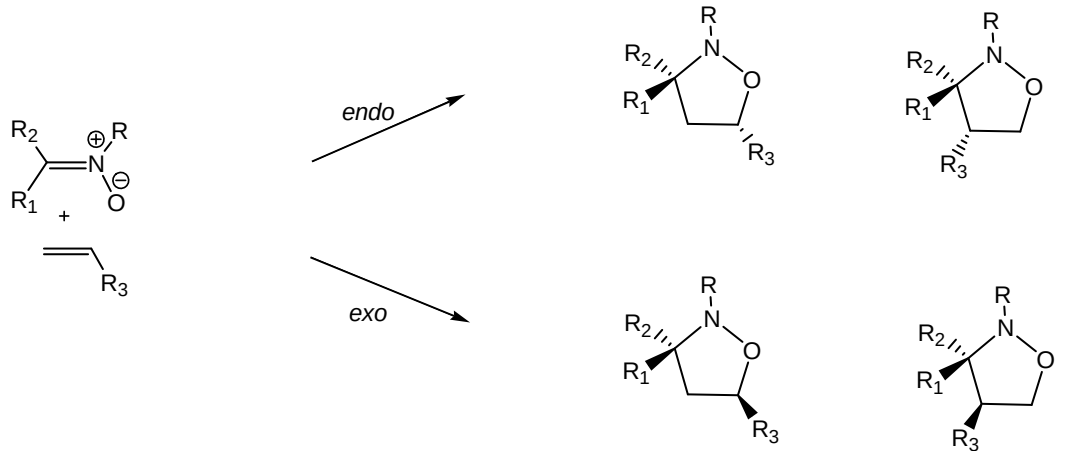
The results obtained for the asymmetric [4+2] cycloaddition catalyzed by titanium chloride can be explained through the complexation of $TiCl_4$ presumably at both oxygen atoms of (*Sp,Sp*)-**155** and thus by decreasing of the activation energy by the lowering the energy of the LUMO, which is required to facilitate the diastereoselective cycloaddition. Recently, the coordination of $GaCl_3$ to the oxygen atom of P=O group of *O,O*-diethyl-*β*-methoxycarbonylvinylphosphonate in a Diels-Alder reaction with 9,10-dimethylantracene was documented.[137]

3.3 The Asymmetric Huisgen Cycloaddition of (*Sp,Sp*)-155 with Acyclic Nitrones

The addition of a 1,3-dipole to an alkene for the construction of a variety of five-membred heterocycles is a powerful reaction in organic chemistry.[138] The general application of 1,3-dipoles in organic chemistry was first established by the systematic studies of Huisgen in the 1960s.[139] At the same time, the new concept of conservation of orbital symmetry, developed by Woodward and Hoffmann, appeared.[140] Their work was a milestone for the understanding of the mechanism of concerted cycloaddition reactions. On the basis of the concept by Woodward and Hoffmann, Houk et al. have further contributed to our present understanding and ability to predict relative reactivity and regioselectivity, of 1,3-dipolar cycloaddition reactions.[141]

Isoxazolidines, the products of 1,3-dipolar cycloaddition reaction between nitrones and alkenes, are saturated, five membered heterocycles containing adjacent nitrogen and oxygen atoms.[142] Best regarded as a concerted but asynchronous [$_{\pi}4_s$ + $_{\pi}2_s$] suprafacial process, the reaction allows up to three contiguous carbon stereocentres to be created in a single step. In a manner analogous to the famous [$_{\pi}4_s$ + $_{\pi}2_s$] cycloaddition reactions, the nitrone-alkene cycloadditions can occur with the nitrone and alkene approaching each other in either of two possible regiochemical senses and in either an *endo*- or *exo*- fashion, the four possible

transition states giving rise to two pairs of regioisomeric and diastereoisomeric products (Scheme 20).[143]

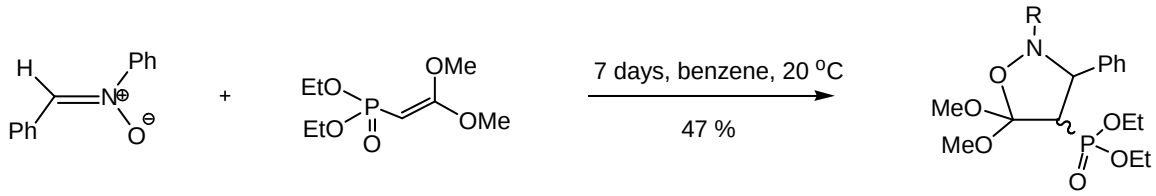


Scheme 20. Regioselectivity in the Huisgen cycloaddition of a nitrone with an alkene

Most studies concerned with the reactions between achiral nitrones and chiral unsaturated carbonyl compounds have concentrated mainly upon the product distribution in terms of regio-, stereo- and facial selectivity in the 1,3-dipolar cycloaddition step. The synthetic utilities of chiral allylic amines,[144] vinylic and allylic ethers,[145] vinylic sulphoxides[146] as precursors to optically active isoxazolidines have also been demonstrated.

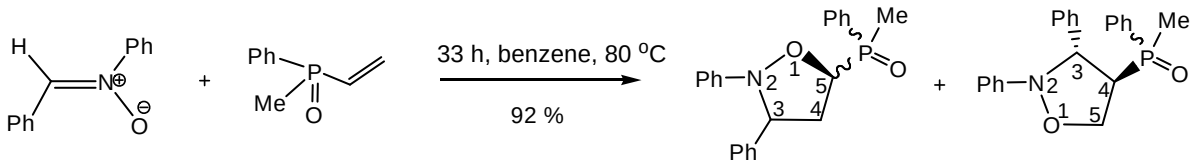
The use of organophosphorus compounds as dipolarophiles for 1,3-dipolar cycloaddition reaction is still limited to few examples and remains to be an important subject in organic chemistry due to the further utility of the phosphorus isoxazolidines as ligands for asymmetric catalysis.[147]

The first 1,3-cycloaddition of organophosphorus dienophiles appeared in 1975, where *C*,*N*-diphenylnitrone (**265**) was reacted with β–substituted vinylphosphonate (**266**) to give isoxazolidine **267** in a moderate yield.[148]



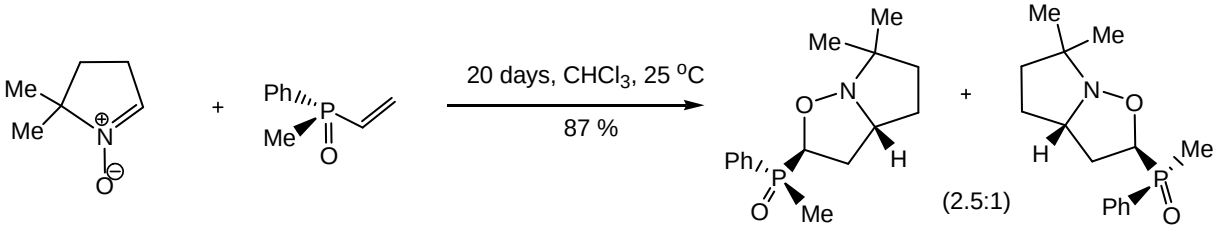
265 **266** **267**

In 1989, Pietrusiewicz et. al. reported the 1,3-dipolar cycloaddition of chiral *racemic* vinylphosphine oxide **97** to various acyclic and cyclic nitrones with ca. 40% *de* diastereofacial selectivity.[149] For example, *C*,*N*-diphenylnitrone (**265**) reacted with *rac*-**97** to form two regioisomeric products **268a** and **268b**, whereas 5-substituted regioisomer **268a** either prevailed in the product mixtures.



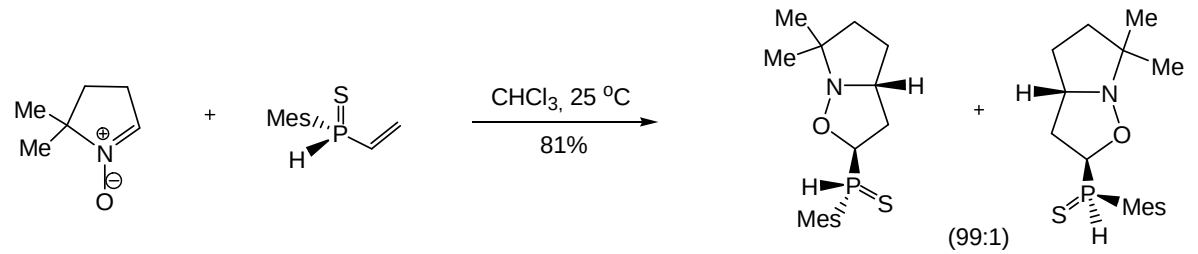
265 *rac*-**97** **268a** (42:29:17:12) **268b** (70:30)

In a related study, the enantiomerically pure vinylphosphine oxide (*Sp*)-**97** reacted with 2,2-dimethyl-3,4-pyrroline *N*-oxide (DMPO) (**269**) to give two diastreoisomers **270a** and **270b** in high yield. The unique sense of induction is consistent with the assumption that vinylphosphorus dipolarophile prefer an *s*-cisoid array of C=C−P=O fragments in their reactive conformations.[150]



269 (*Sp*)-**97** **270a** **270b**

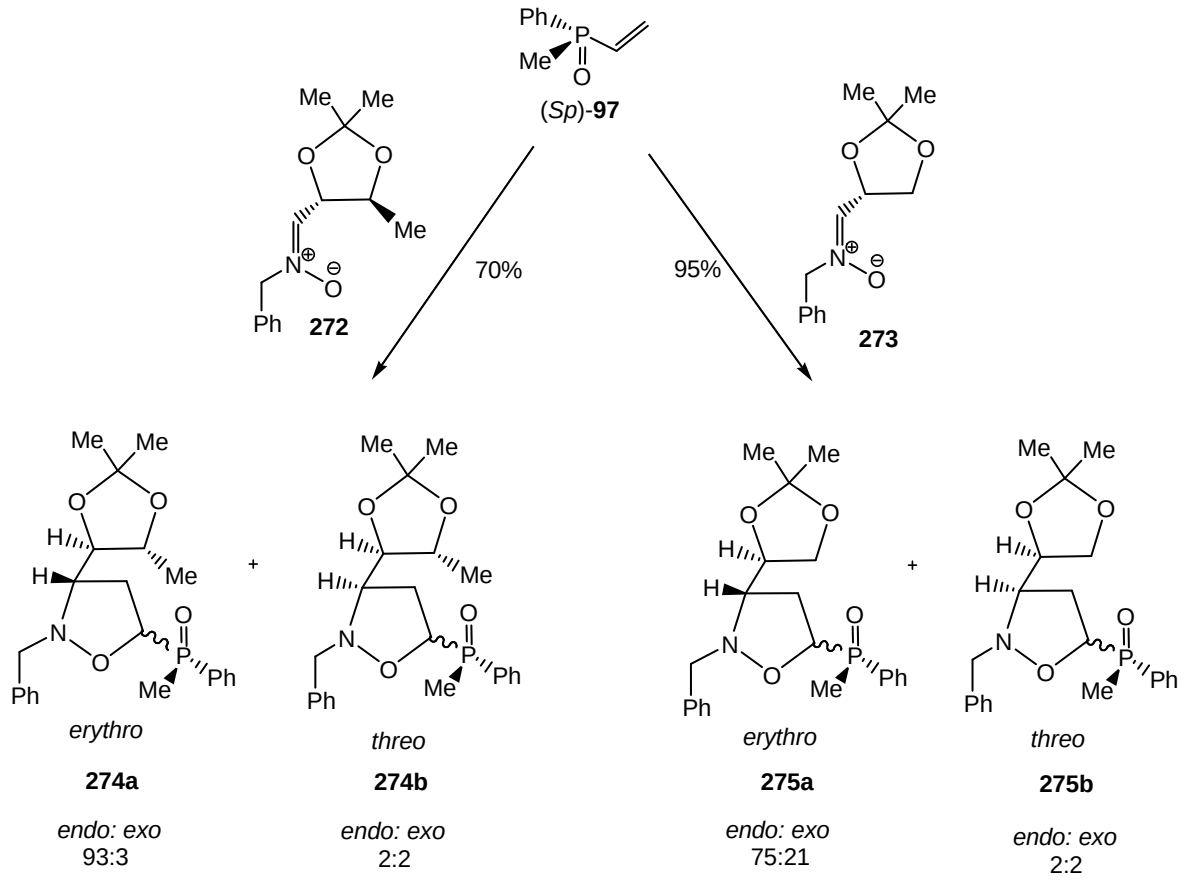
Pietrusiewicz reported that the facial selectivity in 1,3-dipolar cycloaddition of vinyl phosphine chalcogenides can be effectively controlled by the phosphorus stereocenter. For example, a replacement of oxygen with sulphur, and methyl substituent with hydrogen resulted in the improvement of the diastereoselectivity in the 1,3-dipolar cycloaddition of **267**.[151]



269 **267** **271a** **271b**

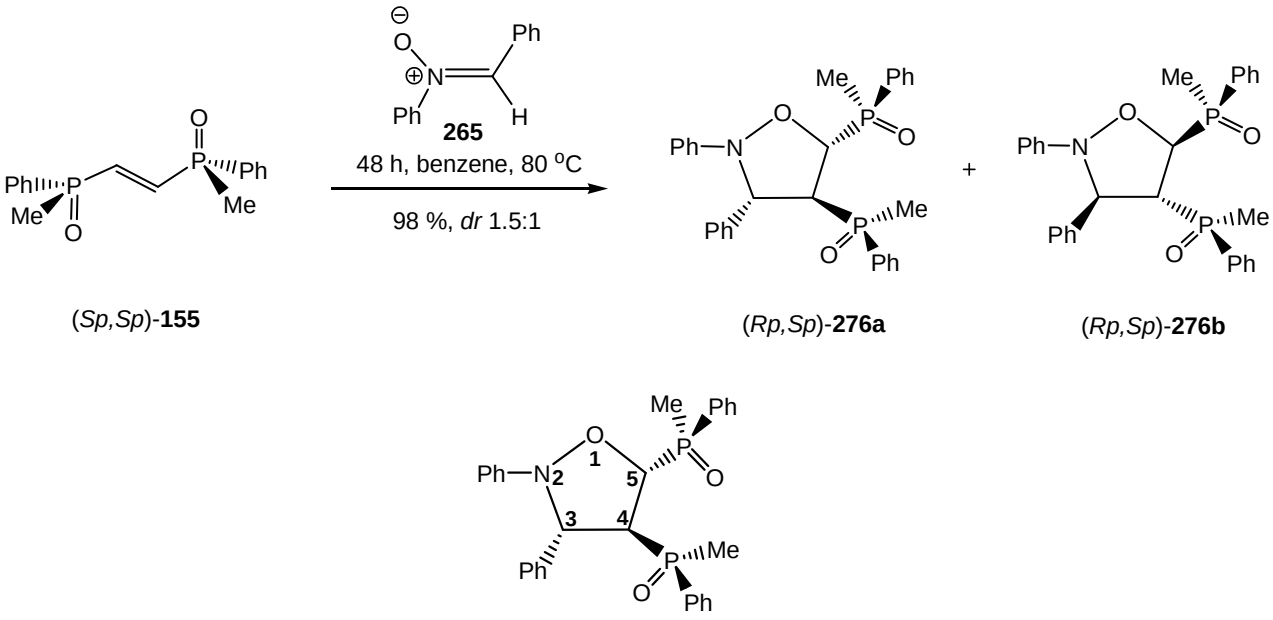
In addition, Pietrusiewicz et. al. studied single and double asymmetric induction in the 1,3-dipolar cycloaddition of chiral nitrones **272** and **273** and the enantiomerically pure (*Sp*)-(**97**).

In fact, this reaction led to four possible 5-substituted regioisomeric adducts with the selectivity in favour of the *erythro* **274a** or **275a** isomer. The presence of the methyl substituent in **272** proved advantageous in terms of *endo* vs. *exo* selectivity which was raised from 3:1 to 30:1 in the cyloaddition with (*Sp*)-(**97**).[152]



Taking into account that (*Sp,Sp*)-**155** underwent the asymmetric Diels-Alder with cyclopentadiene (**243**) the related approach might be possible to use (*Sp,Sp*)-**155** as chiral dipolarophile in an asymmetric Huisgen cycloaddition.

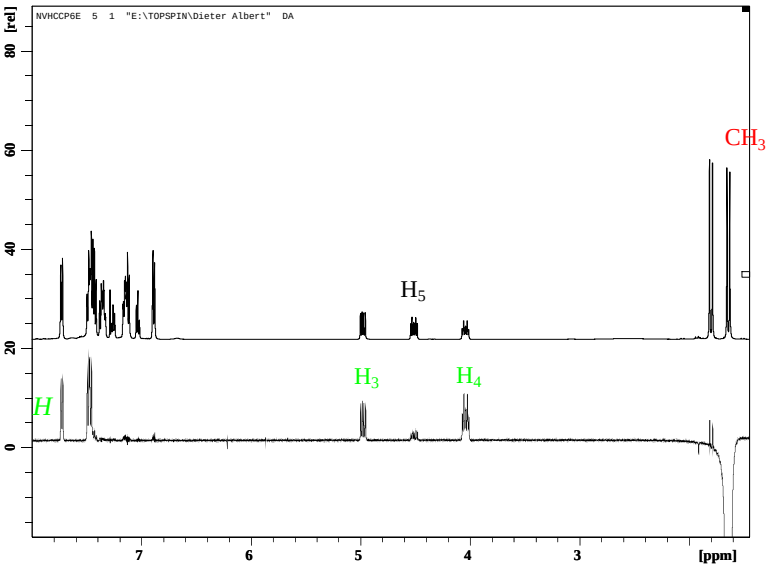
In a sequence to develop a novel approach to unprecetend *P*-chiral bidentate ligands, the *P*-chiral diphosphine dioxide (*Sp,Sp*)-**155** was treated with *C,N*-diphenylnitrone (**265**) in boiling benzene. After two days, the crude reaction mixture showing two doublets of the desired product between δ = + 36 and 40 ppm in the ^{31}P NMR indicating that the reaction was completed. The two products formed in the ratio 1.5:1 are diastreoisomers (*Rp,Sp*)-**276a** and (*Rp,Sp*)-**276b**, which were easily separated by column chromatography and characterized by their ^{1}H, ^{13}C, ^{31}P NMR and IR spectra. In the ^{1}H NMR the methyl groups at phosphorus resonate as doublets, with the coupling constant $^{2}J_{PH}$ = 13.2 Hz.[153]

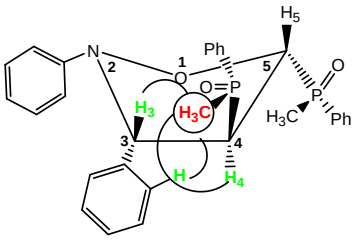


Scheme 21. Isoxozalidine ring numbering in (*Rp,Sp*)-**276a**

The signals of the protons at the isoxazolidine ring in (*Rp,Sp*)-**276a** and (*Rp,Sp*)- **276b** are readily assigned by a combination of HMQC, HMBC and HH-COSY spectra. The signal assigned to 3-H appeared always as a double doublet, whereas 4-H and 5-H give rise to more complicated signals, due of their direct coupling with chiral phosphorus atoms. The signals referred to C-4 and C-5 were assigned on the basis of $^{1}J_{PC}$, which is larger in the case of C-5.[149] This correct assigment was later confirmed by HH-COSY and HMBC spectra. In the ^{13}C NMR spectra all carbon atoms belonging to phenyl groups attached to the phosphorus atom show doublets with appropriate coupling constants to phosphorus, which is in agreement with the literature.[153] The coupling constant of the signals obtained from the ^{31}P NMR spectra for each diastereoisomer are J_{PP} = 20.3 Hz and J_{PP} = 19.8 Hz for the major diastereoisomer, and J_{PP} = 16.4 Hz and J_{PP} = 15.9 Hz for the minor one, indicating the magnetic non-equivalence of the asymmetric phosphorus atoms.

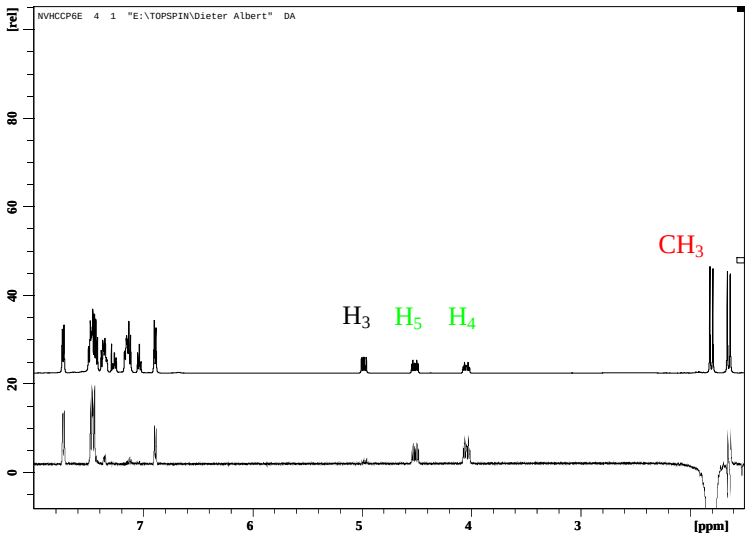
Since, the cycloaddition reactions are known to proceed with complete stereospecifity, it was rational to conclude the *trans* arrangement of the phosphorus substituents in the five-membred ring. The NOE spectra allow assigning of the relative configuration in the isoxazolidine ring. These experiments clearly showed that all the substituents in the isoxazolidine ring are positioned *trans* one to another.

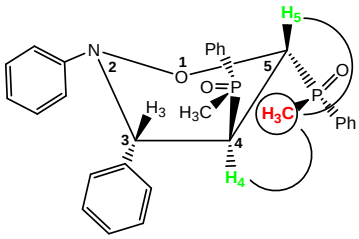




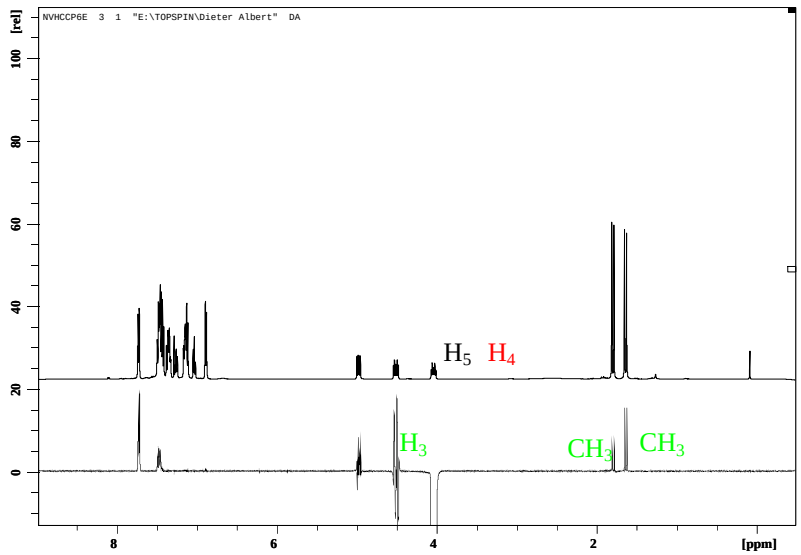
(*Rp*,*Sp*)-**276a**

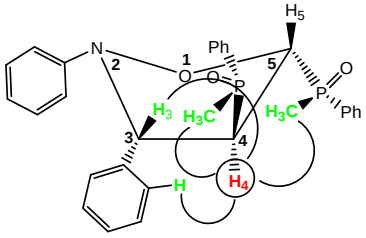
Fig. 5 Irradiation (NOE) of CH_3 at δ = 1.62 ppm





(*Rp*,*Sp*)-**276a**





(*Rp*,*Sp*)-**276a**

Fig. 7 Irradiation (NOE) of H_4 at δ = 4.01 ppm

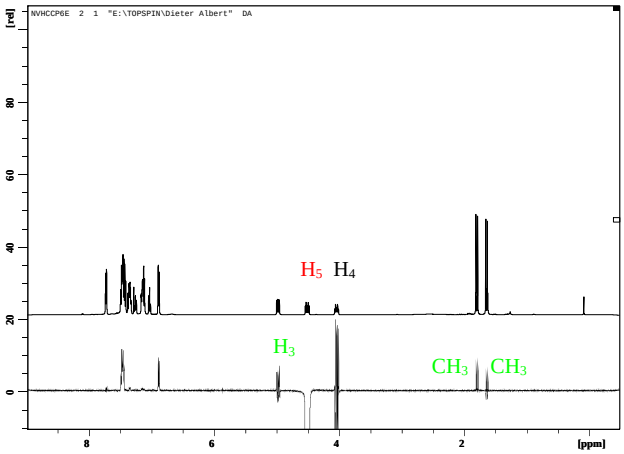
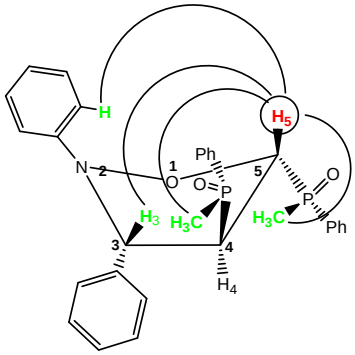


Fig. 8 Irradiation (NOE) of H_5 at 4.47



(*Rp*,*Sp*)-**276a**

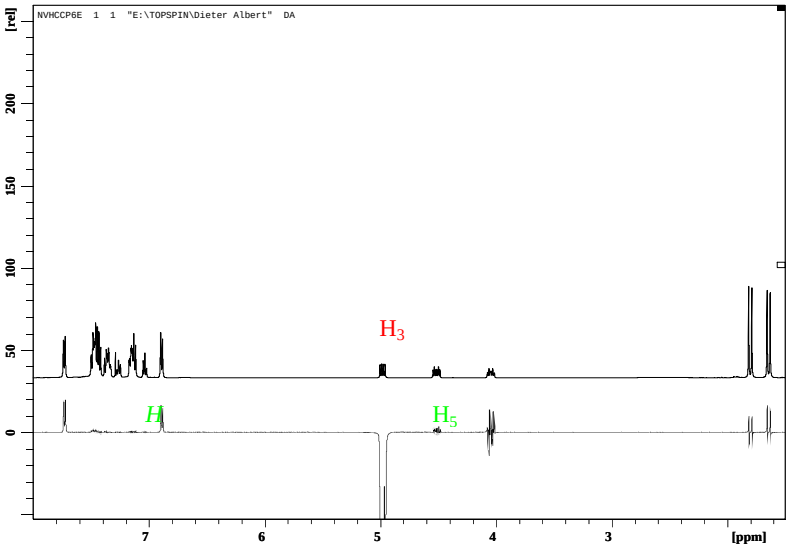
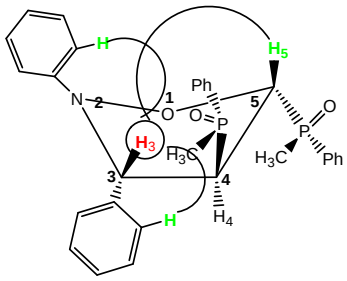


Fig. 9 Irradiation (NOE) of H_3 at 4.96 ppm



(*Rp*,*Sp*)-**276a**

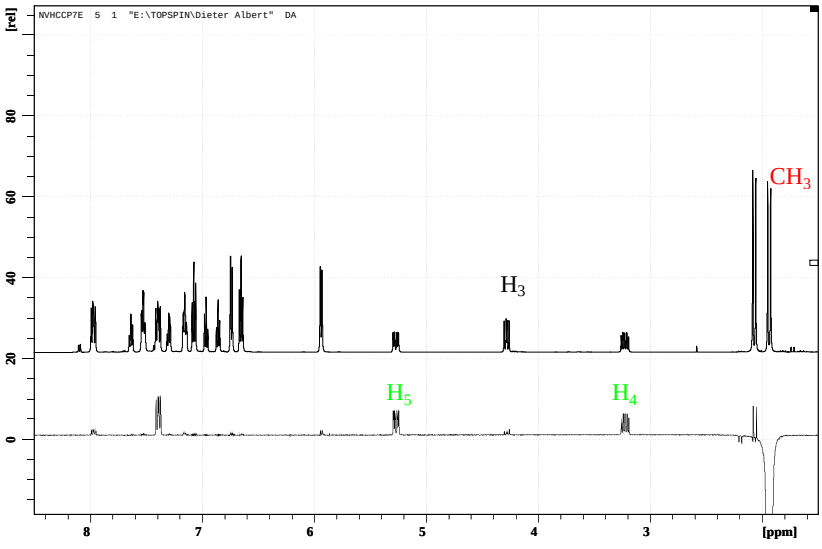
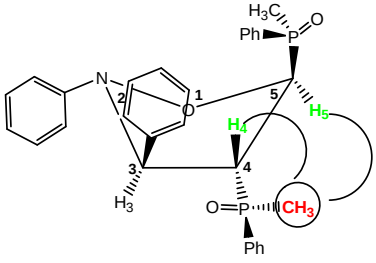


Fig. 10 Irradiation (NOE)of CH_3 at 1.92 ppm



(*Rp*,*Sp*)-**276b**

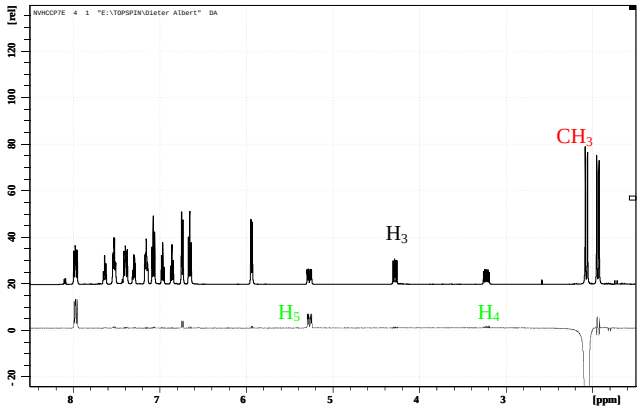
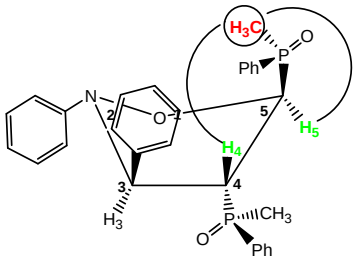


Fig. 11 Irradiation (NOE) of CH_3 at 2.06 ppm



(*Rp*,*Sp*)-**276b**

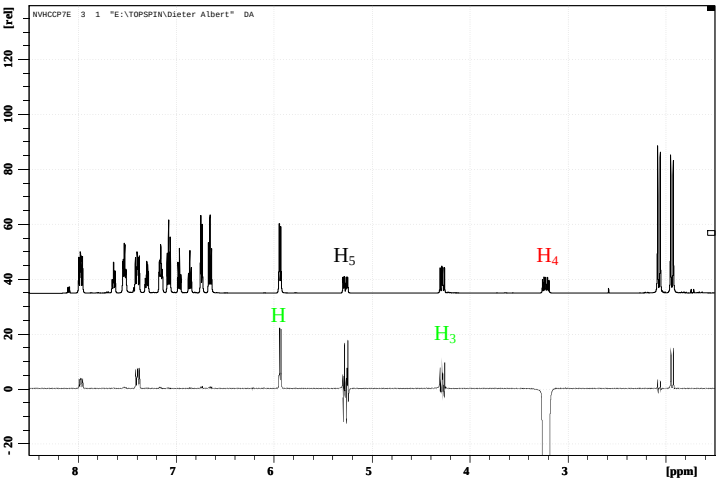
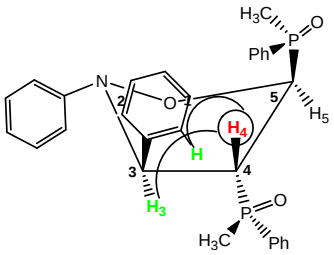


Fig. 12 Irradiation of H_4 at 3.19 ppm



(*Rp*,*Sp*)-**276b**

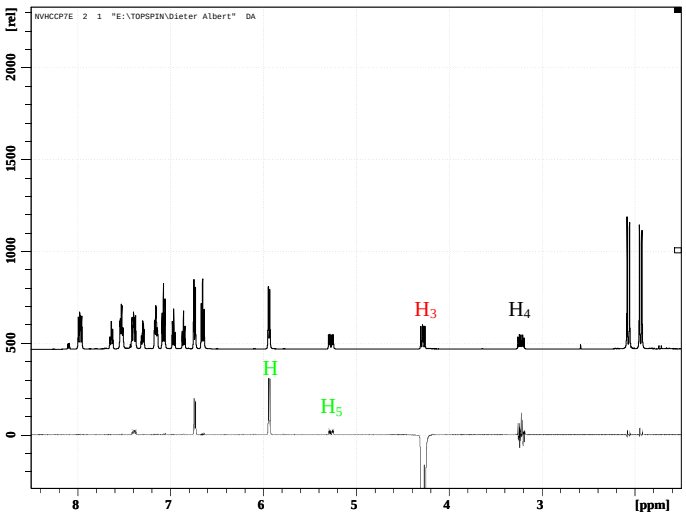
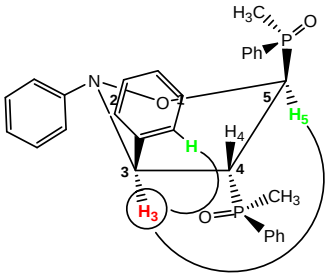
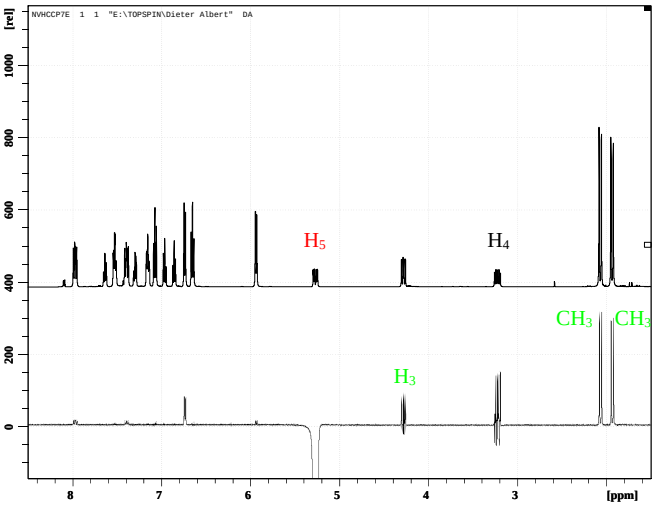
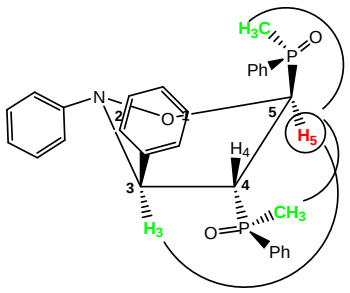


Fig. 13 Irradiation (NOE) of H_3 at 4.26 ppm



(*Rp*,*Sp*)-**276b**

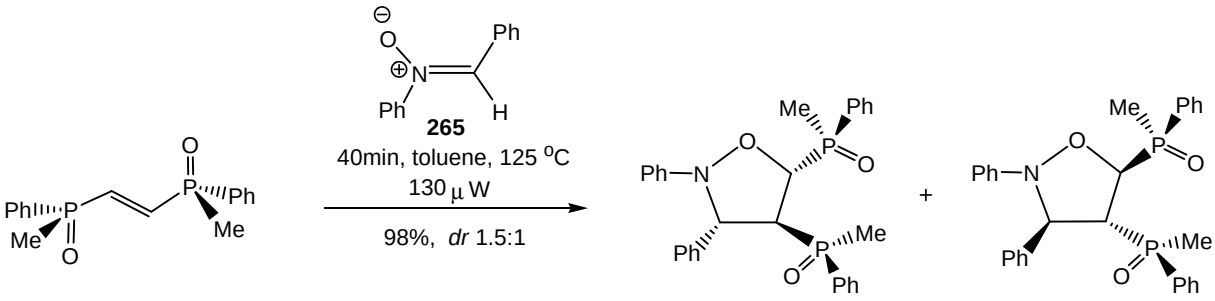




(*Rp*,*Sp*)-**276b**

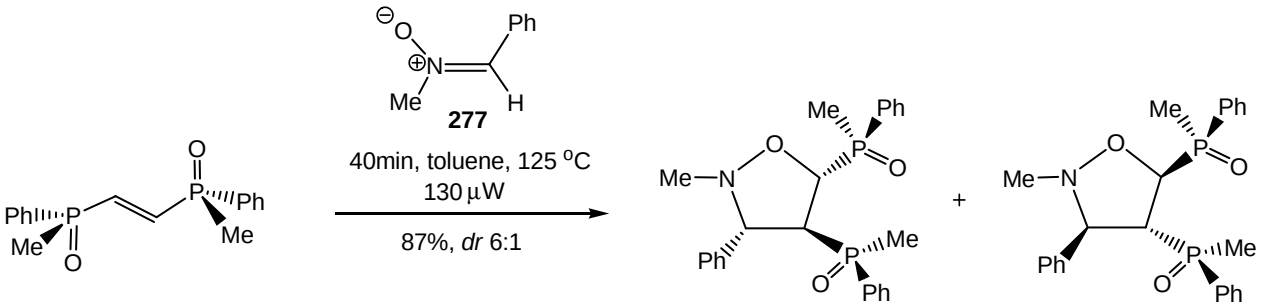
Fig. 14 Irradiation (NOE) of H_5 at 5.23 ppm

This 1,3-dipolar cycloaddition can also be performed under microwave irradiation. By using toluene as the solvent it was possible to reduce the reaction time from 2 days to 40 minutes without decrease of the yield. No alternation of diastereoselectivity was observed.



(*Sp*,*Sp*)-**155** (*Rp*,*Sp*)-**276a** (*Rp*,*Sp*)-**276b**

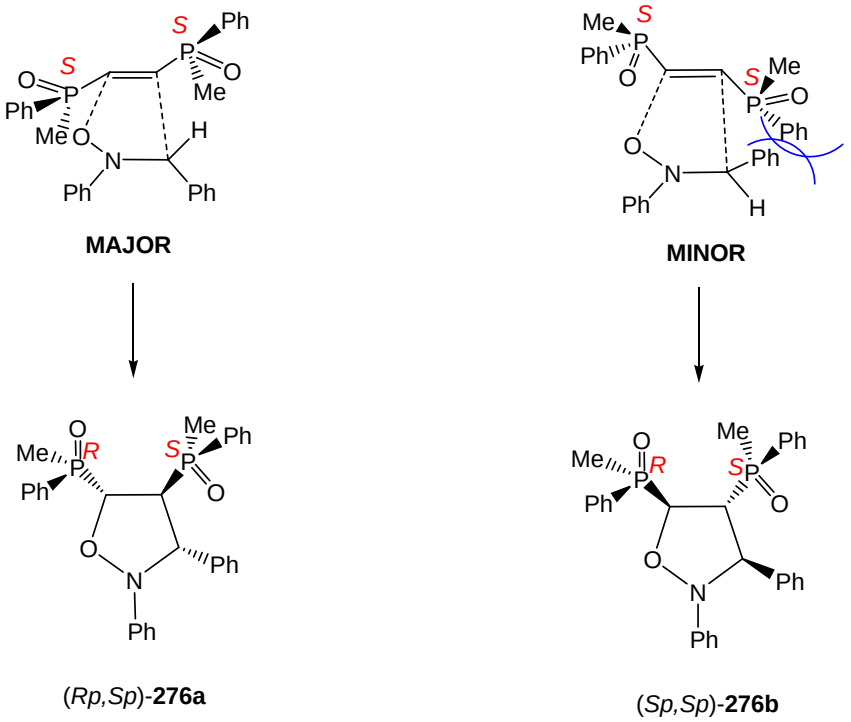
In order to investigate this reaction, (*Sp*,*Sp*)-**155** was treated with *C*-phenyl-*N*-methylnitrone (**274**). The reaction proceeds with higher diastereoselectivity leading to two diastereosiomers in the ratio 6:1 (^{31}P MNR) in high yield.



(*Sp*,*Sp*)-**155** (*Rp*,*Sp*)-**278a** (*Rp*,*Sp*)-**278b**

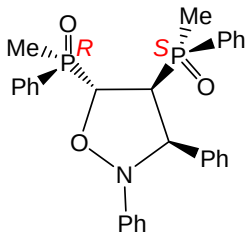
These results are comparable to those obtained by Pietrusiewicz et. al. for the 1,3-dipolar cycloaddition of the (*Sp*)-**97**, which led to diastereoisomeric ratios 60:40 and 87:13 by the use acyclic nitrones **261** and **274**, respectively.[149, 154]

To discuss possible models of diastereoselectivity, firstly it should be mentioned that only two diasteroisomeric isoxazolidines were formed, whereas four possible diastereoisomers could be formed. In order to explain the observed diastereoselectivity trends, two transition states can be taken into account (Scheme 22).



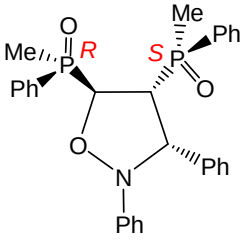
Scheme 22. Proposed models of diastereoselectivity for the formation (*Rp*,*Sp*)-**276a** and (*Rp*,*Sp*)-**276b** Charges are omitted for clarity.

Based on the proposed above transition states, it has been concluded that the reactive conformation of the dipolarophile (*Sp*,*Sp*)-**155**, must be also *s-trans* coplanar. The transition state of major (*Rp*,*Sp*)-**276a** is more preffered as compare to minor (*Rp*,*Sp*)-**276a**, because steric repulsions between the methyl group and the hydrogen are minimized, whereas the formation of (*Rp*,*Sp*)-**276b** disfavoured by the steric interactions between two phenyl groups (minor).



(*Rp*,*Sp*)-**276c**

not formed



(*Sp*,*Sp*)-**276d**

not formed

Scheme 23. Unfavourable (not formed) diastereoisomers (*Rp*,*Sp*)-**276a** and (*Rp*,*Sp*)-**276b**

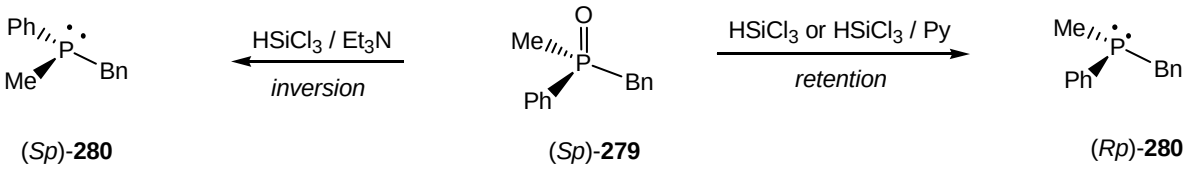
The formation of other two diastereoisomers (*Rp*,*Sp*)-**276c** and (*Rp*,*Sp*)-**276d** is disfavoured presumably because of additional steric interactions between the phosphorus substituent and the phenyl ring, due the *cis*-arrangement of the substituents undesired.

3.4. Reduction of *P*-Stereogenic Diphosphine Dioxides to *P*-Stereogenic Diphosphines

Optically active phosphines possessing their chiral centers at phosphorus atoms have become increasingly important not only in stereochemical studies of organophosphorus compounds but also as chiral ligands in transition metal catalyzed asymmetric reactions.[2,8] The stereospecific reduction of *P*-chiral monophosphine oxides to *P*-chiral monophosphines with *retention* or *inversion* of configuration has been developed,[47] albeit is still limited concerning its applications in the *P*-chiral ligand synthesis. A necessary condition for such a reduction is that it must proceed under mild reaction conditions, because the produced phosphine can racemize by thermally induced pyramidal inversion.[156] $LiAlH_4$ is a powerful reducing reagent and it is often used for the reduction of achiral phosphine oxides. However, the reduction of optically active phosphine oxides by $LiAlH_4$ leads predominantly to the racemized *P*-chiral phosphines owing to pseudorotation of the pentacoordinate intermediates.[157]

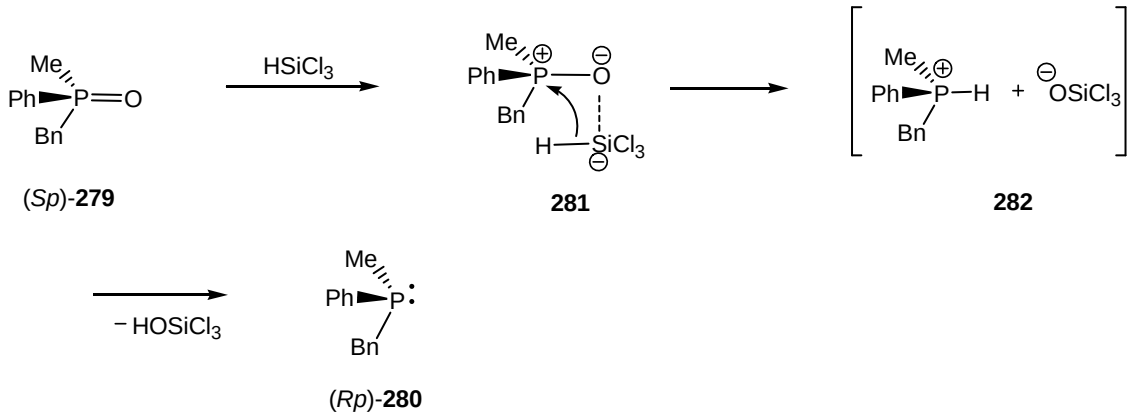
Historically, in 1965 Horner developed the first method for reduction of optically active methylphenylbenzylphosphine oxide (*Sp*)-**279** to appropriate phosphines.[17a] In presence of trichlorosilane the reduction proceeded with retention of configuration, whereas the combination of trichlorosilane with Et_3N led to a *inversion* at phosphorus. Interestingly,

Horner and Balzer observed that in the presence of pyridine and *N*,*N*-diethylaniline the stereochemical course of this reaction is *retention.*[17a]



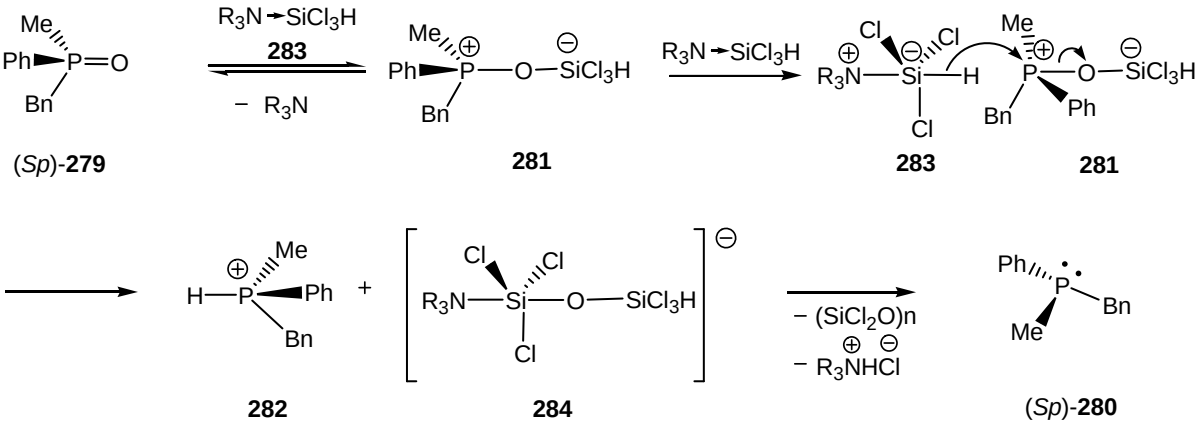
(*Sp*)-**280** (*Sp*)-**279** (*Rp*)-**280**

To rationalize the retention of configuration in the absence of base, Horner and Balzer suggested complexation to **281**, followed by *intramolecular* hydride transfer to **282**, which after a release von $HOSiCl_3$ allowed the formation of the (*Rp*)-**280** with retention of configuration.[17a]



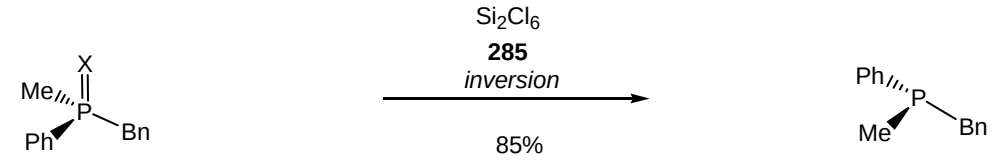
(*Sp*)-**279** **281** **282** (*Rp*)-**280**

To establish the inversion of configuration in the presence of triethylamine it was suggested that complexation to **281** followed by *intermolecular* hydride transfer from a 1:1 triethylamine-trichlorosilane complex **283** in an S_N2 reaction through formation of the the intermediate **282** followed by an elimination of HCl from **284** and the formation of (*Sp*)-**280**.[17a]



(*Sp*)-**279** **281** **283** **281** **282** **284** (*Sp*)-**280**

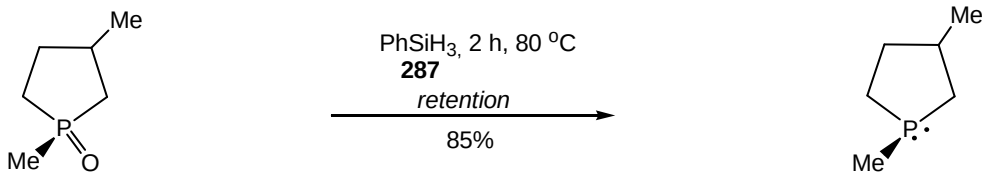
In addition Mislow et. al reported the use of hexachlorodisilane (**285**) as reducing agent for the reduction of optically active phosphine oxide (*Sp*)-**279** and sulphide (*Sp*)-**286** with inversion of configuration.[17b]



(*Sp*)-**279** X = O
(*Sp*)-**286** X = S

(*Sp*)-**280**

In 1974 the use of phenylsilane (**287**) to reduce (*Rp*)-1,3-dimethylphospholane 1-oxide (**288**) with *complete* retention of configuration to yield (*Sp*)-**289** was published by Marsi et. al.[158] Acyclic optically active phosphine oxides were also reduced with *complete* retention of configuration using the same protocol.

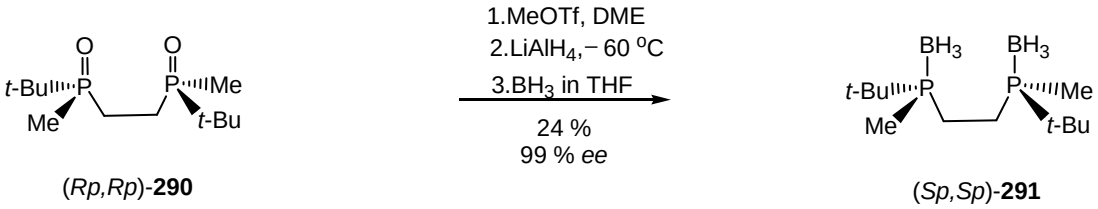


(*Rp*)-**288**

(*Sp*)-**289**

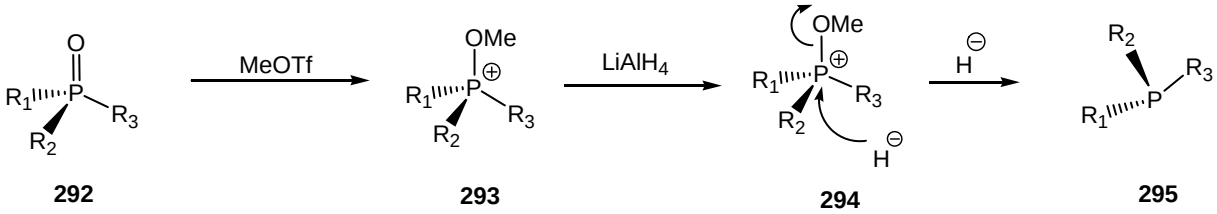
Phenylsilane offers advantages over trichlorosilane as a reducing agent since the later method employs the use of an amine which may be somewhat difficult to separate from the phosphine when the two have similar boiling points. Hexachlorodisilane offers the advantage of reduction with inversion, if that stereochemical operation is required. However, if a configurationally pure phosphine is desired, hexachlorodisilane may not be satisfactory since its use is accomplished by some stereomutation, attributed to the generation of silicon tetrachloride produced *in situ.* Additionally, hexachlorodisilane is currently an expensive reagent.

Recently, Imamoto et. al reported a convenient method for the stereospecific reduction of optically active phosphine oxides. *P*-chiral monophosphine oxides were reduced with *inversion* of configuration in high chemical yield. However, the reduction of *P*-chiral diphosphine dioxide (*Rp,Rp*)-**290** gave low yield of the borane complex (*Sp,Sp*)-**291**.[159]



(*Rp,Rp*)-**290** (*Sp,Sp*)-**291**

Although the detailed reaction mechanism has not yet been studied, it was supposed that the phosphine oxide **292** is methylated by methyl triflate, and the resulting phosphonium salt **293** is subjected to hydride attack **294** from the backside of the methoxy group to give the reduction product **292** (Scheme 24).

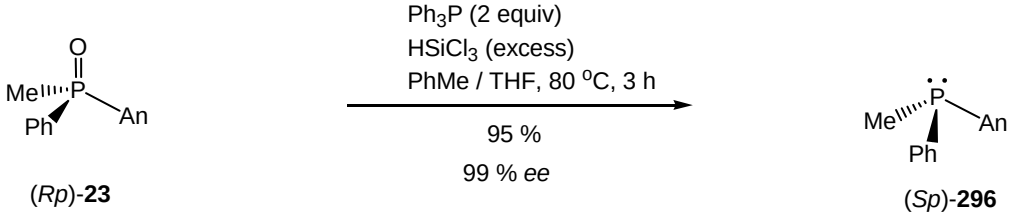


292 **293** **294** **295**

Scheme 24. Proposed formation of **295** by reduction with MeOTf / $LiAlH_4$[159]

However, very low stereospecificity was observed when methyl iodide, methyl methanesulfonate, and methyl *p*-toluenesulfonate were used. In these cases, the methylation of the phosphine oxide was not observed. The reduction probably proceeds in this case through the initial generation of alane by the reaction of methylation reagents with $LiAlH_4$ and subsequent reaction of phosphine oxides with alane.[160]

Lately, a new protocol for deoxygenation of the *P*-chiral monophosphine oxide (*Rp*)-**23** with complete retention of configuration appeared. The use of trichlorsilane and triphenylphosphine as an oxygen acceptor furnished accomplimentary protocol to the $HSiCl_3/Et_3N$ system that normally leads to an inversion. The enantiomerically pure phosphine (*Sp*)-**296** was isolated in high yield and excellent *ee*.[161]

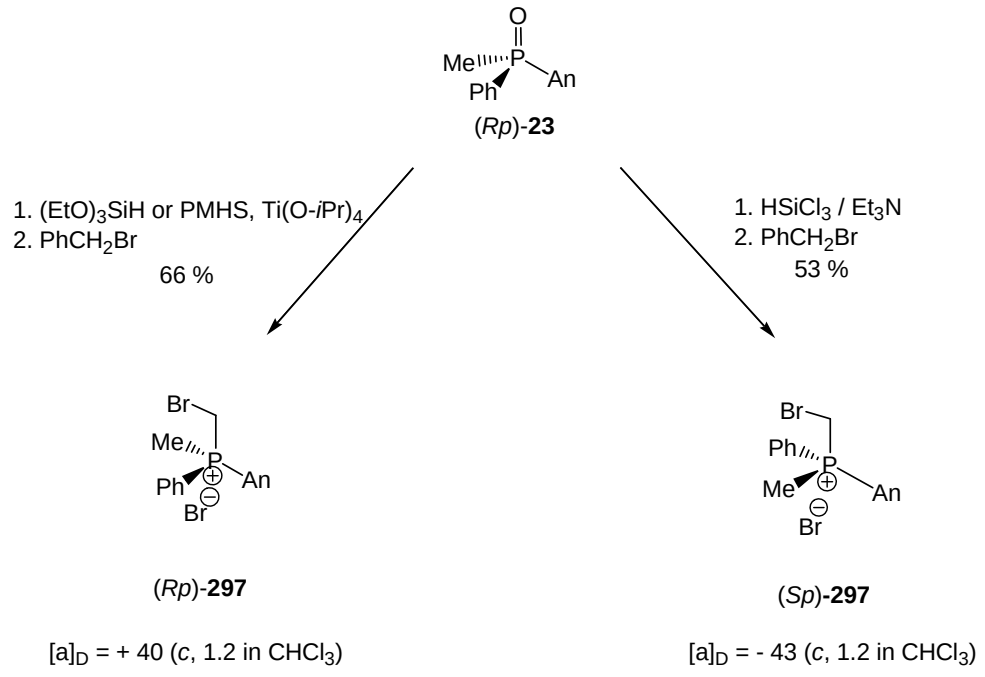


(*Rp*)-**23** (*Sp*)-**296**

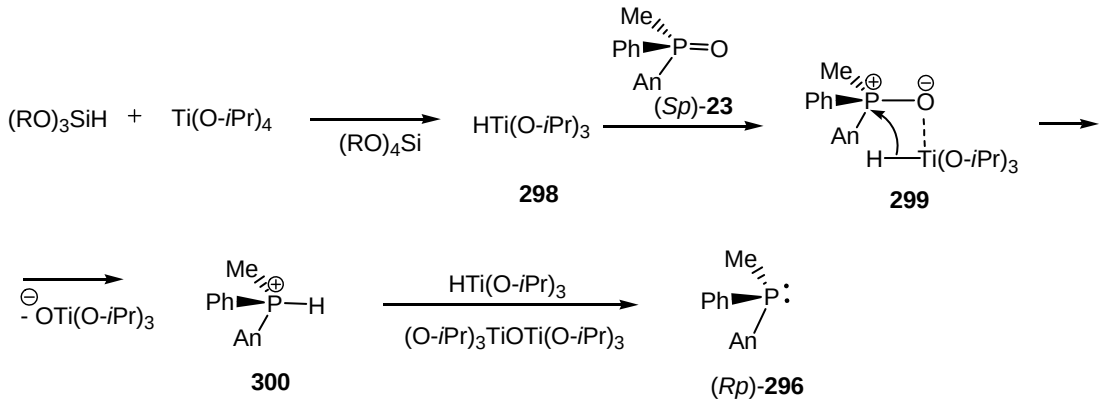
According our synthetic plan, the novel *P*-chiral diphosphine dioxides **262a** and (*Rp,Sp*)-**276a** and (*Rp,Sp*)-**276b** were submitted for the stereospecific reduction. Unfortunately, the use of

the common silane reagents $PhSiH_3$ or $HSiCl_3$ / Et_3N resulted in partial or complete racemization at phosphorus. Since, the N-O bond in **276a** might be cleaved in the presence $LiAlH_4$ as a hydride donor, the Imamoto method was applied only to **262a** however without any success. After many attempts to achieve the desired *P*-chiral diphosphines in diastereomerically pure form by variation of reaction conditions (solvent, temperature, reagents addition, reaction time, concentration) no positive results were obtained.

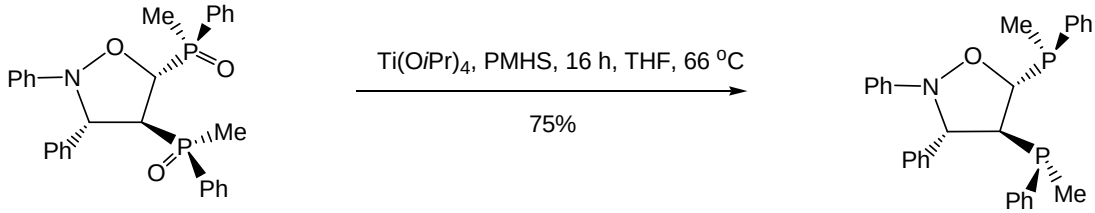
However, recently an interesting method based on the titanium(IV) catalysed reduction of phosphine oxides by triethoxysilane or polymethylhydrosiloxane (PMHS) was reported. The silane/titanium method is evidently proceeding predominantly with retention of configuration of phosphorus, providing an alternative to the phenylsilane and trichlorosilane (in the absence of an amine) methods both of which proceeded with retention.[162, 19] The optically active (*Rp*)-**23** was reduced in the presence of $(EtO)_3SiH$ or PMHS followed by reaction with benzylbromide leading to the phosphonium salt (*Rp*)-**297**, which showed opposite rotation value as compared to the (*Sp*)-**297**.[162]



If the reaction occurs by way of a titanium hydride species **298**, the stereochemistry can be explained by a syn-hydrotitanation type process **299** as the key step to give the protonated phosphine **300** with retention ofconfiguration.[162]



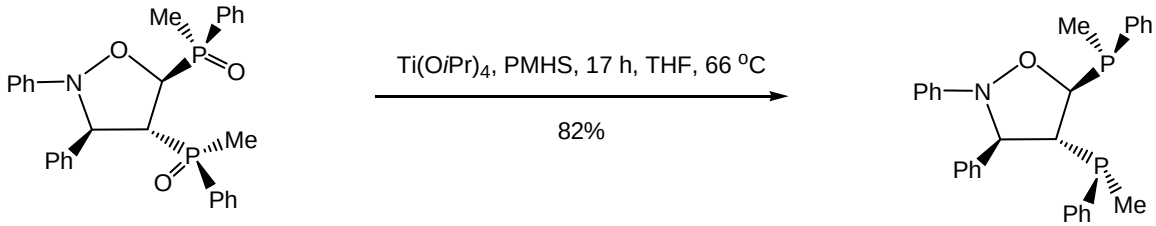
The application of this method to the reduction of (*Rp,Sp*)-**276a** and (*Rp,Sp*)-**276b** showed gratifiyingly that the *P*-stereogenic diphosphine dioxide (*Rp,Sp*)-**276a** was reduced stereospecifically in the presence of Ti(O*i*Pr)$_4$ and polymethylhydrosiloxane (PMHS) to give only one diastereoisomeric diphosphine (*Sp,Rp*)-**301a** as a product in good yield:



(*Rp,Sp*)-**276a**

(*Sp,Rp*)-**301a**

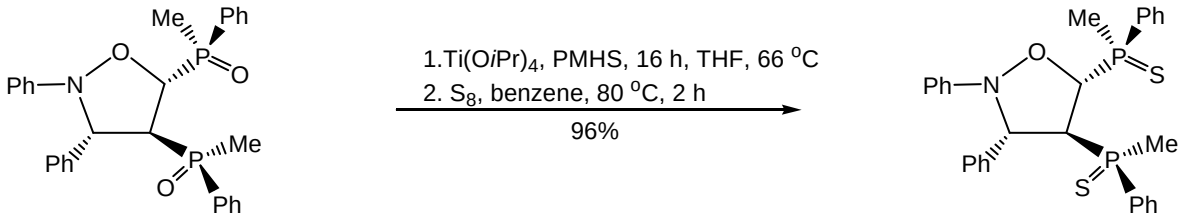
The other *P*-chiral diastereoisomeric diphosphine dioxide (*Rp,Sp*)-**276b** also underwent this stereospecific reduction to give (*Sp,Rp*)-**301b** without any racemization in 82% yield.



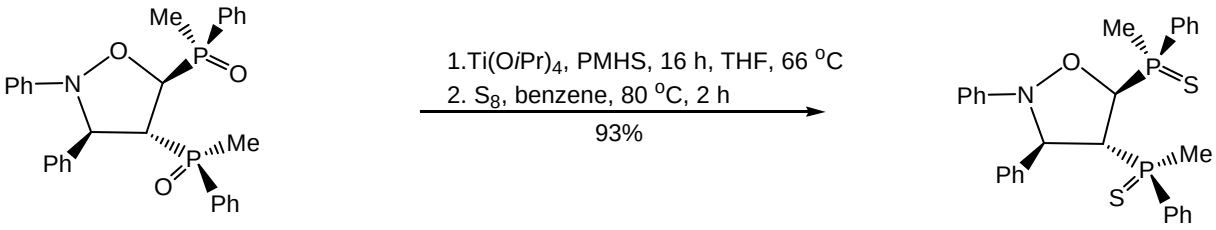
(*Rp,Sp*)-**276b**

(*Sp,Rp*)-**301b**

To prove that the formation of the new *P*-stereogenic diphosphines was stereospecific, each of them was oxidized with elementar sulfur to give desired *P*-stereogenic diphosphine disulfides (*Rp,Sp*)-**302a** and (*Rp,Sp*)-**302b** in high yields and especially as only one diastereoisomer, indicating a highly stereospecific reduction-oxidation sequence.



(*Rp,Sp*)-**276a** (*Rp,Sp*)-**302a**



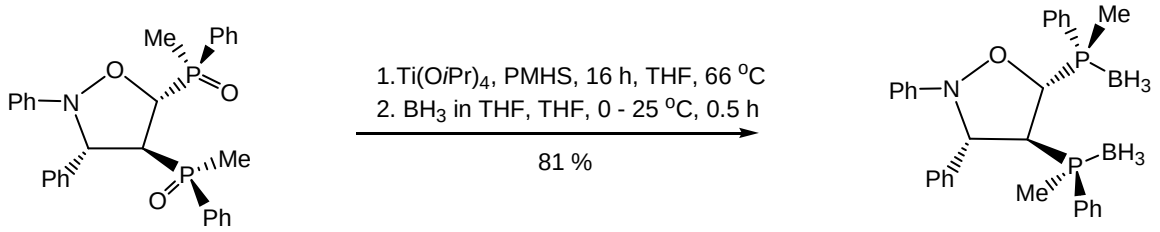
(*Rp,Sp*)-**276b** (*Rp,Sp*)-**302b**

After column chromatography, diastereomerically pure diphosphine disulfides were obtained as pure white solids and characterized by their ^{1}H, ^{13}C, ^{31}P NMR and IR spectra. Replacing phosphinyl oxygen with sulfur resulted in considerable decreases in $^{1}J_{PC}$ coupling constants by ca. 30 Hz.[153] In the ^{1}H NMR spectra the methyl groups at phosphorus resonate as doublets, ($^{2}J_{PH}$ = 12.9 Hz). The ^{31}P NMR spectra of each *P*-chiral diphosphine disulfide shows two doublets which are shielded + 45 to 50 ppm as compared to the diphosphine dioxides (*Rp,Sp*)-**273** (+ 35 and 40 ppm). The coupling constants of the major diastreoisomer (*Rp,Sp*)-**302a** are J_{PP} = 29.7 Hz and J_{PP} = 28.7 Hz, and J_{PP} = 27.2 Hz and J_{PP} = 27.2 Hz for the minor (*Rp,Sp*)-**302b** one, indicating the magnetic non-equivalence of the asymmetric phosphorus atoms.

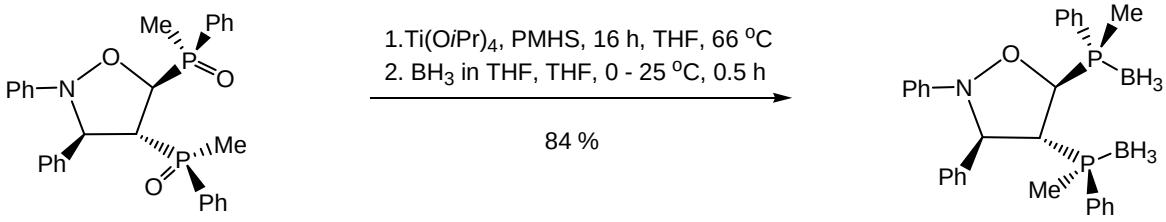
However, it should be mentioned that after reduction of *P*-chiral diphosphine dioxides (*Rp,Sp*)-**276a** and (*Rp,Sp*)-**276b** it was quite difficult to separate completely traces of PMHS from the sample of each diphosphine in order to obtain pure diphosphine directly after reduction. It is well known, that *P*-chiral phosphine-boranes are stable precursors to *P*-chiral phosphines, which can be easily handled in air and purified without decomposition by column chromatography. Usually, the synthesis of phosphine boranes is accomplished *in one pot* by treating a crude reaction mixture, which contains *P*-chiral phosphine, with BH_3 in THF.[24] After column chromatography or distillation pure diphosphine-boranes are usually obtained.

This synthetic procedure was successfully applied to our *P*-stereogenic diphosphines to give diastereomerically pure diphosphine diboranes in high yield. It should be mentioned here that obtained (*Sp,Rp*)-**303a** and (*Sp,Rp*)-**303b** are stable at 25 ºC during 2-3 weeks as solids, but

then they slowly decomposed (^{31}P NMR). Therefore the samples were stored at – 25 ºC in the refrigerator for the period more as 2 months without decomposition (^{31}P NMR).



(*Rp,Sp*)-**276a** (*Sp,Rp*)-**303a**



(*Rp,Sp*)-**276b** (*Sp,Rp*)-**303b**

Diastereomerically pure *P*-stereogenic diphosphine diborane complexes were assayed by their ^{1}H, ^{13}C, ^{31}P NMR spectra. Replacing phosphinyl oxygen by a borane moiety causes decreases in $^{1}J_{PC}$ coupling constants by ca. 20-30 Hz. In the ^{1}H NMR the methyl groups at phosphorus resonate as doublets, with the slightly smaller coupling constant ($^{2}J_{PH}$ = 10.2 Hz).[24] The ^{31}P NMR spectra of each *P*-chiral diphosphine diborane show four doublets which are shielded + 17 to 24 ppm as to ^{31}P NMR of diphosphine dioxides (+ 35 to 40 ppm), with the coupling constants for major diastreoisomer (*Sp,Rp*)-**303a** are J_{PP} = 41.6 Hz and J_{PP} = 45.5 Hz, and J_{PP} = 45.7 Hz and J_{PP} = 44.6 Hz for the minor (*Sp,Rp*)-**303b** one, indicating the magnetic non-equivalence of asymmetric phosphorus atoms.

The *P*-stereogenic diphosphine diborane (*Sp,Rp*)-**303b** crystallized by slow evaporation from a solvent mixture of hexane and EtOAc (3:1) at 25 ºC afforded crystals suitable for a single-crystal X-ray structure analysis (Fig.15).

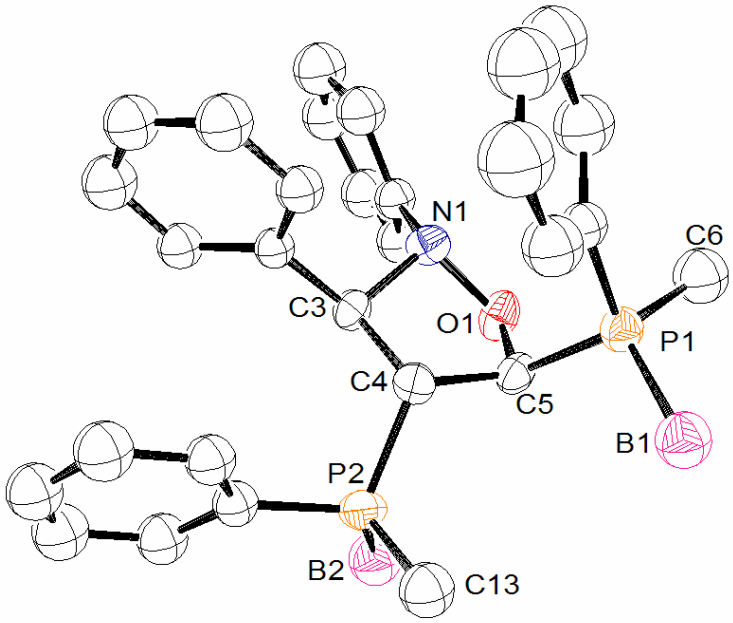
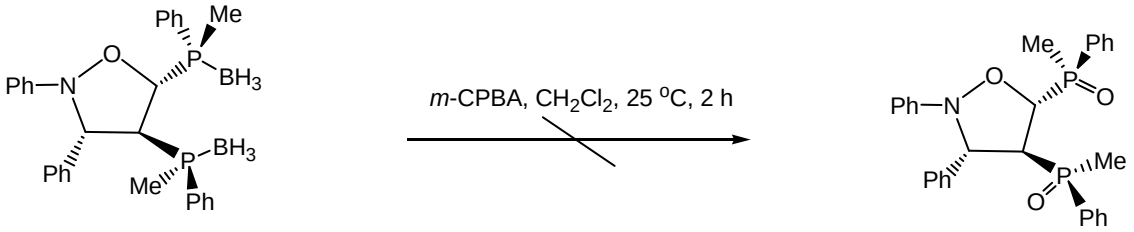


Fig. 15 Structure of (*Sp*,*Rp*)-**303b** in the crystal. Selected bond lengths [pm], angles [°]: P1-B1 189.2(9), P1-C5 185.1(6), P1-C6 178.9(7), P2-B2 188.2(10), P2-C4 184.2(6), O1-C5 142.3(7), O1-N1 146.8(5), N1-C3 149.0(7), C3-C4 155.8(7), C4-C5 155.1(7), C6-P1-C5 103.5(4), C6-P1-B1 113.6(4), C5-P1-B1 110.7(4), C13-P2-C4 105.5(3), C13-P2-B2 111.4(4), C4-P2-B2 115.0(4), C5-O1-N1 102.2(4), O1-N1-C3 100.8 (4), N1-C3-C4 101.7(5), C5-C4-P2 112.3(4), C3-C4-P2 109.9(4), O1-C5-C4 106.7(5), C4-C5-P1 115.3(4), O1-C5-C4 113.7(4).

On the basis of the X-ray analysis, it was possible to assign absolute configuration of both asymmetric phosphorus atoms and carbon atoms of the isoxazolidine ring in (*Sp*,*Rp*)-**303b**. The absolute configurations of phosphorus atoms are *S* (phosphorus substituent at C-5) and *R* (at C-4). The absolute configurations of carbon atoms in the isoxazolidine ring are C-3 – *R*, C-4 – *R*, C-5 – *S*. This assignment is in very good correlation with NOE experiments done for the assignment of the relative configuration in diastereoisomeric diphosphine dioxides (*Rp*,*Sp*)-**276a** and (*Rp*,*Sp*)-**276b**. The main question concerning the stereospecifity of the reduction with the Ti(O*i*Pr)$_4$ / PMHS system also could be answered. Regarding the absolute configuration of the starting diphosphine dioxide (*Rp*,*Sp*)-**276b** it can be concluded that the reduction proceeds with *retention* of configuration at both phosphorus atoms leading to *P*-chiral diphosphine with absolute configuration *Sp*,*Rp*. Since, reaction of a enantiomerically pure phosphine with BH_3 in THF is well known to proceed with retention of

configuration[24, 159], the obtained (*Sp,Rp*)-**303b** clearly confirms that *retention* took place by reduction of *P*-chiral (*Rp,Sp*)-**276b**.

The attempts to oxidize the *P*-chiral diphosphine back to the starting *P*-chiral diphosphine dioxide with H_2O_2[47], in order to check if the reduction proceeded with *retention* or *inversion* of configuration, failed. The treatment of *P*-chiral diphosphine diborane (*Sp,Rp*)-**303a** with *m*-CPBA in dichloromethane[55] did not result in the stereospecific formation of (*Rp,Sp*)-**276a**, but no traces of diphosphine borane (*Sp,Rp*)-**303a** were detected by ^{31}P MNR.



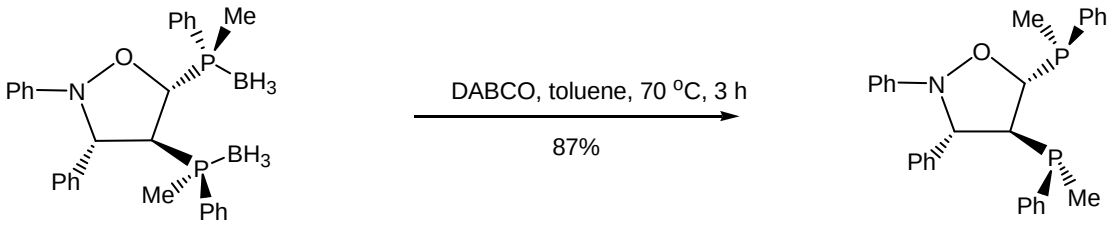
(*Sp,Rp*)-**303a** (*Rp,Sp*)-**276a**

Presumably, this reaction accomplished by partial racemization at phosphorus leading to a mixture of diastereomeric diphosphine dioxides (^{31}P NMR).

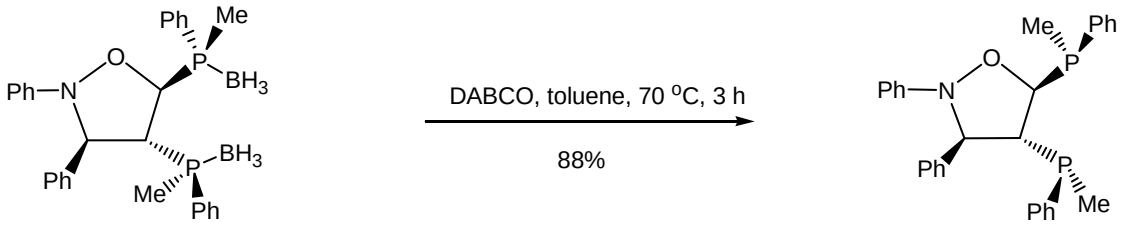
3.5. Synthesis of *P*-Chiral Diphosphines from *P*-Chiral Diphosphine Diboranes

P-chiral phosphine-borane is usually treated with a an excess of amine which has strong nucleophilicity to give after filtration pure phosphine with complete retention of configuration at phosphorus[24] Generally, this deboronation is followed by reaction of an enantiomerically pure phosphine with a transition metal in order to achieve a formation of a chiral complex of the appropriate phosphine.

To apply this procedure to the *P*-stereogenic diphosphine diboranes (*Sp,Rp*)-**303a** and (*Sp,Rp*)-**303b**, they were reacted with 1,4-diazabicyclo[2.2.2]octane (DABCO) in toluene at 70 °C for 3 h.



(*Sp,Rp*)-**303a** (*Sp,Rp*)-**301a**



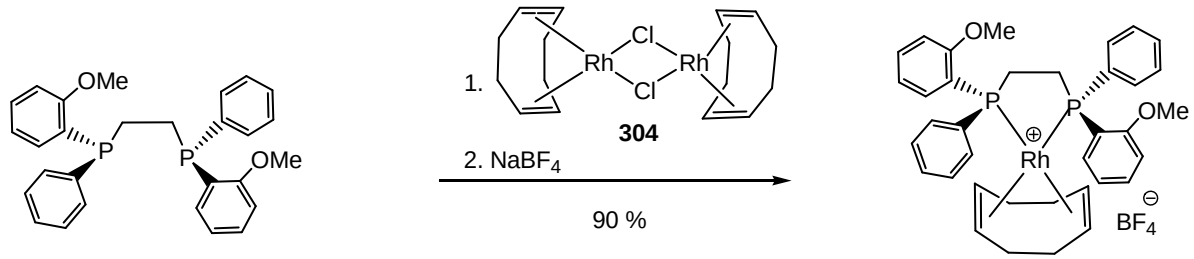
(*Sp,Rp*)-**303b** (*Sp,Rp*)-**301b**

DABCO is a crystalline compound, which can be easily handled, since other amines diethylamine, pyrrollidine or morpholine usually required distillation under argon prior its use. After reaction, DABCO can be easily removed by filtration by using toluene as a solvent. *P*-stereogenic diphosphines (*Sp,Rp*)-**301a** and (*Sp,Rp*)-**301b** formed after deboronation in high yield and are virtually pure according to their ^{1}H, ^{13}C, ^{31}P NMR spectra. In the ^{31}P NMR spectra the signals appear as two doublets in the upfield between – 27 and – 31 ppm. The coupling constants J_{PP} are different and found to be larger for the diphosphine (*Sp,Rp*)-**301a** (J_{PP} = 10.9 Hz), whereas for the (*Sp,Rp*)-**301b** diphosphine the coupling constant is J_{PP} = 7.6 Hz. The methyl groups at phosphorus resonate as doublets in the ^{1}H NMR spectra, with the coupling constant $^{2}J_{PH}$ = 4.3 Hz. In the ^{13}C NMR spectra signals of the carbon atoms of the isoxazolidine ring appear as double doublets indicating a strong coupling with the phosphorus atoms: ($^{1}J_{PC}$ = 32.9 Hz, $^{1}J_{PC}$ = 8.1 Hz, C-4), ($^{1}J_{PC}$ = 30.5, $^{1}J_{PC}$ = 5.2 Hz, C-5), ($^{2}J_{PC}$ = 8.2 Hz, C-3). The obtained new *P*-chiral diphosphines must be carefully handled under argon and stored in the refrigerator at – 25 °C.

3.6. Synthesis of the Rhodium Complex 310 of the Novel *P*-chiral Diphosphine (*Sp,Rp*)-301a

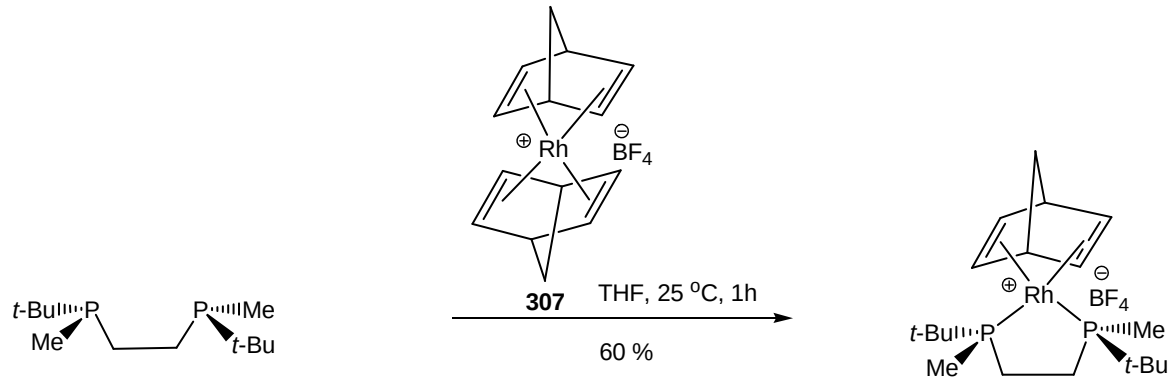
Highly selective catalysts are revolutionizing asymmetric synthesis. The invention of enantiospecific, Rh-based catalysts for the homogeneous hydrogenation of prochiral enamides in the early 1970s initiated intense efforts towards the discovery of new, more effective catalysts and the elucidation of the reaction mechanism.[2, 7, 9]

Originally the synthesis of a rhodium complex of *P*-chiral diphosphine is accomplished by a treatment of a rhodium complex with a solution of phosphine at 25 ºC. For example, the Rh-complex of DIPAMP (**12**) was synthesized with rhodium(1,5-cyclooctadiene) chloride dimer (**304**) and sodium tetrafluoroborate to give the catalyst precursor **305**.[6]



(*S,S*)-**12** **304** **305**

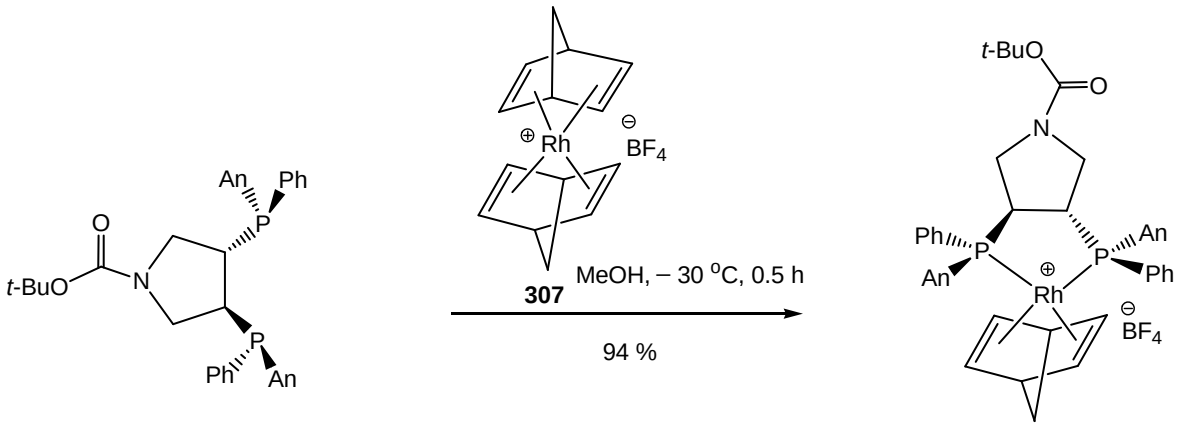
Imamoto reported the synthesis of the Rh-complex **308**, by treatment of $Rh(nbd)_2BF_4$ (**307**) in THF with the solution of the *P*-chiral diphosphine **306**. The Rh-complex **308** was obtained after recrystallization from THF in 60 % yield as red-yellow plates.[163]



306 **307** **308**

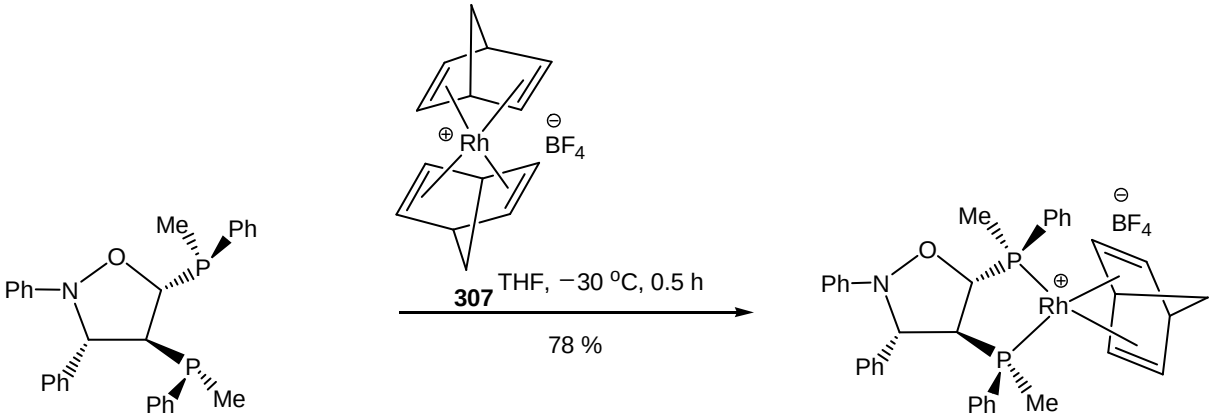
Recently, Nagel et. al. reported the synthesis of a series of *P*-chiral diphosphines and the synthesis of their Rh-and Pd-complexes.[164] The synthesis of the Rh-complex **310** was

achieved in high yield by mixing *P*-chiral diphosphine **309** with rhodium precursor $Rh(nbd)_2BF_4$ (**307**) in methanol at – 30 °C.[164]



309 **310**

The *P*-stereogenic diphosphine (*Sp,Rp*)-**301a** was failed to react with $Rh(nbd)_2BF_4$ in THF at 25 °C, only decomposition was detected by ^{31}P NMR. Due to this fact that the Nagel ligands possess a heterocyclic five-membered ring, it was proposed to use low temperature for the synthesis of the desired Rh-complex. Treatment of *P*-stereogenic diphosphine (*Sp,Rp*)-**301a** in THF at – 30 °C produced the desired Rh-complex in 78 % yield as an orange powder after carefully washing with hexane.



(*Sp,Rp*)-**301a** **310**

The constitution of novel chiral Rh-complex **310** was by ^{31}P NMR and ^{1}H NMR spectroscopy. In the ^{31}P NMR of **310** appear four doublets, which is in agreement with the proposed structure. (Fig. 16) Since two asymmetric phosphorus atoms are chemically not equivalent, the appearance of four doublets can be easily explained.

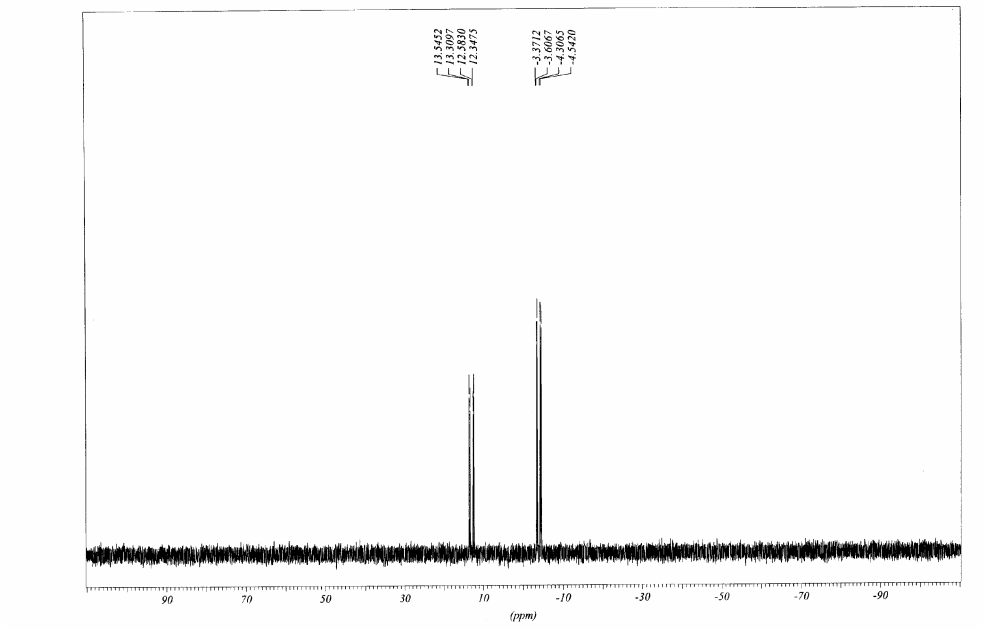


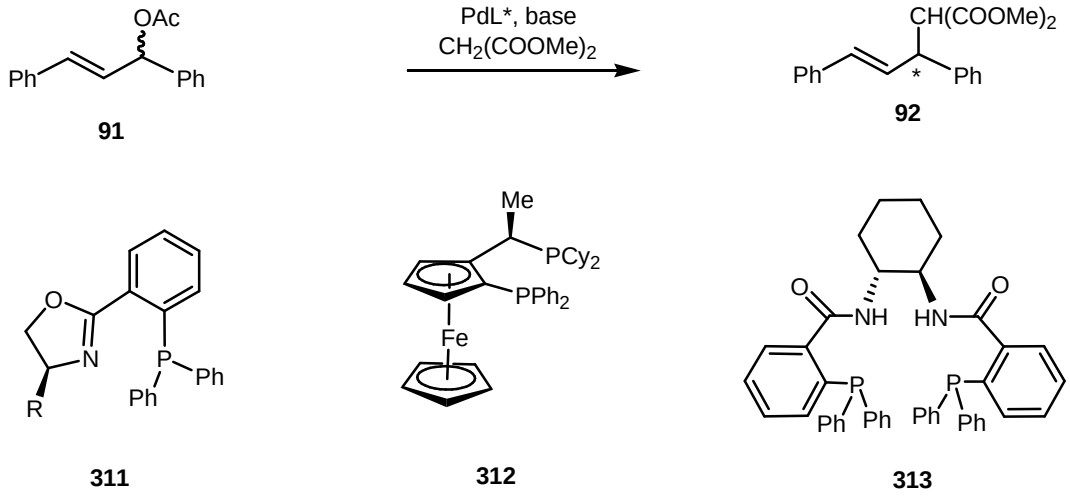
Fig. 16 ^{31}P NMR of the novel rhodium complex **310**

The coupling constant are in very good agreement with literature data[165] δ = – 3.8 (dd, $^{1}J_{RhP}$ = 151.5 Hz, $^{2}J_{PP}$ = 38.1 Hz), + 12.3 (dd, $^{1}J_{RhP}$ = 155.8 Hz, $^{2}J_{PP}$ = 38.1 Hz). In the ^{1}H NMR spectra the methyl groups resonate as two doublets with the very diagnostic coupling constant $^{2}J_{PH}$ = 8.4 Hz[165] showing that both asymmetric phosphorus atoms coordinate to the rhodium atom. The Rh-complex **310** was found to be moderately sensitive to air. It is well soluble in $CDCl_3$, THF, CH_2Cl_2, Et_2O and showed low solubility in hexane.

3.7. Novel *P*-Stereogenic Diphosphine (*Sp,Rp*)-301a in Asymmetric Pd-Catalyzed Allylic Alkylation Reaction

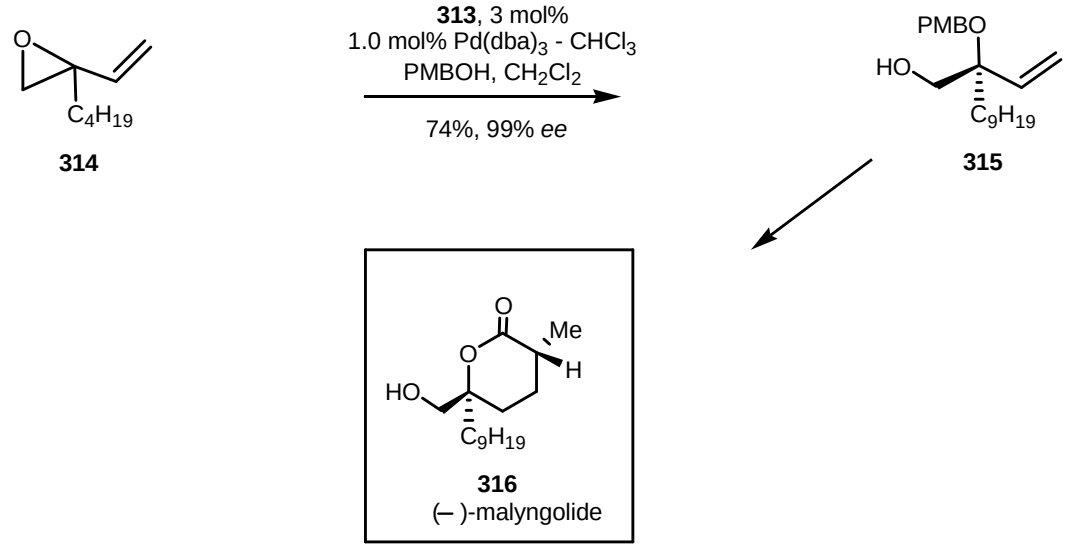
Palladium-catalyzed allylic substitution is a useful synthetic method for the formation of carbon-carbon and carbon-heteroatom bonds.[166] The synthetic utility of transition metal-catalyzed allylic alkylations has soundly been demonstrated since its introduction nearly three decades ago. In contrast to most metal-catalyzed enantioselective processes, asymmetric allylic akylations involve net reaction at sp^3 instead of sp^2 centers. The ability to transform achiral, prochiral, or chiral racemic material to enantiopure material under similar conditions is unique to the asymmetric allylic alkylation reaction. The significant contributions on this field provided the research groups of Trost, Pfaltz, Helmchen and Togni, who developed

highly efficient chiral phosphorus ligands PHOX **311**[167], Josiphos **312**[168], DACH-Phenyl **313**[169] (Scheme 25).

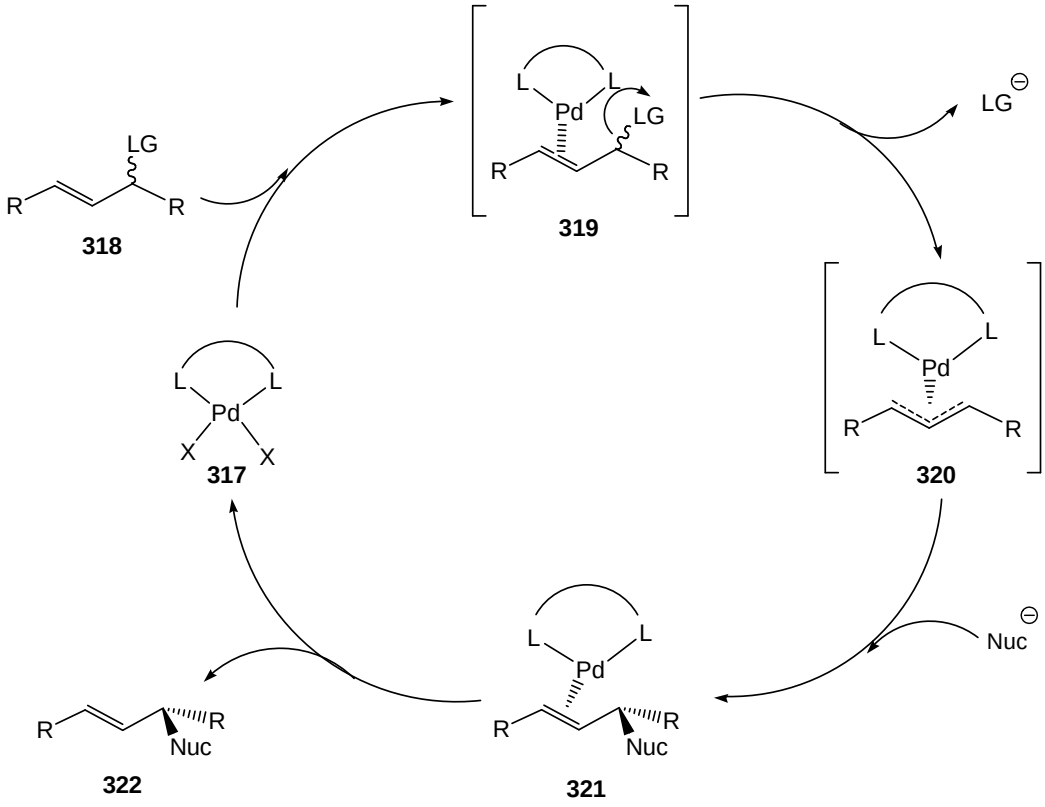


Scheme 25. Highly efficient ligands **311**-**313** for asymmetric Pd-catalyzed allylic alkylation of **91**

The enantioselective palladium allylic substitution was well recognized in the field of total synthesis.[170] Methodology to efficiently synthesize tetrasubstituted carbon centers asymmetrically can play a key role in total synthesis of complex molecules. In this regard, dynamic kinetic asymmetric transformations in asymmetric allylic alkylation has created numerous possibilities for total synthesis, such as that utilized in the synthesis of (–)-malyngolide **97**.[171] This compound is a naturally occurring antibiotic possessing significant activity against *Mycobacterium smegmatis* and *Streptococcus pyogenes*.



The widely accepted mechanism by which Pd oversees the asymmetric allylic substitution reaction is depicted in Scheme 26.

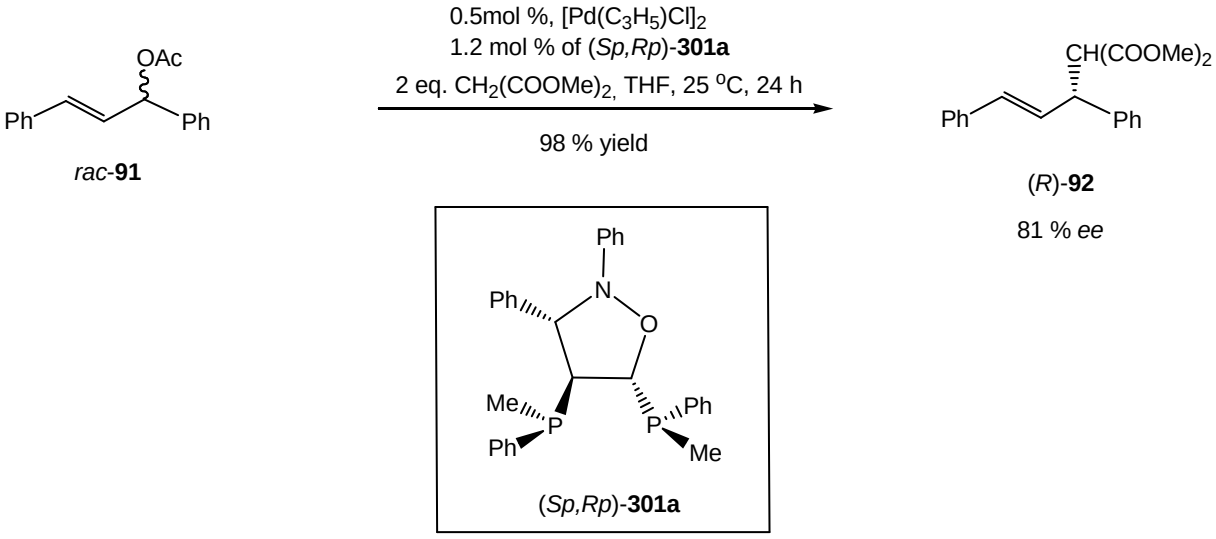


Scheme 26. Generally accepted mechanism for the enantioselective Pd-catalyzed allylic alkylation

The cycle begins by formation of an η^2 π-alkene-Pd^0 complex. Oxidative addition of Pd^0 to form the π-allyl species then occurs with inversion at the leaving group center, providing the key η^3 π-allyl-Pd^{2+} complex. This intermediate has been observed spectroscopically and was crystallographically charcterized[172]. Nucleophillic attack usually occurs from the face opposite the metal and an overall retention of stereochemistry is achieved. Attack generally occurs at the least substituted position for unsymmetrical allyl complexes. Nucleophilic attack results in a formal two electron reduction of the metal producing a Pd(0)-olefin complex. Ligand exchange then occurs resulting in the original Pd(0) catalyst re-entering the cycle and the product of the nucleophilic displacement.

Recently, *P*-chiral diphosphines were used by the Imamoto group in asymmetric allylic substitution reaction.[45, 173]

The novel *P*-stereogenic diphosphine (*Sp,Rp*)-**301a** was employed in enantioselective Pd-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate (**91**) with dimethylmalonate (**320**).



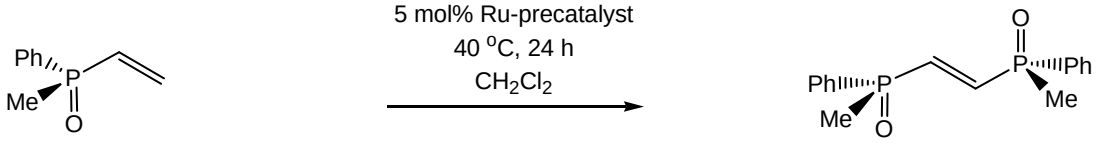
The reaction proceeded smoothly at 25 ºC in THF over 24 h and gave the desired product **92** in nearly quantitative yield after column chromatography. For the determination of enantiomeric excess of the obtained **92** the chiral dirhodium method developed recently by Duddeck et. al. was applied.[174] This method has been proved as an effective practical way for determination of enantiomeric excess of organophosphorus chalcogenides,[175] phosphine-borane complexes[176], aliphatic ethers,[177] alanine esters,[178] oxa- and thiatriazoles,[179] and atropoisomeric diiodobiphenyls.[180] By the use of $[Rh_2(MTPA)_4]$ the *ee* was found to be 81 %, which is a very promising result for the further exploration on the enantioselective asymmetric alkylation employing new *P*-chiral ligands (*Sp,Rp*)-**301**. The assignment of the absolute configuration was established based on the reported optical rotation value for *R* and *S* enantiomer of **92**, respectively.

4. Summary and Outlook

The development of new *P*-stereogenic phosphine ligands has become very important due to expanded utility of transition metal catalyzed asymmetric synthesis such as hydrogenation, hydrosilylation, hydrocarbonylation, C-C coupling reactions and isomerization.[2] Among the large number of optically active phosphine ligands which present in common the 1,2-diphosphanylethane substructure with chiral information located in the carbon backbone connecting the two phosphane fragments, only very few possess a stereogenic center at the phosphorus atom, because of the difficulties in ligand synthesis.[8, 47]

This work is devoted to the synthesis of novel *P*-stereogenic diphosphines for asymmetric catalysis. Previously regarded as not known, the *P*-chiral bidentate phosphorus ligands which possess two asymmetric phosphorus atoms located close to the rigid chiral backbone, were successfully synthesized via Ru-catalyzed olefin cross-metathesis followed by asymmetric Huisgen cycloaddition reaction.

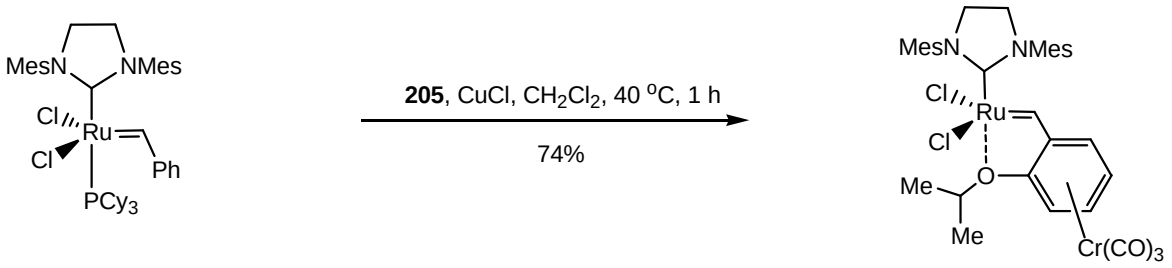
The homo-coupling of *P*-chiral vinylphosphine oxide (*Sp*)-**97** was investigated with an emphasis on the choice of the Ru-precatalyst and the reaction conditions. It was found that homo-coupling of (*Sp*)-**97** proceeded well in the presence of 5 mol % of an appropriate second generation Hoveyda-Grubbs precatalyst and to be more efficient by the use of nitro precatalyst **138**.



(*Sp*)-**97**

(*Sp,Sp*)-**155**

In search for a more active precatalyst for homo-coupling of (*Sp*)-**97** a new Hoveyda-Grubbs alkene metathesis catalyst, in which the benzylidene ligand has been coordinated to a highly electron withdrawing tricarbonylchromium moiety, was synthesized. The synthesis of a new precatalyst was performed by treatment of **205** with **134** in the presence of CuCl as a PCy_3 scavenger, gave the desired bimetallic complex **202** in 74 % yield as an air-stable dark red powder.



134 **202**

The structure of the complex **202** provides evidence for a so far unreported interaction between the benzylidene hydrogen atom and one of the mesityl substituents at the Arduengo carbene ligand.

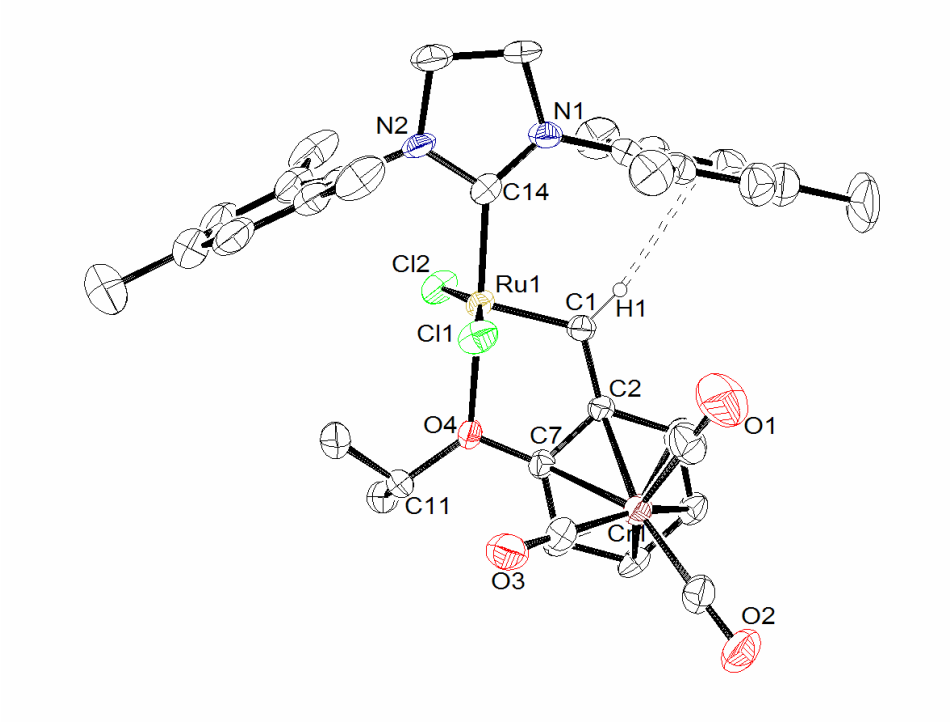
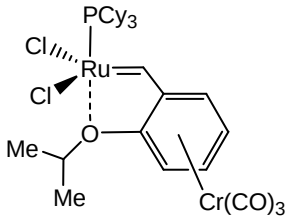


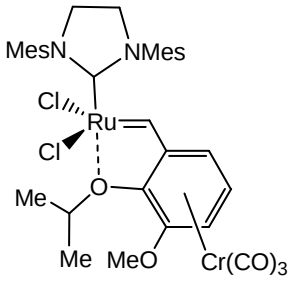
Fig. 3. Structure of **202** in the crystal

Screening of the catalytic properties in ring-closing, enyne, cross, and homo metathesis shows an activity comparable to that of the most highly active catalysts with a chelating isopropoxy moiety. In addition, the (*Sp*)-**97** was homodimerized to give a significantly improved yield of (*Sp*,*Sp*)-**155** in 91% yield, as compared to 80% with **138**.

The synthesis of other bimetallic olefin metathesis precatalysts **236** and **239** has been accomplished.



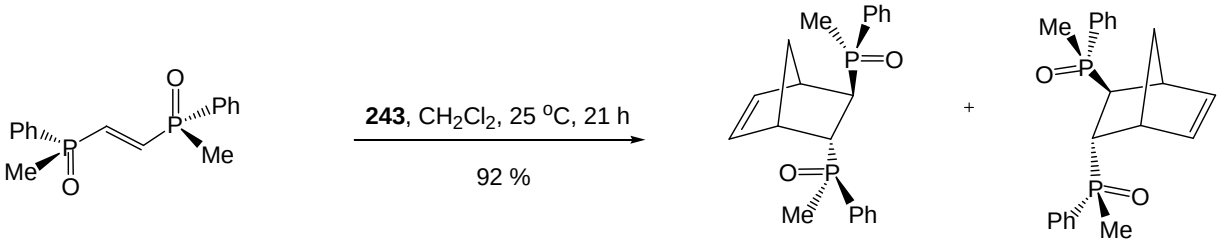
236



239

An important aspect is the potential employment of bimetallic catalysts **202** and **236** in alkene metathesis of electron-deficient olefins, which should be pursued in the near future.

To construct the new *P*-chiral diphosphine ligands, the *P*-stereogenic diphosphine dioxide (*Sp,Sp*)-**155** as a chiral dienophile underwent an asymmetric Diels-Alder reaction with cyclopentadiene (**239**) to produce two diastereoisomeric diphosphine dioxides (*Sp,Sp*)-**262a** and (*Sp,Sp*)-**262b** in the ratio 1.3:1

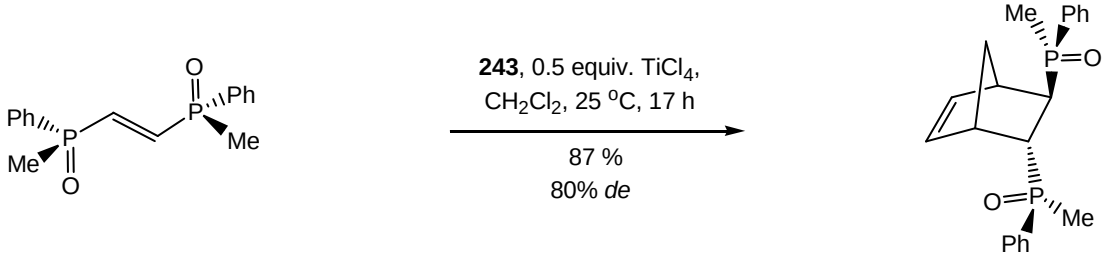


(*Sp,Sp*)-**155**

(*Sp,Sp*)-**262a**

(*Sp,Sp*)-**262b**

The use of titanium(IV) chloride as a Lewis acid for asymmetric Diels-Alder reaction was found to affect the ratio of the desired diastereoisomers leading to (*Sp,Sp*)-**262a** in 80% *de*. The absolute configuration of the main diastereoisomer was confirmed by the X-ray diffraction. From developed transition states for this reaction it has been concluded that (*Sp,Sp*)-**155** preferred the *s-trans* conformation during the cycloaddition.



(*Sp,Sp*)-**155**

(*Sp,Sp*)-**262a**

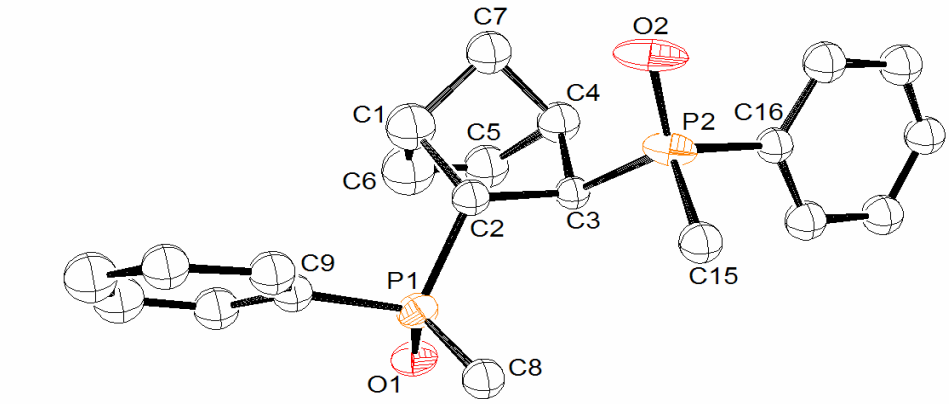
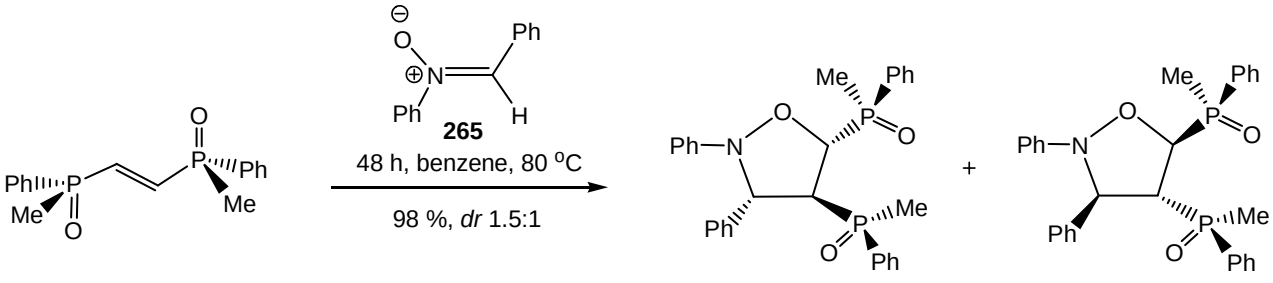
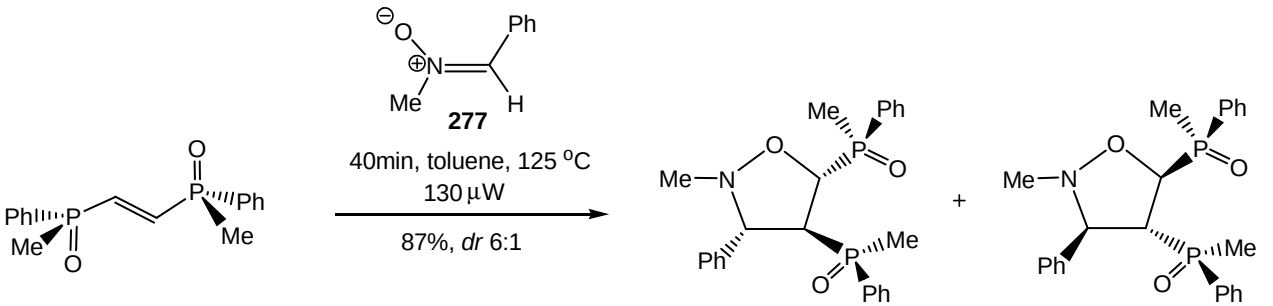


Fig. 4 Structure of (*Sp*,*Sp*)-**262a** in the crystal

The microwave assisted asymmetric Huisgen cycloaddition of the *P*-stereogenic 1,2-diphosphanylethene dioxide with acyclic nitrones **261** and **274** afforded the desired diastreomerically pure isoxazolidines (*Rp*,*Sp*)-**276a** and (*Rp*,*Sp*)-**276b** and (*Rp*,*Sp*)-**278a** and (*Rp*,*Sp*)-**278b** in high yields.

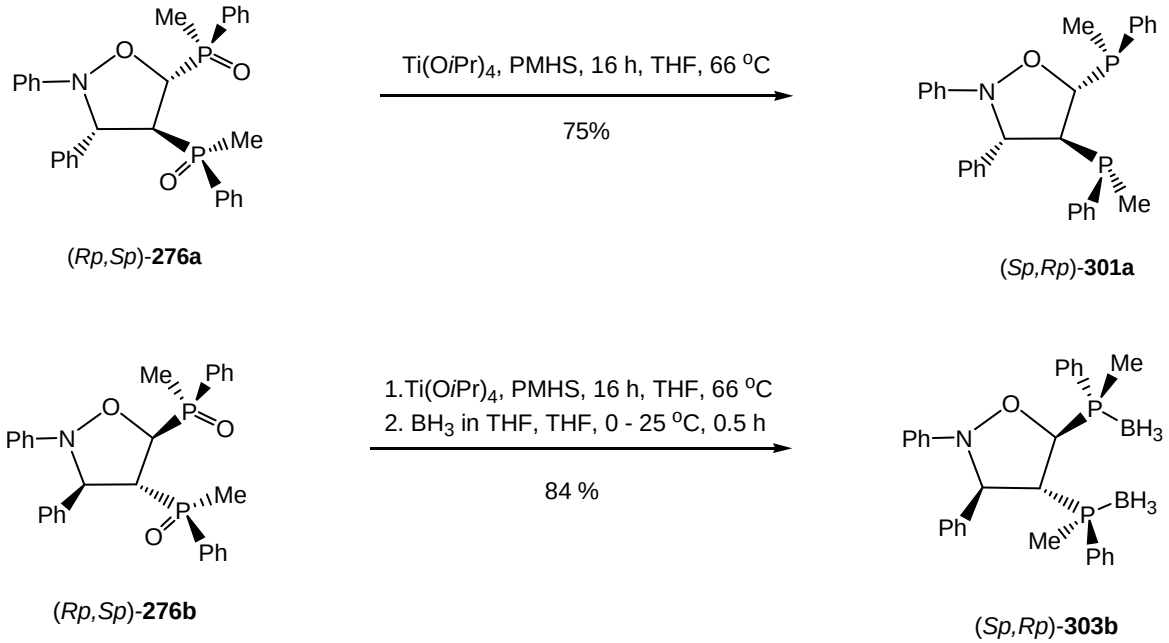


(*Sp*,*Sp*)-**155** (*Rp*,*Sp*)-**276a** (*Rp*,*Sp*)-**276b**



(*Sp*,*Sp*)-**155** (*Rp*,*Sp*)-**278a** (*Rp*,*Sp*)-**278b**

The novel *P*-stereogenic diphosphine dioxides (*Rp*,*Sp*)-**276a** and (*Rp*,*Sp*)-**276b** were successfully reduced to the respective *P*-chiral diphosphines (*Sp*,*Rp*)-**301a** and (*Sp*,*Rp*)-**301b** by the use of Ti(O*i*Pr)$_4$/polymethylhydrosiloxane (PMHS) in THF with complete retention of configuration at the phosphorus in high yields. This was proven by assignment of the absolute configuration by the X-ray analysis of the (*Sp*,*Rp*)-**303b**.



(*Rp*,*Sp*)-**276a** (*Sp*,*Rp*)-**301a**

(*Rp*,*Sp*)-**276b** (*Sp*,*Rp*)-**303b**

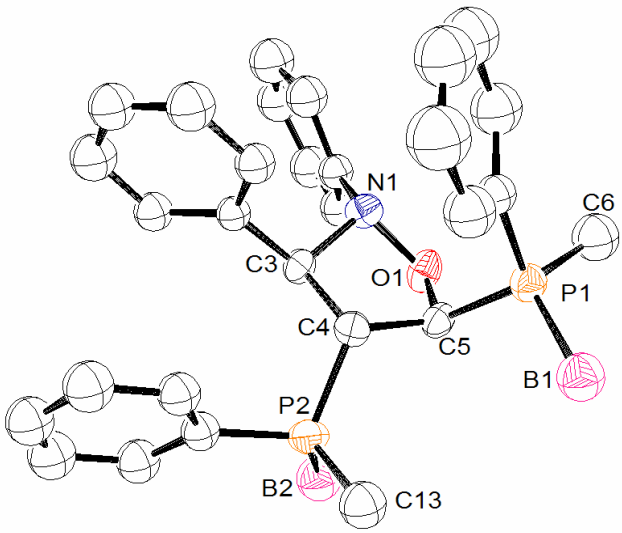
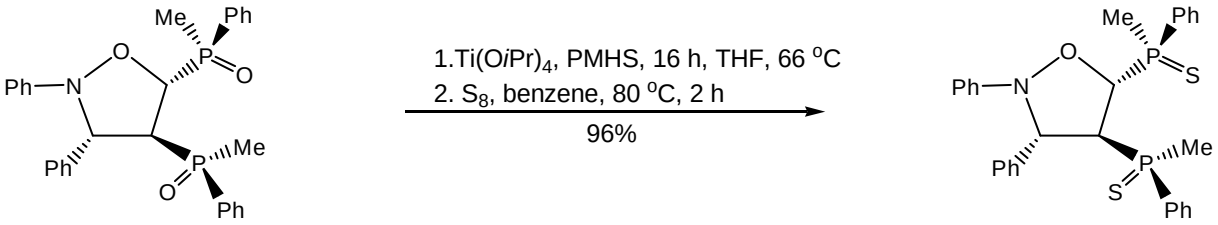


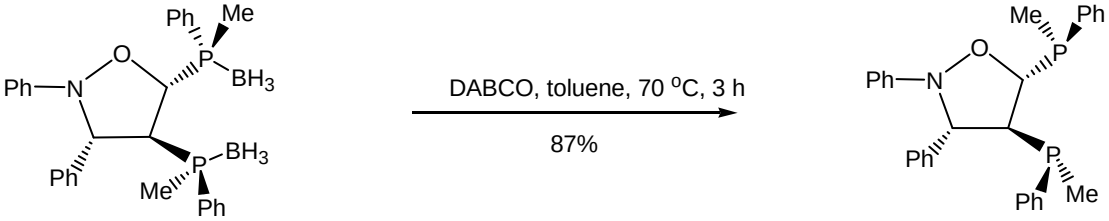
Fig. 15 Structure of (*Sp*,*Rp*)-**303b** in the crystal

The obtained *P*-stereogenic diphosphine (*Sp,Rp*)-**301a** was oxidized by treatment *in situ* of a crude reaction mixture with sulphur allowing the formation of diastereomerically pure *P*-chiral diphosphine disulfide (*Rp,Sp*)-**302a** in high yield.

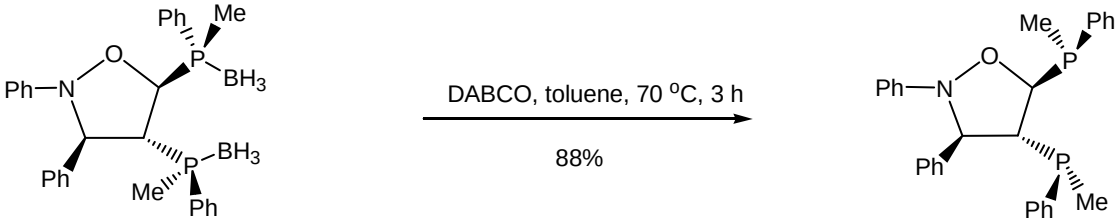


(*Rp,Sp*)-**276a** (*Rp,Sp*)-**302a**

P-stereogenic diphosphine diboranes (*Sp,Rp*)-**303a** and (*Sp,Rp*)-**303b** were reacted with 1,4-diazabicyclo[2.2.2]octane (DABCO) in toluene at 70 °C for 3 h to form (*Sp,Rp*)-**301a** and (*Sp,Rp*)-**301b,** respectively.

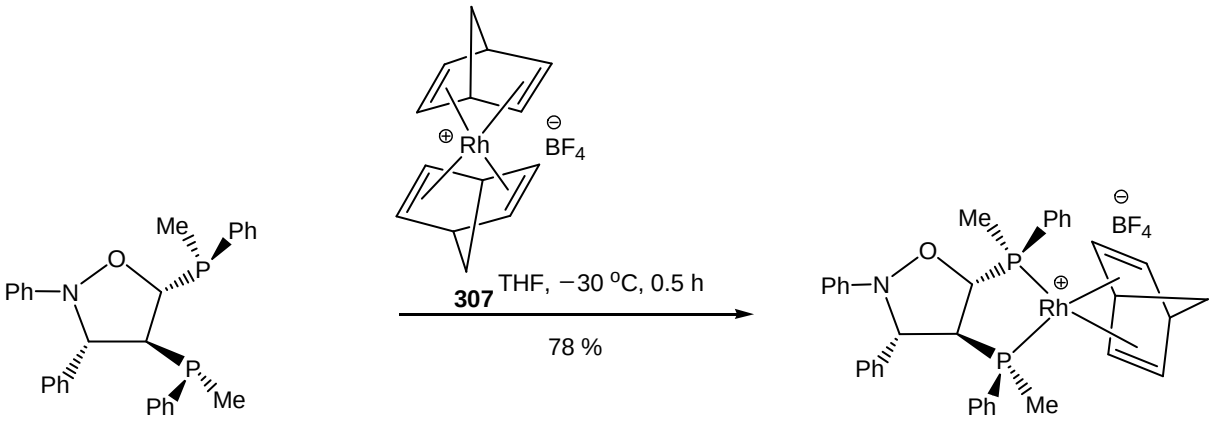


(*Sp,Rp*)-**303a** (*Sp,Rp*)-**301a**



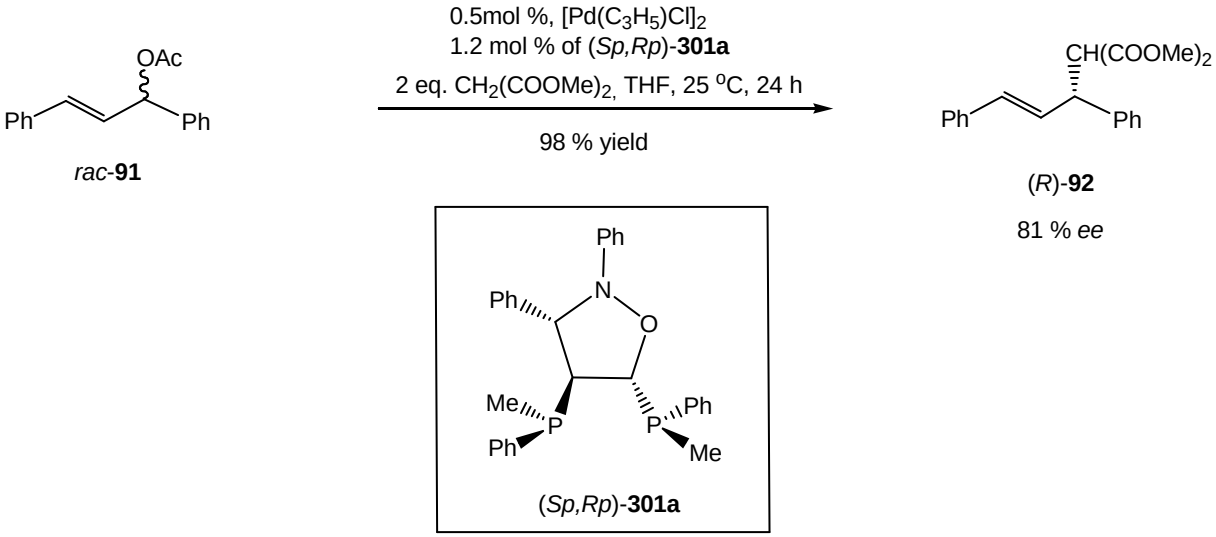
(*Sp,Rp*)-**303b** (*Sp,Rp*)-**301b**

The treatment of novel *P*-stereogenic diphosphine (*Sp,Rp*)-**301a** in THF at – 30 °C produced the novel chiral Rh-complex **310** in 78 %.



(*Sp,Rp*)-**301a** **310**

To test the ability of the novel *P*-chiral diphosphines in asymmetric catalysis, the novel *P*-stereogenic diphosphine (*Sp,Rp*)-**301a** was employed in the enantioselective Pd-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate (**91**) with dimethylmalonate (**320**). In unoptimized conditions the desired product was formed in nearly quantitative yield and 81 % *ee*.

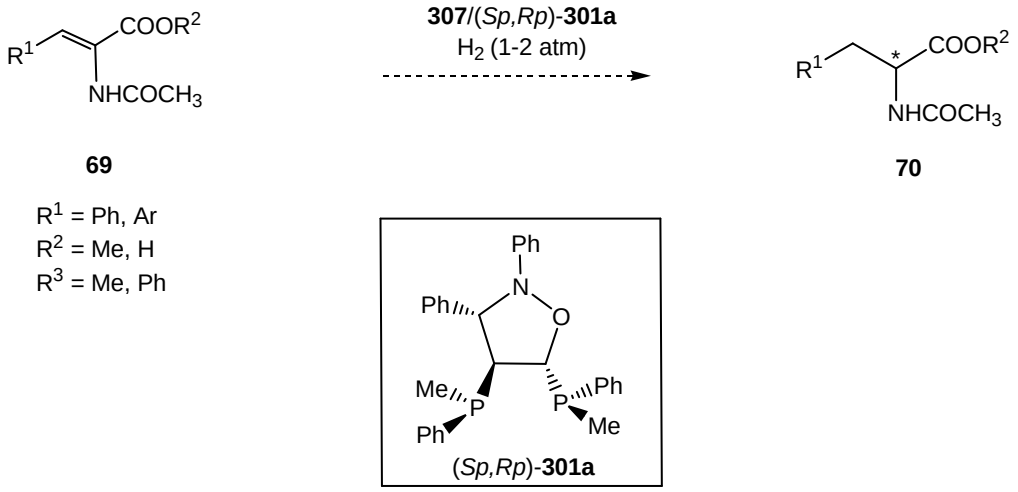


rac-**91** (*R*)-**92**

81 % *ee*

(*Sp,Rp*)-**301a**

It is of great interest to employ the novel *P*-stereogenic bidentate ligands in Rh-catalyzed asymmetric hydrogenation of prochiral olefins. It could be interesting to study the mechanism of asymmetric hydrogenation with regard to the structure of these novel ligands. Recently, Imamoto proposed an alternative mechanism for Rh-catalyzed asymmetric hydrogenation with BisP* ligands.[180]

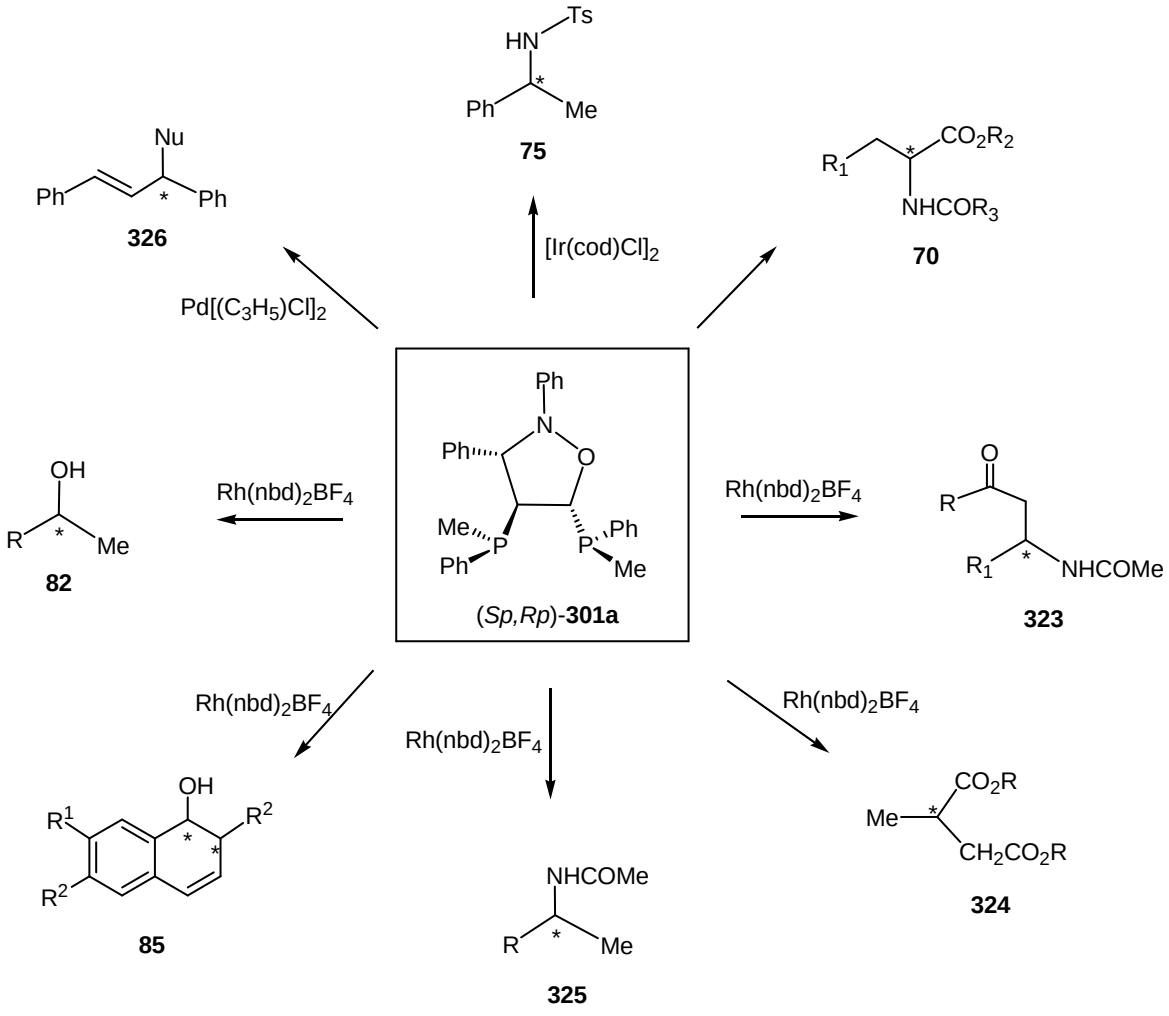


69 **70**

R^1 = Ph, Ar
R^2 = Me, H
R^3 = Me, Ph

(*Sp,Rp*)-**301a**

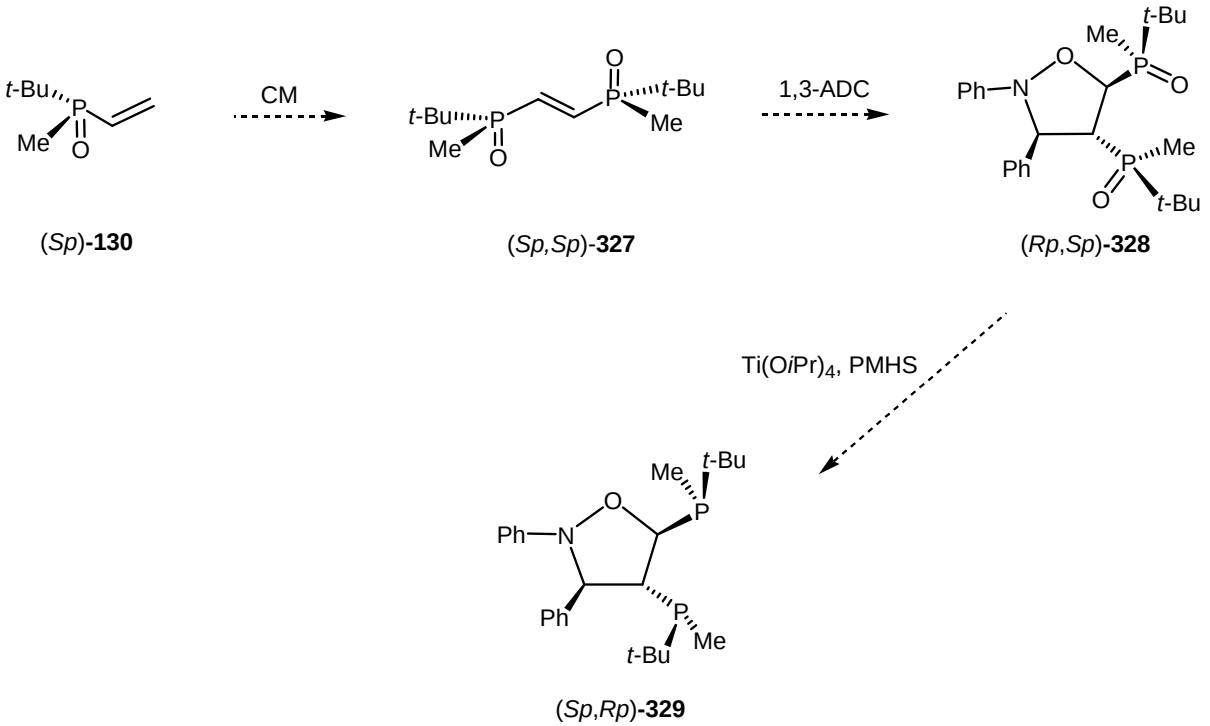
The utility of these new *P*-stereogenic bidentate ligand systems in the enantioselective alkylative ring opening of oxabenzonorbornadienes to **85,** Pd-catalyzed asymmetric alyllic alkylation to **326**, Ir-catalyzed asymmetric hydrogenation of imines to **75**, Rh-catalyzed asymmetric hydrosilylation reactions to **82** and asymmetric hydrogenation of enamides, dehydroamino acids, itaconic acid derivatives and α- acylaminoacrylic acids and esters will be explored. (Scheme 27).



Scheme 27. The proposed utility of new *P*-chiral diphosphine (*Sp*,*Rp*)-**301a** in asymmetric catalysis

To summarize this work devoted to the synthesis of novel *P*-stereogenic diphosphine ligands, it should be mentioned that the concept based on olefin metathesis-asymmetric cycloaddition-stereoselective reduction sequence, was successfully realized and should find applications in the future.

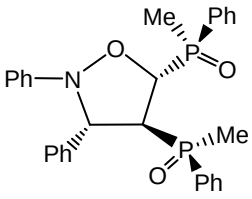
For example, a displacement of the phenyl group by a *tert*-butyl one is one of the possible improvements in this field. The respective approach would be based on the homo-coupling of (*Sp*)-**130** to (*Sp*,*Sp*)-**327** followed by an asymmetric Huisgen cycloaddition to the appropriate (*Rp*,*Sp*)-**328**, which after stereoselective reduction would give the desired *P*-stereogenic diphosphine (*Sp*,*Rp*)-**329**.



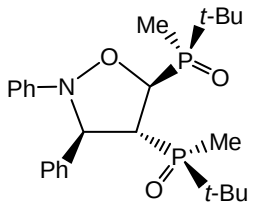
(*Sp*)-**130** (*Sp*,*Sp*)-**327** (*Rp*,*Sp*)-**328**

(*Sp*,*Rp*)-**329**

The cleavage of the isoxazolidine ring in (*Rp*,*Sp*)-**276a** or (*Rp*,*Sp*)-**329** might be accomplished by hydrogenation on 10% Pd/C[138] or by the use of $Mo(CO)_6$[181] in acetonitrile to give the desired 1,3-aminoalcohols (*Rp*,*Sp*)-**276a** or (*Rp*,*Sp*)-**329**, which could also be used as precursors to *P*-stereogenic diphosphine ligands.



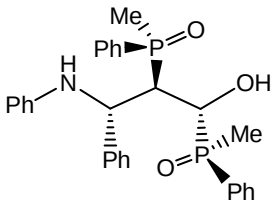
(*Rp,Sp*)-**276a**



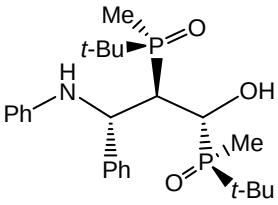
(*Rp*,*Sp*)**-328**

H_2, 10% Pd/C or $Mo(CO)_6$

H_2, 10% Pd/C or $Mo(CO)_6$



(*Rp*,*Sp*)**-330a**



(*Rp*,*Sp*)**-331**

5. Experimental Part

5.1 General

All operations involving air-sensitive organometallic and organophosphorus compounds were carried out in an argon or nitrogen atmosphere, using standard vacline and Schlenk techniques. All glassware was flame-dried at reduced pressure and filled with a protective gas (repeated 3 times). The following solvents were distilled before use under a slight positive pressure of nitrogen or argon. Diethyl ether (DEE), toluene, benzene, dimethoxyethane (DME), hexane and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl. Methylene chloride (DCM) and triethylamine (Et_3N) were distilled from calcium hydride. Petroleum ether (PE) and *tert*-butyl methyl ether (TBME) were distilled from calcium chloride.

^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra were measured at 25 ºC with Bruker AM 400 (^{1}H: 400.1, ^{13}C: 100.1, ^{31}P NMR: 162 MHz), 500 (^{1}H: 500, ^{13}C: 125 MHz) or WP 200 SY (^{1}H: 200.1, ^{13}C: 50.3 MHz) spectrometers. The chemical shifts refer to δ_{TMS} = 0 ppm or to residual solvent signals as internal standard. For ^{31}P NMR a solution of H_3PO_4 30 % in water is used as external reference. The multiplicity of the peaks are abbreviated as s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. The deuterated solvents [D_6]-benzene, $CDCl_3$ and CD_2Cl_2 were distilled under argon and used immediately. Atom numbering is arbitrary and does not correspond to the IUPAC.

Infrared spectra (IR) were recorded on a Perkin-Elmer FT-IR 580 and 1710 spectrometers. Signal intensities are abbreviated s (strong), m (medium) or w (weak).

Mass spectra (MS) were measured on a Micromass LCT with Lock-Spray-unit (ESI). The injection was made in Loop-Modes in a HPLC-Alliance 2695 (Waters). All values are given in atomic units of mass per elemental charge (*m/z*). The intensity is given as a percentage of the base peak.

High resolution mass spectra (HRMS) were recorded with the peak-matching method in Micromass LCT with Lock-Spray-unit (ESI). All values are given in atomic units of mass per elemental charge (*m/z*).

Optical rotations were determined with a Perkin Elmer PE-241 instrument at 20 °C with the light frequency of 589 nm (D-line of a sodium vapour lamp) in a cuvette (length *d* =1 dm or *d* = 0.1 dm; concentration (*c*) is given in g / 100 mL).

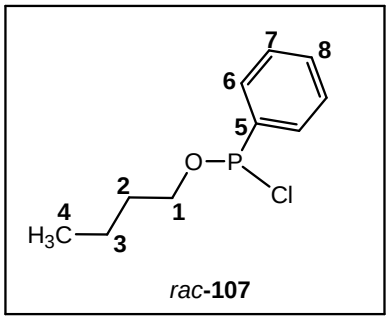
Melting points were determined with the Electrothermal IA 9200.

Elemental analysis (EA) Microanalyses were conducted with a Elementar Vario EL instrument with acetamide as standard. All values are given as mass percentages.

Microwave Oven (µW) Microwave heating was carried out with a CEM Corporation Discover® LabMate™ single-mode microwave cavity operating at 300 W.

5.2 Synthesis of Organophosphorus Compounds

5.2.1 *rac*-Butylchlorophenylphosphinite (107)[48]

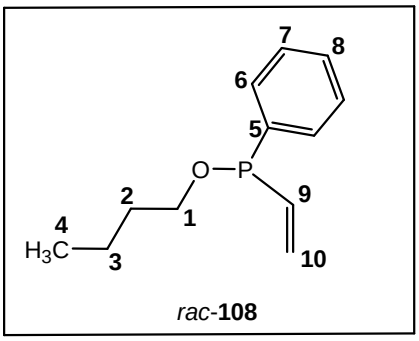


rac-**107**

A mixture of 1-butanol (22.30 g, 0.3 mol) and *N*,*N*-diethylaniline (44.80 g, 0.3 mol) in petroleum ether (50 mL) was added dropwise over 1 hour at –30 ºC to mechanically stirred dichlorophenylphosphine (54.00 g, 0.3 mol) in degassed petroleum ether (300 mL). After completed addition, the reaction mixture was stirred for one additional hour at –30 ºC. Thereafter the white precipitate was filtered off, washed with degassed petroleum ether (3×100 mL), and solvents were removed at reduced pressure to give 42.2 g (0.2 mol, 65 %) of **107**. The colourless residue was used for next step without distillation avoiding decomposition of **107**.

rac-(**107**): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.95 (t, J = 7.4 Hz, 4-H), 1.42 (m, 2H, 1-H), 1.68 (m, 2H, 2-H), 3.93 (m, 2H, 3-H), 7.45-7.48 (m, 3H$_{Ar}$), 7.80-7.84 (m, 2H$_{Ar}$) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = + 175.95 ppm.

5.2.2 *rac*-Butylphenylvinylphosphinite (108)[49]

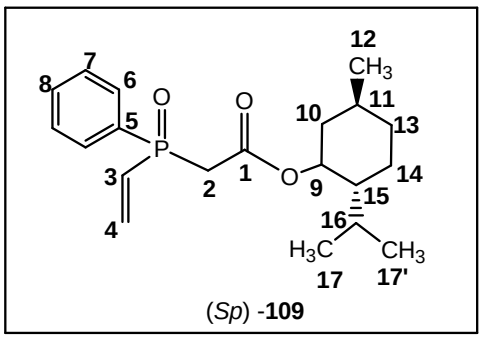


rac-**108**

A solution of vinyl magnesium bromide prepared from of magnesium 18.60 g (0.78 mol) and vinyl bromide 90.00 g (60 mL, 0.85 mol) in THF (100 mL), was added dropwise at – 65 ºC in THF (150 mL) over 1-2 h to mechanically stirred of *rac*-butylchlorophenylphosphinite (**107**) 145.00 g (0.671 mol) in THF (300 mL). After complete addition, the reaction mixture was allowed to stir at 25 °C for 1 h. THF was removed from the reaction flask in high vacuum and to yellow pasty residue was added petroleum ether (250 mL) and freshly distilled pyridine (50 mL) with vigorous mechanically stirring. The white-yellow precipitate was grinded with a spoon, filtered off and effectively washed with petroleum ether (500 mL). Solvents were evaporated under high vacuum (2 Torr) and the residue distilled under vacuum to give pure phosphinite **108** in 65.6 g (0.32 mol, 47 %).

rac-(**108**): ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.97 (t, J = 7.2 Hz, 4-H), 1.46 (m, 2H, 3-H), 1.69 (m, 2H, 2-H), 3.81 (m, 2H, 1-H), 5.82-6.07 (m, 2H, 10-H), 6.47-6.70 (m, 1H, 9-H), 7.41-7.66 (m, 5H$_{Ar}$) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = – 14.96 ppm.

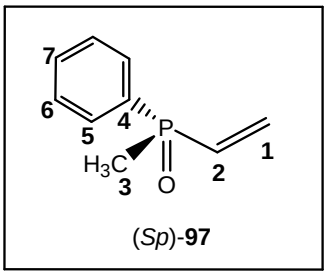
5.2.3 (*Sp*)-(-)-(Ethenylphenylphosphinyl)acetic acid menthyl ester (109)[51]



(*Sp*) -**109**

In a 250 mL 3-necked flask charged with a cooling condenser, thermometer, dropping funnel and magnetic stirrer was placed (–) menthyl bromoacetate (36.00 g, 0.129 mol) and preheated to 100-105 °C. *rac*-**108** (distilled twice, 27.00 g, 0.129 mol), was added dropwise (without external heating of the oil bath) at a rate as to keep the reaction temperature around 100-110° C only by the exothermic process. After completed addition, the reaction mixture was kept at this temperature by stirring for one additional hour. After cooling to 25° C toluene (8 mL) was added and vacuum was applied to remove it with most of the butylbromide. The final residue after evaporation had consistency of mead (crystallization). The white precipitate was washed with cold benzene (300 mL) in a Büchner funnel and recrystallized from benzene until constant optical rotation value. White powder 14.80 g (0.0425 mol, 32.9 %). M. p. = 152 °C. (*Sp*)-(**109**): $[\alpha]^{D}_{20}$ = – 93 (*c* = 4.8, $CHCl_3$)[51]. – IR (ATR): $\tilde{\nu}$ = 2960 (w) cm^{-1}, 2922 (w), 2863 (w), 1717 (s, C=O), 1442 (w), 1279 (s, P=O), 1190 (s), 1115 (s), 1001 (w), 972 (w), 856 (w), 836 (w), 800 (w), 732 (s), 716 (w), 696 (w), 682 (w). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.59 (d, *J* = 6.8 Hz, 17-H), 0.78 (d, *J* = 6.8 Hz, 17'-H), 0.85 (d, *J* = 6.5 Hz, 3H, 12-H), 0.92 (m, 2H, 10'-H, 11-H), 1.24 (m, 1H, 15-H), 1.36 (m, 1H, 13-H), 1.60 (m, 3H, 14-H, 13-H), 1.84 (m, 1H, 10'-H) 3.18 (d, *J* = 15.1 Hz, 2H, 2-H, 2'-H), 4.54-4.61 (dt, 1H, 9-H), 6.21-6.32 (ddd, $^{3}J_{PH}$ = 27.9 Hz, $^{3}J_{HH}$ = 12.3 Hz, $^{2}J_{HH}$ = 1.37 Hz, 1H, 4-H), 6.34-6.44 (ddd, $^{3}J_{PH}$ = 28.0 Hz, $^{3}J_{HH}$ = 18.4 Hz, $^{2}J_{HH}$ = 1.4 Hz, 1H, 4-H), 6.58 (dddd, $^{3}J_{PH}$ = 27.9 Hz, $^{3}J_{HH}$ = 18.4 Hz, 1H, $^{3}J_{HH}$ = 12.3 Hz, $^{2}J_{HH}$ = 1.37 Hz, 3-H), 7.43-7.53 (m, $3H_{Ar}$), 7.71-7.76 (m, $2H_{Ar}$) ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, HMQC, HMBC, H,H-COSY, $CDCl_3$): δ = 16.6 (C-17), 21.3 (C-18), 22.5 (C-12), 23.8 (C-13), 26.4 (C-14), 32.0 (C-16), 34.7 (C-11), 39.1 (d, ^{2}J = 68.6 Hz, C-2), 41.2 (C-10), 46.5 (C-15), 76.4 (C-9), 129.2 (d, ^{3}J = 12.4 Hz, C-7), 130.9 (d, ^{1}J = 97.6 Hz, C-3), 131.2 (d, ^{2}J = 9.8 Hz, C-6), 132.8 (d, ^{4}J = 2.9 Hz, C-8), 135,7 (C-4), 166.4 (d, ^{2}J = 4.4 Hz, C-1) ppm. – ^{31}P NMR ($CDCl_3$, 162.0 MHz): δ = + 20.47 ppm. – MS (EI) *m/z* (%): 349 [M^{+}+H], 211 (96), 193 (68), 166 (21), 151 (100). – HR-MS (ESI) calcd. for $[M + Na]^{+}$ ($C_{20}H_{29}O_3PNa$): 371.1752, found. 371.1857. – Anal ($C_{20}H_{29}O_3P$): Calcd. C 68.94, H 8.39; found C 68.49, H 8.19.

5.2.4 (*Sp*)-Methylphenylvinylphosphine oxide (97)[52]

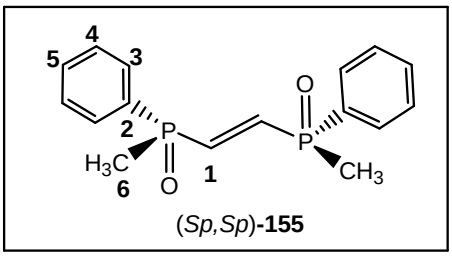


(*Sp*)-**97**

In a 1L three necked round bottom flask were placed (S_p)-**109** (20.4 g, 0.059 mol), water (1.1 mL), lithium chloride (4.98 g, 0.117 mol) and dimethylsulfoxide (400 mL) and heated at reflux for 4 h. Dimethylsulfoxide was completely distilled off and chloroform (200 mL) was added in order to precipitate LiCl, which was filtered off, and the residue was distilled 137 – 140 ºC / 3 Torr to give (*Sp*)-**97** 6.014 g (0.036 mol, 61 %) as a colourless liquid, which on standing crystallizes in white crystals. M. p. = 79-80 °C.

(*Sp*)-**97**: $[\alpha]^{D}_{20}$ = – 80 (*c* = 2.6, $CHCl_3$)[52]. – IR (ATR): $\tilde{\nu}$ = 1590 (w) cm^{-1}, 1486 (w), 1439 (w), 1415 (w), 1392 (w), 1293 (w), 1169 (s, P=O), 1113 (s), 1072 (w), 1002 (w), 965 (s), 889 (s), 765 (w), 746 (s), 697 (s), 672 (w). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.75-1.79, (d, $^2J_{PH}$ = 13.3 Hz, 3H, 3-H), 6.35-6.49 (ddd, $^3J_{PH}$ = 28.3 Hz, $^3J_{HH}$ = 12.3 Hz, $^2J_{HH}$ = 1.6 Hz, 1H, 1-H), (ddd, $^3J_{PH}$ = 23.1 Hz, $^3J_{HH}$ = 18.4 Hz, $^2J_{HH}$ = 1.6 Hz, 1H, 1-H), (dddd, $^3J_{PH}$ = 24.9 Hz, $^3J_{HH}$ = 12.3 Hz, $^3J_{HH}$ = 18.4 Hz, $^2J_{HH}$ = 1.6 Hz, 1H, 2-H), 7.46 – 7.52 (m, 3H$_{Ar}$), 7.68 – 7.73 (m, 2H$_{Ar}$) ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, HMQC, $CDCl_3$): δ = 15.9 (d, ^1J = 74.4 Hz, C-3), 128.6 (d, ^3J = 11.8 Hz, C-6), 130.0 (d, ^2J = 9.7 Hz, C-5), 131.7 (d, ^4J = 2.7 Hz, C-7), 132.8 (C-1), 132.9 (d, ^1J = 95.3 Hz, C-2), 133.7 (d, ^1J = 102.2 Hz, C-4) ppm. – ^{31}P NMR ($CDCl_3$, 162.0 MHz): δ = + 28.2 ppm. – MS (EI) *m/z* (%): 166 [M^+], 151 (75), 139 (56), 133 (15), 125 (23), 109 (14), 104 (73), 91 (24), 77 (90), 63 (11). – HR-MS (ESI) calcd. for [M + H]$^+$ ($C_9H_{11}OPNa$): 167.0626, found. 167.0630.

5.2.5 (*Sp*,*Sp*)-(-)-(*E*)-Ethene-1,2-diylbis[methyl(phenyl)phosphine] dioxide (155)



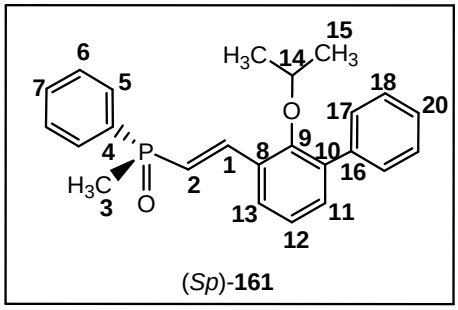
(*Sp*,*Sp*)-**155**

In a 100-mL Schlenk flask were placed (*Sp*)-**97** (500 mg, 3.01 mmol) in dichloromethane (12 mL). Thereafter, Ru-precatalyst **138** (115 mg, 0.15 mmol) in dichloromethane (3 mL) was added via syringe. The reaction mixture was stirred at 40 ºC for 24 h. Solvents were removed at reduced pressure and brown residue was purified by column chromatography (SiO_2, 25×4 cm, $CHCl_3$ / MeOH 9:1) to give 80 % (368 mg, 1.2 mmol) of (*Sp*,*Sp*)-**155** as a white powder. M. p. = 238 ºC.

(*Sp*,*Sp*)-**155**: $[\alpha]^{D}_{20}$ = – 255.0 (*c* = 1, CH_2Cl_2). – IR (ATR): $\tilde{\nu}$ = 3056 (w) cm^{-1}, 2989 (w), 1590 (w), 1483 (w), 1437 (w), 1174 (s, P=O), 1112 (s), 1071 (w), 1032 (w), 1024 (s), 890 (s), 881 (s), 820 (w), 737 (s), 692 (s). – ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.83 (t, $^{2}J_{PH}$ = 13.1 Hz, 6H, 3-H), 7.33 (t, J_{AX} + J_{BX} = 50.0 Hz, 2H, 1-H), 7.53-742 (m, 6H$_{Ar}$), 7.68-7.62 (m, 4H$_{Ar}$) ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, HMQC $CDCl_3$): δ = 16.7 (d, $^{1}J_{PC}$ = 74.5 Hz, C-6), 128.8 (t, ^{3}J = 12.1 Hz, C-4), 129.9, (t, ^{2}J = 9.9 Hz, C-3), 131,3 (d, $^{1}J_{PC}$ = 103.3 Hz, C-2), 132.1 (d, ^{4}J = 2.7 Hz, C-5), 140.9 (d, $^{1}J_{PC}$ = 23.6 Hz, C-1) ppm. – ^{31}P NMR ($CDCl_3$, 162.0 MHz): δ = + 26.4 ppm. – MS (EI) *m/z* (%): 304 [M^+]. – HR-MS (ESI) calcd. for [M + Na]$^+$ ($C_{16}H_{18}O_2P_2Na$): 327.0674, found 327.0690. – ($C_{16}H_{18}O_2P_2$): Calcd. C 63.16, H 5.96; found C 62.34, H 6.18.

The by-products **159**-**161** were isolated after homo-coupling of (*Sp*)-**97** with ruthenium precatalysts **138**, **156**, **137**, respectively.

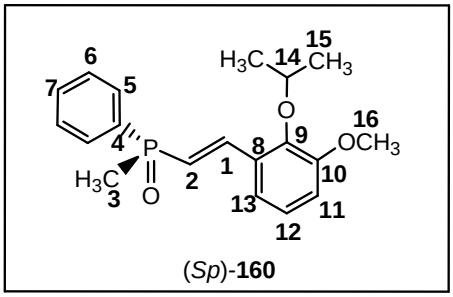
5.2.6 (*Sp*)-(-)-(*E*)-[2-(2-Isopropoxy-1,1'-biphenyl-3-yl)vinyl](methyl)phenylphosphine oxide (161)[92]



(*Sp*)-**161**

(*Sp*)-(**161**): Brown-green pasty oil, 47.2 mg (0.12 mmol, 5 %). – $[\alpha]^{D}_{20}$ = + 11.4 (*c* = 1.7, CH_2Cl_2). – IR (ATR): $\tilde{\nu}$ = 2927 (w) cm^{-1}, 1602 (w), 1421 (s), 1381 (w), 1258 (w), 1220 (s), 1173 (s, P=O), 1104 (s), 1008 (w), 931 (w), 906 (w), 787 (s), 759 (s), 696 (s). – ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.89 (dd, *J* = 6.2, 10.9 Hz, 6H, 14-H); 1.91 (d, $^2J_{PH}$ = 13.3 Hz, 3H, 3-H), 3.72 (spt, *J* = 6.1 Hz, 1H, 14-H), 6.75 (dd, *J* = 18.0 Hz, 20.5 Hz, 1H, 1-H), 7.17 (t, *J* = 7.5 Hz, 1H, 12-H), 7.34-7.30 (m, $2H_{Ar}$), 7.41 (t, *J* = 7.2 Hz, 1H, 16-H), 7.53-7.48 (m, $6H_{Ar}$), 7.74 (dd, *J* = 17.8, 20.8 Hz, 1H, 2-H), d = 7.82-7.77 (m, $2H_{Ar}$) ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, HMQC $CDCl_3$): δ = 17.2 (d, $^1J_{PC}$ = 75.0 Hz, C-3), 21.9 (d, *J* = 7.7 Hz, C-15), 76.2 (C-14), 121.4 (C-13), 132.4 (C-12), 123.9 (C-11), 126.0 (d, $^5J_{PC}$ = 1.3 Hz, C-10), 128.2 (C-18), 128.6 (d, $^3J_{PC}$ = 11.8 Hz, C-6), 129.0 (C-17), 130.3 (d, $^1J_{PC}$ = 17.6, C-2), 130.4 (d, $^2J_{PC}$ = 9.6 Hz, C-5), 131.6 (d, $^4J_{PC}$ = 2.7 Hz, C-7), 132.8 (C-20), 134.2 (d, $^1J_{PC}$ = 102.4 Hz, C-4), 136.3 (d, $^3J_{PC}$ = 1.1 Hz, C-8), 138.7 (C-16), 141.6 (d, $^2J_{PC}$ = 5.7 Hz, C-1), 153.9 (C-9) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = + 29.8 ppm. – MS (EI) *m/z* (%) 376 [M^+], 334 (95), 317 (29), 252 (10), 236 (29), 221 (32), 194 (97), 182 (31), 165 (81), 152 (42), 140 (100), 125 (78), 115 (32), 109 (16). – HR-MS (ESI) for $[M+H]^+$ ($C_{24}H_{26}O_2P$): calcd. 377.1670, found: 377.1685.

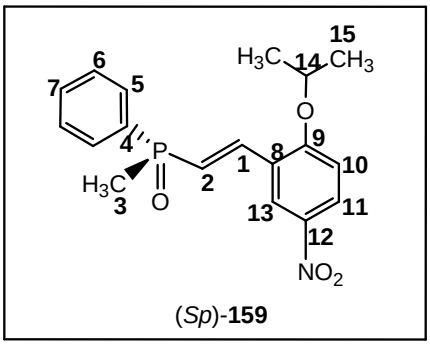
5.2.7 (*Sp*)-(-)-(*E*)-[2-(2-Isopropoxy-3-methoxyphenyl)vinyl](methyl)phenylphosphine oxide (160)[92]



(*Sp*)-**160**

(*Sp*)-(**160**): Brown solid, 45.2 mg (0.13 mmol, 5%). – M. p. = 131-131.5 °C. – $[\alpha]^{D}_{20}$ = + 37.6 (*c* = 0.5, CH_2Cl_2). – IR (ATR): $\tilde{\nu}$ = 2973 (w) cm^{-1}, 1573 (s), 1475 (w), 1453 (w), 1438 (w), 1372 (w), 1297 (w), 1261 (s), 1255 (w), 1172 (s, P=O), 1105 (s), 1066 (s), 995 (w), 932 (w), 896 (s), 772 (s), 695 (s). – ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 1.20 (dd, *J* = 9.8, 6.14 Hz, 6H, 15-H), 1.88 (d, $^{2}J_{PH}$ = 13.2 Hz, 3H, 3-H), 3.82 (s, 3H, 16-H), 4.44 (sept, *J* = 6.1, 1H, 14-H), 6.70 (dd, *J* = 20.6, 17.7 Hz, 1H, 1-H), 6.90 (dd, *J* = 1.4, 8.2 Hz, 1H, 13-H), 7.03 (t, *J* = 7.9 Hz, 1H, 12-H), 7.13 (dd, *J* = 1.4, 7.9 Hz, 1H, 11-H), 7.55-7.46 (m, $3H_{Ar}$), 7.67 (dd, *J* = 20.6, 17.8 Hz, 1H, 2-H), 7.80-7.75 (m, $2H_{Ar}$) ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, HMQC $CDCl_3$): δ = 17.1 (d, $^{1}J_{PC}$ = 74.9 Hz, C-3); 22.4 (d, *J* = 6.1 Hz, C-15), 55.8 (C-16), 75.8 (C-14), 113.6 (C-9), 118.7 (d, $^{3}J_{PC}$ = 1.15 Hz, C-8), 121.5 (C-13), 122.5 (C-14), 123.6 (C-11), 128.6 (d, $^{3}J_{PC}$ = 11.9 Hz, C-6), 130.2 (d, $^{1}J_{PC}$ = 17.6, C-2), 130.4 (d, $^{2}J_{PC}$ = 9.8 Hz, C-5), 131.6 (d, $^{4}J_{PC}$ = 2.9 Hz, C-7), 134.3 (d, $^{1}J_{PC}$ = 102.5 Hz, C-4), 141.3 (d, $^{2}J_{PC}$ = 5.6 Hz, C-1), 145.9 (C-10), 153.4 (d, $^{4}J_{PC}$ = 1.40 Hz, C-9) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = + 29.7 ppm. – MS (EI) *m/z* (%) 330 [M^+], 322 (22), 288 (98), 279 (12), 272 (48), 257 (10), 245 (23), 226 (17), 214 (15), 194 (12), 177 (20), 165 (44), 149 (89), 140 (100), 125 (81), 110 (24). – HR-MS (ESI) for $[M+H]^+$ ($C_{19}H_{24}O_3P$): calcd. 331.1463, found 331.1472.

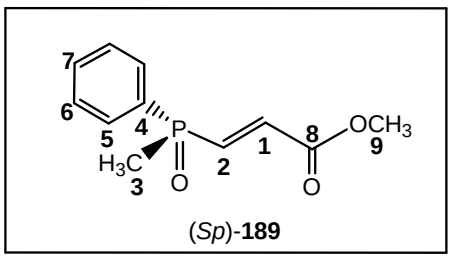
5.2.8 (*Sp*)-(-)-(*E*)-[2-(2-Isopropoxy-5-nitrophenyl)vinyl](methyl)phenylphosphine oxide (159) [83, 92]



(*Sp*)-**159**

(*Sp*)-(**159**): Brown-green solid, 51.9 mg (0.15 mmol, 5 %). – M. p. = 103–104 °C. – $[\alpha]^{D}_{20}$ = – 29.2 (*c* = 1, CH_2Cl_2). – ^{1}HNMR ($CDCl_3$, 400.1 MHz): δ = 1.41 (dd, *J* = 6.0, 2.3 Hz, 6H, 15-H); 1.89 (d, $^2J_{PH}$ = 13.2 Hz, 3H, 3-H), 4.73 (sept, *J* = 6.0 Hz, 1H, 14-H), 6.78 (dd, *J* = 23.5, 17.5 Hz, 1H, 2-H), 6.95 (d, *J* = 9.2 Hz, 1H, 10-H), 7.58–7.48 (m, $3H_{Ar}$), 7.74 (dd, *J* = 20.0, 17.6 Hz, 1H, 1-H), 7.82– 7.76 (m, $2H_{Ar}$), 8.20 (dd, *J* = 9.2, 2.8 Hz, 1H, 13-H), 8.39 (d, *J* = 2.8 Hz, 1H, 11-H) ppm. – ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 16.9 (d, $^1J_{CP}$ = 75.2 Hz, C-3), 21.8 (C-15), 72.1 (C-14), 112.6 (C-11), 123.6 (C-10), 124.7 (C-8), 125.4 (d, $^1J_{CP}$ = 18.0 Hz, C-2), 126.4 (C-13), 128.8 (d, $^3J_{CP}$ = 11.8 Hz, C-6), 130.1 (d, $^2J_{CP}$ = 9.7 Hz, C-5), 132.9 (d, $^4J_{CP}$ = 2.7 Hz, C-7) 133.5 (d, $^1J_{CP}$ = 102.9 Hz, C-4), 139.0 (d, $^2J_{CP}$ = 4.5 Hz, C-1), 140.9 (C-12), 160.8 (C-9) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = + 28.1 ppm.

5.2.9 (*Sp*)-(-)-(*E*)-(2-methoxycarbonylvinyl)(methyl)phenylphosphine oxide (189)[92]



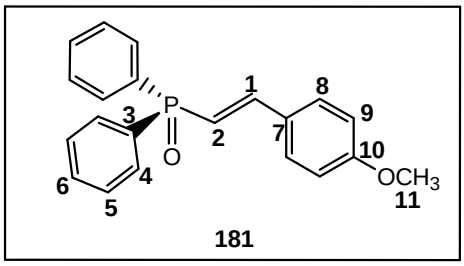
(*Sp*)-**189**

To a mixture of vinylphosphine oxide (*Sp*)-**97** (41.5 mg, 0.25 mmol) and precatalyst **138** (16.80 mg, 0.3 mmol) in dichloromethane (13 mL) via syringe was added methyl acrylate

(**188**) (645.7 mg, 7.5 mmol). The resulting mixture was stirred at 40 ºC for 24 h. The solvent was removed under reduced pressure. The crude product (*Sp*)-**189** was purified by flash chromatography (SiO_2, 25×4 cm, EtOAc / MeOH 20:1) to afford pure product as a brownish powder 34.8 mg (0.16 mmol, 62 %). – M. p. = 88-89 ºC.

(*Sp*)-(**189**): $[\alpha]^{D}_{20}$ = + 38.3 (*c* = 0.74, CH_2Cl_2). – IR (ATR): $\tilde{\nu}$ = 2980 (w) cm^{-1}, 1716 (s, C=O), 1619 (w), 1437 (s), 1324 (w), 1275 (w), 1234 (s), 1158 (s, P=O), 1112 (s), 996 (s), 890 (s), 858 (w), 825 (s), 769 (w), 738 (s), 691 (s). – ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.80 (d, $^{2}J_{PH}$ = 26.8 Hz, 3H, 3-H), 3.37 (s, 3H, 9-H), 6.80 (t, $^{3}J_{PH}$ = 17.4 Hz, 1H, 1-H), 7.37 (dd, $^{2}J_{PH}$ = 17.1 Hz, J_{PH} = 22.9 Hz, 1H, 2-H), 7.52-7.49 (m, $3H_{Ar}$), 7.72-7.65 (m, $2H_{Ar}$) ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, HMQC $CDCl_3$): δ = 16.7 (d, ^{1}J = 75.3 Hz, C-3), 52.3 (C-9), 128.9 (d, ^{3}J = 12.0 Hz, C-6), 130.1 (d, ^{2}J = 10.0 Hz, C-5), 131.3 (d, ^{4}J = 2.7 Hz, C-7), 132.4 (d, ^{1}J = 104.5 Hz, C-4), 134.1 (d, ^{2}J = 4.0 Hz, C-1), 138.5, (d, ^{1}J = 90.3 Hz, C-2), 165.1 (d, ^{3}J = 19.0 Hz, C-8) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = + 26.3 ppm. – MS (EI) *m/z* (%): 224 [M^+], 209 (52), 193 (16), 181 (12), 165 (24), 149 (59), 139 (55), 131 (100), 123 (38), 103 (65), 91 (50), 77 (83), 63 (35). – HR-MS (ESI): calcd for ($C_{11}H_{14}O_3P$) 225.0681, found 225.0689.

5.2.10 (*E*)-[2-(4-Methoxyphenyl)vinyl]diphenylphosphine oxide (181)

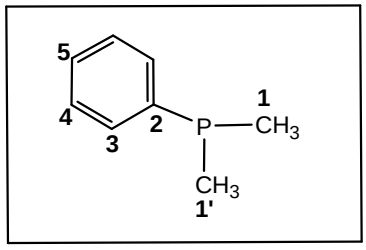


181

To a mixture of diphenylvinylphosphine oxide **168** (62 mg, 0.27 mmol) and precatalyst **138** (9.1 mg, 0.02 mmol) in dichloromethane (13 mL) via syringe was added 4-methoxystyrene **180** (0.11ml, 0.81 mmol). The resulting mixture was stirred at 40 ºC for 24 h. The solvent was removed under reduced pressure. The crude product **181** was purified by flash chromatography (SiO_2, 25×4 cm, EtOAc / MeOH 20:1) to afford pure product as a colorless solid 75.2 mg (0.225 mmol, 83%). M. p. = 108-109 ºC.

(**181**): IR (ATR): $\tilde{\nu}$ = 2924 (w) cm^{-1}, 1604 (s), 1571 (w), 1513 (s), 1439 (w), 1422 (w), 1300 (w), 1263 (s), 1239 (w), 1176 (s, P=O), 1103 (s), 1028 (s), 955 (s), 852 (w), 817 (s), 799 (s), 745 (s), 722 (s), 691 (s). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3H, 11-H), 6.67 (dd, J = 17.3, 22.3 Hz, 1H, 2-H), 6.94-6.86 (m, 2H$_{Ar}$), 7.45-7.38 (m, 1H, 2-H), 7.51-7.45 (m, 6H$_{Ar}$), 7.57-7.51 (m, 2H$_{Ar}$), 7.79-7.72 (m, 4H$_{Ar}$) ppm. – ^{13}C NMR (125 MHz, BB, DEPT, HMQC, $CDCl_3$): δ = 55.4 (C-11), 114.2 (C-8), 116.0 (C-9), 127.9 (d, $^{1}J_{PC}$ = 17.7 Hz, C-2), 128.5 (d, $^{3}J_{PC}$ = 12.1 Hz, C-5), 129.4 (C-7), 131.4 (d, $^{2}J_{PC}$ = 10.3 Hz, C-4), 131.8 (d, $^{4}J_{PC}$ = 2.6 Hz, C-6), 133.1 (d, $^{1}J_{PC}$ = 106.0 Hz, C-3), 147.2 (d, $^{2}J_{PC}$ = 4.2 Hz, C-1), 161.2 (C-10) ppm. – ^{31}P NMR (162 MHz, $CDCl_3$): δ = + 24.9 ppm. – MS (EI) *m/z* (%): 334 [M^{+}], 319 (11), 257 (9), 202 (50), 198 (13), 183 (11), 155 (20), 77 (10), 47 (11). – HR-MS (ESI) calcd for [M]+($C_{21}H_{19}O_2P$): 334.1122; found: 334.1116.

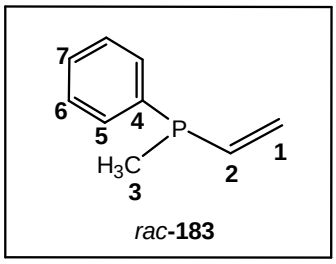
5.2.11 Dimethylphenylphosphine[25]



To mechanically stirred and cooled with an ice-bath methylmagnesium iodide prepared from magnesium (8.00 g, 0.33 mol) and methyl iodide (45.00 g, 0.28 mol) in diethyl ether (100 mL) was slowly during 2 hours added dichlorophenylphosphine (20.00 g, 0.11 mol) in diethyl ether (50 mL). The reaction mixture was stirred over night at 25 °C and well degassed ammonium chloride saturated solution (250 mL) was added with ice-bath cooling. After extraction with ether (3×70), the residue was dried over sodium sulphate. After filtration and vacuum distillation, dimethylphenylphosphine were obtained in 10.8 g (0.08 mol, 71 %).

^{1}HNMR ($CDCl_3$, 200 MHz): δ = 1.39 (d, $^{2}J_{PH}$ = 2.8 Hz, 6H, 1-H), 7.36 (m, 3H$_{Ar}$), 7.56 (m, 2H$_{Ar}$) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = – 44.4 ppm.

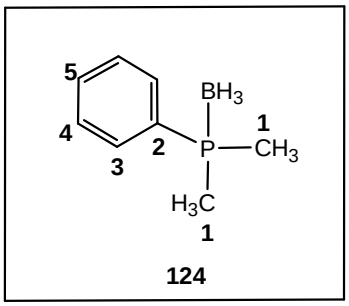
5.2.12 *rac*-Methylphenylvinylphosphine (183)[49]



rac-**183**

To a stirred solution of *rac*-**97** (1.00 g, 0.006 mol) in benzene (2 mL) at 20 ºC was added phenylsilane (1.5 equiv., 1.00 mL, 0.009 mol) and the reaction mixture was stirred at reflux for 15 h. After reaction was completed, the residue was distilled from reaction flask leading to *rac*-methylphenylvinylphosphine (**183**) 545 mg (3.63 mmol, 61 %). B.p. = 90 ºC/13 Torr *rac*-(**183**): ^{1}HNMR ($CDCl_3$, 200 MHz): δ = 1.46 (d, $^{2}J_{PH}$ = 2.8 Hz, 3H, 3-H), 5.66 (dd, J = 13.05 Hz, J = 18.32, 1-H), 5.79 (dd, J = 11.8 Hz, J = 28.5 Hz, 1-H), 6.45 (m, 1H, 2-H), 7.36 (m, 3H$_{Ar}$), 7.52 (m, 2H$_{Ar}$) ppm. – ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 11.6 (d, J = 12.9 Hz, C-3), 125.7 (d, $^{1}J_{PC}$ = 18.28 Hz, C-4), 128.2 (t, $^{1}J_{PC}$ = 6.7 Hz, C-5), 131.4 (C-6), 131.6 (C-7), 132.9 (d, $^{1}J_{PC}$ = 18.42 Hz, C-2), 149.4 (d, $^{2}J_{PC}$ = 14.9 Hz, C-1). – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = – 30.1 ppm.

5.2.13 Dimethylphenylphosphine borane (124)[25]

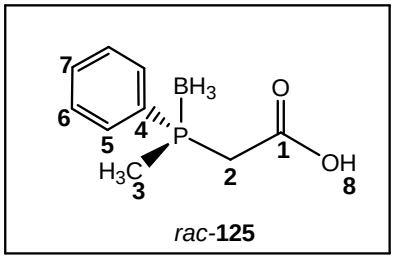


124

In a Schlenk flask were placed dimethylphenylphosphine (5.0 g, 0.036 mol) in freshly distilled tetrahydrofurane (15 mL). Borane-THF complex (6.18 mL, 0.07 mol) was added over 0.5 h at 0 ºC and stirred over night at 20 ºC. After the reaction was completed according TLC (hexane / EtOAc 9:1), to the reaction mixture 2 N hydrochloric acid (10 mL) was added. Extraction with ethylacetate (3×20 mL), drying over $MgSO_4$ evaporation of the solvent gave an oil as residue, which was distilled in vacuum to afford **124** 5.25 g (0.034 mol, 96 %).

(**124**): ^{1}HNMR ($CDCl_3$, 400 MHz): δ = 1.51 (d, $^2J_{PH}$ = 10.4 Hz, 6H, 1-H), 7.42 (m, 3H$_{Ar}$), 7.66 (m, 2H$_{Ar}$) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 3.5-4.9 (m) ppm.

5.2.14 *rac*-Boranato[(methyl)phenylphosphino]acetic acid (125)[182]



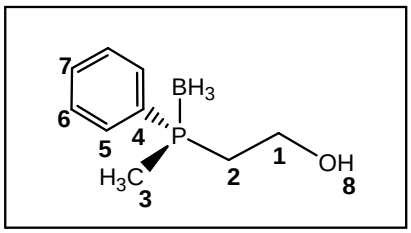
rac-**125**

At – 78 ºC to dimethylphenylphosphine-borane (820.8 mg, 5.4 mmol) (**124**) in Et_2O (43 mL) was added *sec*-BuLi (5 mL, 1.4 M in cyclohexane) and reaction mixture was stirred at – 78 ºC for 5 h. Dry ice (500 mg) was added as a solid and the reaction mixture allowed to reach 25 ºC with stirring 14 h. The reaction mixture was carefully poured into ice-water containing HCl and the organic layer was separated, and the aqueous layer was extracted with $CHCl_3$. The combined organic extracts were washed with 0.5 M aqueous Na_2CO_3, and to the aqueous layer was added 4 M HCl (50 mL) and $CHCl_3$ (100 mL). The organic layer was separated, and the aqueous layer was extracted with $CHCl_3$ (4×50 mL). The combined organic extracts were washed with brine and dried over Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure, to give the desired *rac*-boranatophosphinoacetic acid *rac*-**125** 603 mg (3.1 mmol, 57 %) as viscous colourless oil.

rac-(**125**): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.49-0.95 (m, 3H, B*H*$_3$), 1.77 (d, $^2J_{PH}$ = 10.2 Hz, 3-H), 2.89 (m, 2H, 2-H), 7.46 (m, 3H$_{Ar}$), 7.72 (m, 2H$_{Ar}$), 10.26 (brs, 1H, 8-H) ppm. – ^{13}C NMR (125 MHz, BB, DEPT, HMQC, $CDCl_3$): δ = 9.8 (d, J = 38.2 Hz, C-3), 34.8 (d, $^1J_{PC}$= 26.3 Hz, C-2), 127.4 (d, $^1J_{PC}$ = 54.3 Hz, C-4), 128.9 (d, $^3J_{PC}$ = 10.2 Hz, C-6), 131.4 (d, $^2J_{PC}$ =

9.9 Hz, C-5), 132.1 (d, $^{4}J_{PC}$ = 2.5 Hz, C-7), 173.1 (d, $^{2}J_{PC}$ = 5.9 Hz, C-1) ppm. – ^{31}P NMR (162 MHz, $CDCl_3$): δ = 10.4 (d, J = 67.0 Hz) ppm.

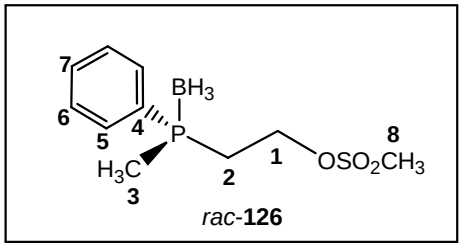
5.2.15 *rac*-2-[Boranato(methyl)phenylphosphino]ethanol[30]



BH_3 ·THF (7.5 mL of a 1.0 M THF solution, 7.5 mmol) was added at 0 °C, under argon, to a stirred solution of **125** (300 mg, 1.5 mmol) in THF (6 mL). The mixture was stirred at 25 °C for 2 h. The reaction was quenched by addition of ice/water and organic layers were separated, and the aqueous layer was extracted with EtOAc (3×40 mL). The combined extracts were washed with brine and dried with $MgSO_4$, and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography (SiO_2, 25×4 cm, EtOAc) to afford pure product as a white powder 270 mg (1.5 mmol, 97 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.44 (m, 3H, *BH*$_3$), 1.60 (d, $^{2}J_{PH}$ = 10.5 Hz, 3-H), 2.14 (m, 2H, 1-H), 2.23 (br, 1H, 8-H), 3.74 (m, 2H, 2-H), 7.46 (m, 3H$_{Ar}$), 7.75 (m, 2H$_{Ar}$) ppm. – ^{13}C NMR (125 MHz, BB, DEPT, HMQC, $CDCl_3$): δ = 11.3 (d, $^{1}J_{PC}$ = 39.3 Hz, C-3), 30.5 (d, $^{1}J_{PC}$ = 35.5 Hz, C-2), 57.5 (C-1), 128.9 (d, $^{3}J_{PC}$ = 9.9 Hz, C-6), 129.3 (d, $^{1}J_{PC}$ = 55.1 Hz, C-4), 131.3 (d, $^{2}J_{PC}$ = 9.4 Hz, C-5), 131.5 (d, $^{4}J_{PC}$ = 2.5 Hz, C-7) ppm. – ^{31}P NMR (162 MHz, $CDCl_3$): δ = 6.4-7.2 (m) ppm.

5.2.16 *rac*-Methanesulfonic acid (methyl)phenylboranatophosphino] ethyl ester (126)[30]

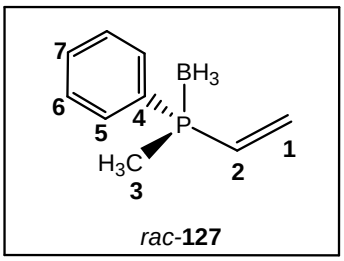


rac-**126**

Methanesulfonyl chloride (0.3 mL, 0.002 mol) was added at 25 °C, to a stirred solution of *rac*-boranato(methyl)phenylphosphino]ethanol (200 mg, 1.1 mmol) in pyridine (2 mL). The mixture was stirred for 12 h at the same temperature. The reaction was quenched by addition of 1M HCl. The organic layers were separated, and the aqueous layer was extracted three times with ethylacetate (20 mL). The combined extracts were washed with aqueous $NaHCO_3$ (50 mL) and brine (75 mL) and dried with $MgSO_4$, and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography (SiO_2, 25×4 cm, EtOAc / hexane 1:9) to afford pure product as colourless viscous oil 82 % (234.1 mg, 0.90 mmol).

rac-(**126**): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.61-0.95 (m, 3H, *BH*$_3$), 1.65 (d, $^2J_{PH}$ = 10.24 Hz, 3-H), 2.33 (m, 2H, 2-H), 2.93 (s, 3H, 8-H), 4.29 (m, 1H, 1-H), 4.44 (m, 1H, 1-H), 7.48 (m, 3H$_{Ar}$), 7.69 (m, 2H$_{Ar}$) ppm. – ^{13}C NMR (125 MHz, BB, DEPT, HMQC, $CDCl_3$): δ = 11.4 (d, $^1J_{PC}$ = 39.1 Hz, C-3), 27.9 (d, $^1J_{PC}$ = 34.5 Hz, C-2), 37.5 (C-8), 64.7 (d, $^2J_{PC}$ = 3.3 Hz, C-1), 128.1 (d, $^1J_{PC}$ = 54.6 Hz, C-4), 129.1 (d, $^3J_{PC}$ = 10.2 Hz, C-6), 131.3 (d, $^2J_{PC}$ = 9.8 Hz, C-5), 131.9 (d, $^4J_{PC}$ = 2.5 Hz, C-7) ppm. – ^{31}P NMR (162 MHz, $CDCl_3$): δ = + 7.7 (d, J = 64.5 Hz).

5.2.17 *rac*-Methylphenylvinylphosphine borane (127)



rac-**127**

To a stirred solution of *rac*-**126** (60 mg, 0.23 mmol) in toluene (2 mL) was added as a powder potassium *tert*-butoxide (30 mg, 0.3 mmol). The mixture was stirred at 25 °C for 1 h. The reaction was quenched by addition of water. The organic layers were separated, and the aqueous layer was extracted with ethylacetate (3×10 mL). The combined extracts were

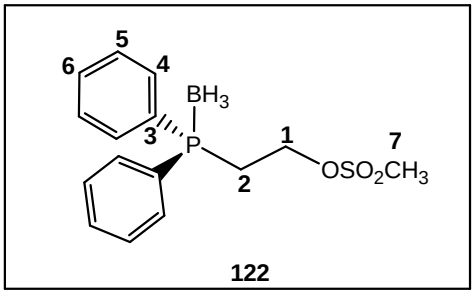
washed with aqueous $NaHCO_3$ (20 mL) and brine (30 mL) and dried with $MgSO_4$, and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography (SiO_2, 25×4 cm, EtOAc) to afford pure product as an oil 37.9 mg (0.203 mmol, 86 %). To prevent decomposition *rac*-**127** was stored as a solution in dichloromethane at –25 °C.

rac-(**127**): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.48 (m, 3H, BH_3), 1.61 (d, $^2J_{PH}$ = 10.3 Hz, 3-H), 6.04 (m, 2H, 1-H), 6.29 (m, 1H, 2-H), 7.43 (m, 3H$_{Ar}$), 7.66 (m, 2H$_{Ar}$) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 11.1 (d, $^1J_{PC}$ = 40.8 Hz, C-3), 128.7 (d, $^3J_{PC}$ = 9.9 Hz, C-6), 129.1 (d, $^1J_{PC}$ = 57.3 Hz, C-4), 129.3 (d, $^1J_{PC}$ = 52.2 Hz, C-2), 131.1 (d, $^4J_{PC}$ = 2.3 Hz, C-7), 131.3 (d, $^2J_{PC}$ = 9.4 Hz, C-5), 133.1 (d, $^2J_{PC}$ = 3.8 Hz, C-1) ppm. – ^{31}P NMR (162 MHz, $CDCl_3$): = 7.1-8.2 (m) ppm.

Synthesis of *rac*-methylphenylvinylphosphine borane from *rac*-methylphenylvinylphosphine

To a stirred solution of *rac*-methylphenylvinylphosphine (200 mg, 1.33 mmol) in THF (2 mL) was added BH_3 (115 mg, 1.4 mL, 1.4 mmol, 1.0 M in THF) at 0 °C. The mixture was allowed to reach 20 °C for 2 h. The reaction was quenched by addition of 2N HCl (3 mL). The organic layers were separated, and the aqueous layer was extracted with ethylacetate (3×20 mL). The combined extracts were washed with aqueous $NaHCO_3$ (20 mL) and brine (30 mL) and dried with $MgSO_4$, and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography (SiO_2, 25×4 cm, EtOAc / cyclohexane 2:5) to afford pure product as an colourless viscous oil 101 mg (0.62 mmol, 46 %). To prevent decomposition **127** was stored as a solution in dichloromethane at –25 °C.

5.2.18 Methanesulfonic acid (diphenylboranatophosphino] ethyl ester (122)[30]

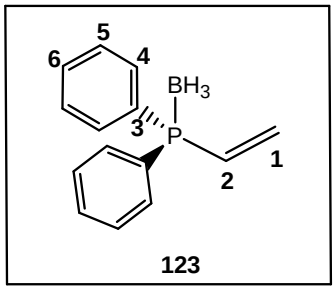


122

Methanesulfonyl chloride (0.5 mL, 4.9 mmol) was added at 0 °C, to a stirred solution of **121** (1.0 g, 4.1 mmol) in pyridine (1.5 mL). The mixture was stirred at 25 °C for 2 h . The reaction was quenched by addition of 1M HCl (5 mL). The organic layers were separated, and the aqueous layer was extracted with ethylacetate (3×20 mL). The combined extracts were washed with aqueous $NaHCO_3$ (10 mL) and brine (20 mL) and dried with $MgSO_4$, and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography (SiO_2, 25×4 cm, EtOAc / hexane 1:1) to afford **122** as a white low melting solid 1.1 g (0.34 mol, 84 %).

(**122**): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (m, 3H, BH_3), 2.72 (m, 2H, 2-H), 2.86 (s, 1H, 7-H), 4.42 (m, 2H, 1-H), 7.45 (m, 6H$_{Ar}$), 7.66 (m, 4H$_{Ar}$) ppm. ^{13}C NMR (100.6 MHz, BB, HMQC, $CDCl_3$): δ = 26.3 (d, $^1J_{PC}$ = 35.3 Hz, C-2), 37.4 (C-7), 64.6 (d, $^2J_{PC}$ = 7.1 Hz, C-1), 127.6 (d, $^1J_{PC}$ = 56.2 Hz, C-3), 129.1 (d, $^3J_{PC}$ = 10.2 Hz, C-5), 131.7 (d, $^4J_{PC}$ = 2.5 Hz, C-6), 131.9 (d, $^2J_{PC}$ = 9.8 Hz, C-4) ppm. – ^{31}P NMR (162 MHz, $CDCl_3$): = + 12.9 (d, J = 63.7 Hz) ppm.

5.2.19 Diphenylvinylphosphine borane (123)



123

To a stirred solution of **122** (100 mg, 0.31 mmol) in toluene (5 mL) was added as a powder potassium *tert*-butoxide (70 mg, 0.63 mmol). The mixture was stirred at 25 °C for 2 h. The reaction was quenched by addition of water. The organic layers were separated, and the aqueous layer was extracted with ethylacetate (3×15 mL). The combined extracts were washed with aqueous $NaHCO_3$ (20 mL) and brine (30 mL) and dried with $MgSO_4$, and the

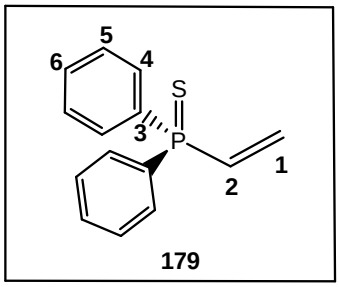
solvents were removed under reduced pressure. The crude product was purified by flash chromatography (SiO_2, 25×4 cm, EtOAc / hexane 3:7) to afford pure product as an colourless viscous oil 63.1 mg (0.28 mmol, 90 %). To prevent decomposition **123** was stored as a solution in dichloromethane at –25 °C.

(**123**): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (m, 3H, BH_3), 6.04 (m, 2H, 1-H), 6.01 (ddd, J = 1.4 Hz, J = 18.3 Hz, J = 19.9 Hz, 1H, 1-H$_{cis}$), 6.22 (ddd, J = 1.4 Hz, J = 12.0 Hz, J = 39.7 Hz, 1H, 1-H$_{trans}$), 6.64 (ddd, J = 12.0 Hz, J = 14.3 Hz, J = 26.3 Hz, 1H, 2-H), 7.43-7.51 (m, 6H$_{Ar}$), 7.62-7.68 (m, 4H$_{Ar}$) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 127.7 (d, $^1J_{PC}$ = 54.3 Hz, C-2), 128.3 (d, $^1J_{PC}$ = 58.7 Hz, C-1), 128.6 (d, $^2J_{PC}$ = 10.0 Hz, C-4), 131.1 (d, $^3J_{PC}$ = 2.6 Hz, C-6), 132.3 (d, $^3J_{PC}$ = 9.6 Hz, C-5), 134.9 (d, $^2J_{PC}$ = 4.8 Hz, C-1) ppm. – ^{31}P NMR (162 MHz, $CDCl_3$): = +16.3 (d, J_{PB} = 70.5 Hz) ppm.

Synthesis of diphenylvinylphosphine borane (123) from diphenylvinylphosphine

To a stirred solution of diphenylvinylphosphine (500 mg, 2.4 mmol) in THF (5 mL) was added BH_3 (203 mg, 2.4 mmol, 1.0 M in THF) at 0 °C. The mixture was allowed to reach 20 °C for 2 h. The reaction was quenched by addition of water. The organic layers were separated, and the aqueous layer was extracted with ethylacetate (3×20 mL). The combined extracts were washed with aqueous $NaHCO_3$ (20 mL) and brine (30 mL) and dried with $MgSO_4$, and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography (SiO_2, 25×4 cm, EtOAc / cyclohexane 2:5) to afford pure product as an colourless viscous oil 135 mg (0.64 mmol, 27 %). To prevent decomposition **123** was stored as a solution in dichloromethane at –25 °C.

5.2.20 Diphenylvinylphosphine sulfide (179)[183]

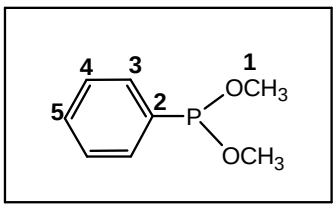


179

To a stirred solution of diphenylvinylphosphine (1.59 g, 0.008 mol) in benzene (5 mL) was added as a powder sulfur (240 mg, 7.5 mmol). The mixture was refluxed for 2 h. After evaporation of benzene, the black residue was purified by column chromatography (SiO_2, 25×4 cm, EtOAc / MeOH 10:1) to afford pure product **179** as an colourless crystals 1.38 g (0.006 mol, 71 %).

(**179**): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.15 (m, 3H, 1-H, 2-H), 7.42-7.57 (m, 6H$_{Ar}$), 7.72-7.84 (m, 4H$_{Ar}$) ppm. – ^{31}P NMR (162 MHz, $CDCl_3$): = + 38.2 ppm.

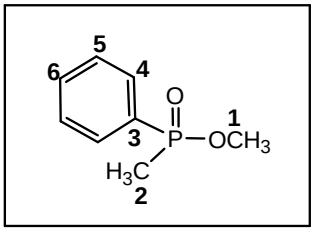
5.2.21 Dimethylphenylphosphonite[53]



Freshly distilled pyridine (18 g, 0.22 mol) was carefully added dropwise to a solution of dichlorophenylphosphine (20 g, 0.11 mol) in 200 mL of hexane (degassed) under argon at 25 °C. After stirring for 30 min. the mixture was cooled to 0 ºC. Whilst vigorous stirring was maintained, methanol (12 mL, 0.22 mol) was added dropwise. The reaction was stirred for 3-4 h, and the pyridine hydrochloride salt was removed by filtration. The solvent was then removed and the residue was distilled at reduced pressure to yield the product as a colorless liquid 17.8 g (0.11 mol, 95%). B. p. 53-54 ºC / 1 Torr.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.57 (d, $^2J_{PH}$ = 10.7 Hz, 6H, 1-H), 7.41-7.45 (m, 3H$_{Ar}$), 7.58-7.64 (m, 2H$_{Ar}$) ppm. – ^{31}P NMR (162 MHz, $CDCl_3$): = + 161.7 ppm.

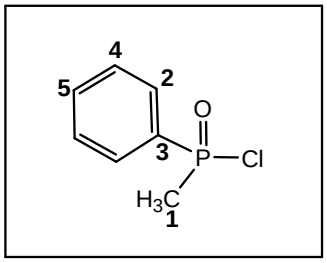
5.2.22 Methylphenyl phosphinic acid methyl ester[53]



Methyl iodide (14 g, 0.1 mol) was placed in a two-necked round bottom flask equipped with magnetic stirring and condenser, which was flushed with argon. Dimethylphenylphosphonite (17 g, 0.1 mol) was added carefully dropwise at 25 °C until an exothermic reaction was initiated. The addition was then controlled at a rate sufficient to maintain a steady reflux. When the addition was complete, the mixture was stirred for a further 3 h, and then it was distilled under reduced pressure. The product was obtained as a colorless liquid, 15.0 g (0.09 mol, 88 %). B. p. 95-96 ºC / 1 Torr.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (d, $^{2}J_{PH}$ = 14.5 Hz, 3H, 2-H), 1.45 (d, $^{2}J_{PH}$ = 11.3 Hz, 3H, 1-H), 7.31-7.39 (m, 3H$_{Ar}$), 7.58-7.67 (m, 2H$_{Ar}$) ppm. – ^{31}P NMR (162 MHz, $CDCl_3$): = + 45.2 ppm.

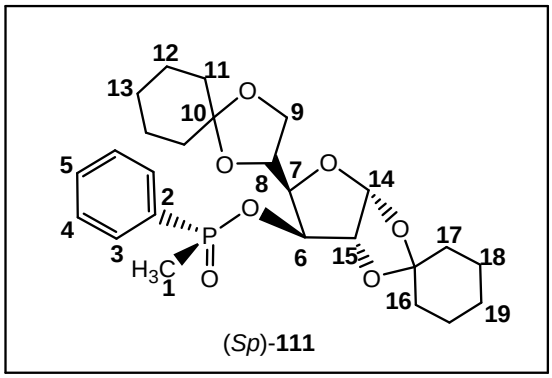
5.2.23 Methylphenyl phosphinic chloride[53]



Methylphenyl phosphinic acid methyl ester (16 g, 0.1 mol) and CCl_4 (60 mL) were placed in a two-necked round bottom flask, equipped with magnetic stirrer bar and condenser. Phosphorus pentachloride (26 g, 0.13 mol) was added slowly in *ca.* 3 g portions at 25 °C. When addition was complete, the mixture was refluxed for 3 h. After the removal of the solvent, the residue was distilled under reduced pressure to give 15.7 g (0.09 mol, 90%) of colourless liquid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.10 (d, $^{2}J_{PH}$ = 14.1 Hz, 3H, 1-H), 7.44-7.54 (m, 3H$_{Ar}$), 7.73-7.85 (m, 2H$_{Ar}$) ppm. – ^{31}P NMR (162 MHz, $CDCl_3$): = + 53.1 ppm.

5.2.24 Dicyclohexylidene-D-glucose-(*Sp*)-methylphenylphosphinate ester (111)[53]



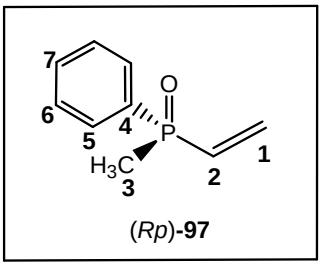
(*Sp*)-**111**

Triethylamine (1.0 g, 1.4 mL, 10 mmol) was added to an ice-cold solution of methylphenyl phosphinic chloride (1.8 g, 10 mmol) in toluene (25 mL) and stirred for 10 min. A solution of di-*o*-cyclohexylidene-R-D-glucofuranose (4.1 g, 12 mmol) in toluene (30 mL) was then added slowly over 15 min. The reaction mixture was allowed to warm to 25 °C, and stirring was continued 15 h. The reaction mixture was filtered, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (SiO_2, 50×6 cm, PE / acetone 9:1) to give (*Sp*)-**111** as a white powder 3.55 g (7.4 mmol, 62%).

M. p. = 52 °C.

(*Sp*)-(**111**): $[\alpha]^{D}_{20}$ = – 59 (*c* = 1.0, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (m, 20H, CH_2), 1.66 (d, $^2J_{PH}$ = 14.7 Hz, 3H, 1-H), 3.92-3.98 (m, 2H, 9-H, 8-H), 4.08 (dd, *J* = 8.6 Hz, *J* = 5.9 Hz, 1H, 9-H), 4.23 (ddd, *J* = 8.6 Hz, *J* = 5.4 Hz, *J* = 4.5 Hz, 1H, 8-H), 4.40 (dd, $^2J_{PH}$ = 6.8 Hz, J_{HH} = 2.3 Hz, 1H, 6-H), 5.08 (d, *J* = 3.6 Hz, 1H, 15-H), 5.94 (d, *J* = 3.6 Hz, 1H, 14-H), 7.46-7.55 (m, 3H$_{Ar}$), 7.87-7.97 (m, 2H$_{Ar}$) ppm. – ^{31}P NMR (162 MHz, $CDCl_3$): = + 46.3 ppm.

5.2.25 (*Rp*)-Methylphenylvinylphosphine oxide (97)[53]



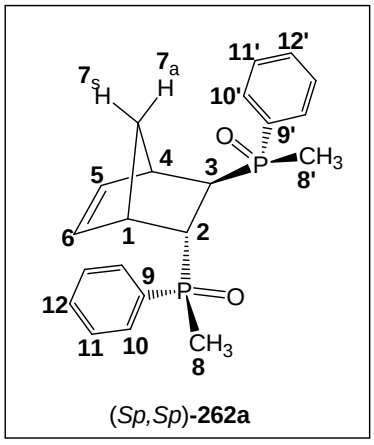
(*Rp*)-**97**

Vinylmagnesium bromide (6 mL, 1 M solution in THF, 2 equiv.) was added dropwise, via syringe, to a solution of (*Sp*)-**111** (1.44 g, 3 mmol) in THF (40 mL) at –78 °C. The mixture was heated gradually to –40 °C and stirred for 10 h. The reaction mixture was quenched by transfer via cannula into a solution of 1 M aqueous NH_4Cl (70 mL) at 0 °C. Following

separation, the aqueous layer was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine (50 mL), and dried over $MgSO_4$, filtered, and evaporated to furnish the crude product as an oil, which was purified by flash chromatography (SiO_2, 50×2.5 cm, $CHCl_3$ / MeOH 9:1) to give (*Rp*)-**97** as a white solid 403 mg, (2.4 mmol, 80 %).
M. p. = 81-82 °C.
(*Rp*)-(**97**): $[\alpha]^{D}_{20}$ = + 81.9 (*c* = 2.0, $CHCl_3$)[53]. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.75-1.79, (d, $^2J_{PH}$ = 13.3 Hz, 3H, 3-H), 6.35-6.49 (ddd, $^3J_{PH}$ = 28.3 Hz, $^3J_{HH}$ = 12.3 Hz, $^2J_{HH}$ = 1.6 Hz, 1H, 1-H), (ddd, $^3J_{PH}$ = 23.1 Hz, $^3J_{HH}$ = 18.4 Hz, $^2J_{HH}$ = 1.6 Hz, 1H, 1-H), (dddd, $^3J_{PH}$ = 24.9 Hz, $^3J_{HH}$ = 12.3 Hz, $^3J_{HH}$ = 18.4 Hz, $^2J_{HH}$ = 1.6 Hz, 1H, 2-H), 7.46 – 7.52 (m, 3H$_{Ar}$), 7.68 – 7.73 (m, 2H$_{Ar}$) ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, HMQC $CDCl_3$): δ = 15.9 (d, ^1J = 74.4 Hz, C-3), 128.6 (d, ^3J = 11.8 Hz, C-6), 130.0 (d, ^2J = 9.7 Hz, C-5), 131.7 (d, ^4J = 2.7 Hz, C-7), 132.8 (C-1), 132.9 (d, ^1J = 95.3 Hz, C-2), 133.7 (d, ^1J = 102.2 Hz, C-4) ppm. – ^{31}P NMR ($CDCl_3$, 162.0 MHz): δ = + 28.2 ppm.

5.3 Synthesis of New *P*-chiral Diphosphine Dioxides

5.3.1 (*Sp,Sp*)-(-)-Bis-(2*R*,3*R*)-([methyl(phenyl)phosphinyl]-bicyclo[2.2.1]hept-2-ene dioxide (262a)



(*Sp,Sp*)-**262a**

To a stirred solution of (*Sp,Sp*)-**155** (50 mg, 0.2 mmol) in dichloromethane (5 mL) at – 78 ºC was carefully added $TiCl_4$ (1M in CH_2Cl_2) (0.5 equiv. 15.6 mg, 0.1 mmol) dropwise over 3 min. The reaction mixture was stirred at – 78 ºC for 10 min. and freshly distilled cyclopentadiene (10 equiv., 108.3 mg, 1.6 mmol) was added as a cold solution in dichlromethane (5 mL) during 15 min. After completed addition reaction mixture was allowed to reach 20 ºC and stirred for 17 h under TLC control (benzene / EtOH 4:1). The reaction was quenched by addition of water (5 mL). The organic layers were separated, and the aqueous layer was extracted three times with CH_2Cl_2 (30 mL). The combined extracts were washed with brine (30 mL) and dried with $MgSO_4$, and the solvents were removed under

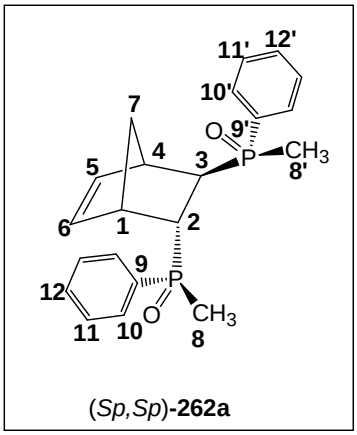
reduced pressure. The crude product was purified by flash chromatography (SiO_2, 25×2, $CHCl_3$ / MeOH 9:1) to afford pure product as a white powder 55.6 mg (0.15 mmol, 91 %). (80 % *de*). M. p. = 191-192 ºC.

(*Sp*,*Sp*)-**262a**: $[\alpha]^{D}_{20}$ = – 119 (*c* = 0.5, $CHCl_3$). – IR (ATR): $\tilde{\nu}$ = 2973 (w) cm^{-1}, 1483 (w), 1335 (w), 1299 (w), 1173 (s, P=O), 1112 (s), 1070 (w), 891 (s), 857 (w), 792 (w), 729 (s), 685 (s), 643 (w). – ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 1.06 (m, 1H, 7-Hs), 1.46 (d, J_{HH} = 8.7 Hz, 7a-H), 1.86 (d, $^2J_{PH}$ = 12.7 Hz, 8-H), 1.87 (d, $^2J_{PH}$ = 12.7 Hz, 8-H'), 2.34 (m, 1H, 3-H), 2.76 (m, 1H, 4-H), 2.80 (brs, 1H, 1-H), 2.93 (m, 1H, 2-H), 5.59 (m, 1H, 6-H), 6.02 (m, 1H, 5-H), 7.48 (m, 6H$_{Ar}$), 7.70 (m, 4H$_{Ar}$) ppm. – ^{13}C NMR (100.6 MHz BB, DEPT, HMQC, HMBC, HH-COSY, NOE, $CDCl_3$): δ = 9.2 (d, $^1J_{PC}$ = 64.2 Hz, C-8), 13.2 (d, $^1J_{PC}$ = 65.3 Hz, C-8'), 41.9 (d, $^1J_{PC}$ = 73.9 Hz, C-3), 42.1 (dd, $^1J_{PC}$ = 65.2 Hz, $^1J_{PC}$ = 1.2 Hz, C-2), 45.8 (q, C-4), 45.9 (d, $^2J_{PC}$ = 4.4 Hz, C-1), 48.1 (d, $^3J_{PC}$ = 11.3 Hz, C-7), 128.5 (d, $^3J_{PC}$ = 11.3 Hz, C-11), 128.6 (d, $^3J_{PC}$ = 11.3 Hz, C-11'), 130.4 (d, $^4J_{PC}$ = 1.3 Hz, C-12), 130.5 (d, $^4J_{PC}$ = 1.3 Hz, C-12'), 131.6 (d, $^2J_{PC}$ = 2.7 Hz, C-10), 131.7 (d, $^2J_{PC}$ = 2.7 Hz, C-10'), 132.5 (d, $^1J_{PC}$ = 90.1 Hz, C-9), 133.5 (d, $^1J_{PC}$ = 90.1 Hz, C-9'), 135.1 (d, $^3J_{PC}$ = 4.0 Hz, C-6), 137.1 (d, $^3J_{PC}$ = 11.9 Hz, C-5) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = + 38.6, (d, *J* = 8.9 Hz), + 39.8, (d, *J* = 8.9 Hz) ppm. MS (EI) *m/z* (%): 370 [M^+], 305 (17), 231 (100), 165 (28), 139 (37), 91 (18), 77 (20). – HR-MS (ESI) calcd for: $[M+H]^+$ ($C_{21}H_{24}O_2P_2$ Na): calcd. 393.1149, found 393.1152. – Anal ($C_{21}H_{24}O_2P_2$): Calcd C 68.10, H 6.53; found: C 67.46, H 6.61.

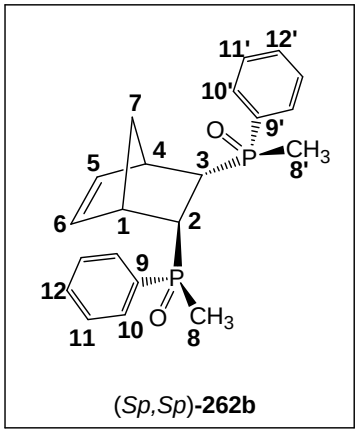
Crystal Structure Analysis of (*Sp*,*Sp*)-**262a**: Crystals were obtained by slow evaporation from chloroform : MeOH (9:1) at 20 ºC. Empirical formula $C_{21}H_{24}O_2P_2$, formula weight 370.34 g/mol, crystal system orthorombic, space group P $2_12_12_1$, unit cell dimensions *a* = 11.857(3), *b* = 16.383(13), *c* = 20.093(8) Å, α = 90º, β = 90º, γ = 90º, *V* = 3903(4) $Å^3$, *Z* = 8, $d_{Calc.}$ = 1.260 g/cm^3, μ = 0.234 mm^{-1}, crystal size 0.15 x 0.15 x 0.18 mm , F (000) = 1568, refinement method full-matrix least-squares on F^2, STOE IPDS one-axis diffractometer with imaging plate detector, *T* = 300(2) K, $Mo_{K\alpha}$ radiation (λ= 0.71073 Å), θ-range 1.99 to 24.32º, reflections collected / unique 12481 / 6266 [*R*(int) = 0.1301], completeness of data θ = 24.3 (99.7%), index ranges –13≤ *h* ≤ 13, 0≤ *k* ≤ 18, 0 ≤ *l* ≤ 23, direct methods, full-matrix least-squares refinement on F^2, goodness-of-fit on F^2 = 0.729, R_1 = 0.0623 ($I > 2\sigma_I$), wR_2 = 0.0879, *R*-indices [all data] R_1 = 0.2372 , wR_2 = 0.1144, final difference electron density map 0.347 and –0.229 $eÅ^{-3}$.

To (*Sp,Sp*)-**155** (50 mg, 0.2 mmol) in dichloromethane (3 mL) was added freshly distilled cyclopentadiene (10 equiv., 108.3 mg, 1.6 mmol) and the reaction mixture was stirred at 20 ºC for 24 h under TLC control (benzene / EtOH 4:1). Thereafter the solvent was removed at reduced pressure, and yellow residue was purified by flash chromatography (SiO_2, 20×2, $CHCl_3$ / MeOH 9:1) to afford pure product as a white powder 58.0 mg (0.19 mmol, 95 %). Ratio of diastereoisomers (1.3:1). $[\alpha]^D_{20}$ = – 62.4 (*c* = 0.5, $CHCl_3$). M. p. = 187.5-188.5 ºC.

5.3.2 Diastereoisomers separation with dibenzoyl- (+)-(L)-tartaric acid monohydrate



(*Sp,Sp*)-**262a**



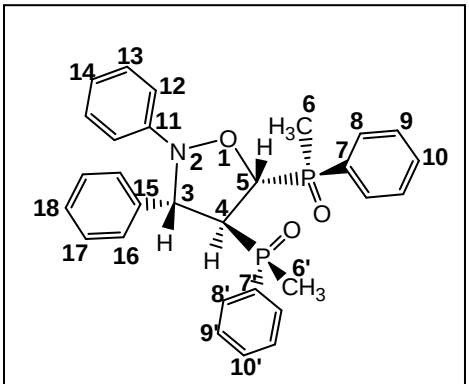
(*Sp,Sp*)-**262b**

To a solution of (*Sp,Sp*)-**262a** and (*Sp,Sp*)-**262b** (1.3:1) (100 mg, 0.270 mmol) in methanol (4 mL) was added as pulver dibenzoyl-(+)-(L)-tartaric acid monohydrate (L)-DBT·H_2O (101.6 mg, 0.270 mmol) and resulted suspension was stirred at reflux for 5h. Than after cooling to 25 ºC, ethyl acetate (2 mL) was added and again the solution refluxed for 2 h. After being cooled to 25 ºC, the white precipitate was filtered off, and washed with EtOAc (10 mL). The precipitate was then treated with 2N NaOH solution (3 mL) and extracted with CH_2Cl_2 (3×10), dried with $MgSO_4$ and evaporated to afford (*Sp,Sp*)-**262a** (96% *de*) as white solid 31 mg (0.101 mmol, 31%). $[\alpha]^D_{20}$ = – 83.5 (*c* = 0.69, $CHCl_3$). M. p. = 207-208 ºC.

The filtrate was also treated with 2N NaOH (5 mL), and extracted with CH_2Cl_2, dried to give (*Sp,Sp*)-**262b** (90% *de*) as white solid. (41 mg, 0.1134 mmol, 41%). $[\alpha]^{D}_{20}$ = + 15.4 (*c* = 0.72, $CHCl_3$). M. p. = 211.5-212 ºC.

(*Sp,Sp*)- (**262b**)-minor (90 % *de*): ^{31}P NMR ($CDCl_3$, 162 MHz): δ = + 38.3, (d, *J* = 9.5 Hz), + 39.5, (d, *J* = 9.5 Hz) ppm.

5.3.3 (4*Sp*,5*Rp*)-(−)-Bis-(4*S*,5*R*)-([methyl(phenyl)phosphinyl]-(*N*,3*S*)-diphenylisoxazolidine dioxide (276a)

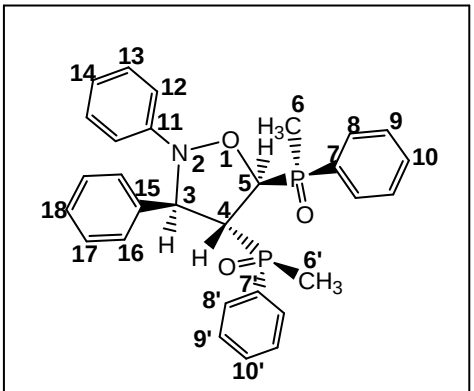


(*Rp,Sp*)-**276a**

In a 80-mL microwave tube were placed (*Sp,Sp*)-**155** (500 mg, 1.64 mmol) and *C,N*-diphenylnitrone **265** (730 mg, 3.7 mmol) in toluene (5 mL). Reaction mixture was heated for 40 min at 125 ºC (130 W). After reaction, toluene was removed at reduced pressure, and black-brownish residue was separated at the column (SiO_2, MeOH / CH_2Cl_2 (20:1) to give 501 mg (1 mmol, 62 %) of the (*Rp,Sp*)-**276a** and 310 mg (0.6 mmol, 36 %) of (*Rp,Sp*)-**276b** as white viscous liquids, which after addition of petroleum ether crystallized in white solids. Ratio of diastereoisomers 1.5:1 (^{31}P NMR)

(*Rp*,*Sp*)-(**276a**)-major: M. p. = 172 ºC. – $[\alpha]^{D}_{20}$ = + 100.8 (*c* = 0.5, $CHCl_3$). – IR (ATR): $\tilde{\nu}$ = 3049 (w) cm^{-1}, 1593 (w), 1488 (w), 1437 (w), 1286 (w), 1190 (s, P=O), 1116 (s, C-N), 1045 (w), 874 (s), 784 (w), 757 (w), 735 (s), 689 (s). – ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 1.66 (d, $^2J_{PH}$ = 13.1 Hz, 3H, 6-H), 1.79 (d, $^2J_{PH}$ = 13.4 Hz, 3H, 6'-H), 4.04 (m, 1H, 4-H), 4.54 (dt, *J* = 5.8 Hz, $^2J_{PH}$ = 12.7 Hz, 1H, 5-H), 4.98 (dd, J_{HH} = 7.5 Hz, $^2J_{PH}$ = 14.3 Hz, 1H, 3-H), 7.2-7.8 (m, 20H_{Ar}) ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, HMQC, HH-COSY, NOE, $CDCl_3$): δ = 13.0 (d, $^1J_{PC}$ = 70.9 Hz, C-6), 16.4 (d, $^1J_{PC}$ = 70.6 Hz, C-6'), 54.8 (dd, $^1J_{PC}$ = 68.5 Hz, *J* = 2.8 Hz, C-4), 72.1 (C-3), 77.2 (d, $^1J_{PC}$ = 76.3 Hz, C-5), 118.8 (C-12, C-12'), 124.9 (C-14), 129.0 (C-18), 128.3 (C-10'), 128.42 (C-10), 128.45 (C-16), 128.5 (C-17), 128.6 (C-13), 129.9 (d, $^3J_{PC}$ = 9.4 Hz, C-9'), 130.4 (d, $^3J_{PC}$ = 9.2 Hz, C-9), 131.2 (d, $^1J_{PC}$ = 97.9 Hz, C-7'), 131.7 (d, $^2J_{PC}$ = 2.9 Hz, C-8'), 131.9 (d, $^2J_{PC}$ = 2.7 Hz, C-8), 132.9 (d, $^1J_{PC}$ = 93.2 Hz, C-7), 138.6 (d, $^3J_{PC}$ = 2.3 Hz, C-15), 147.9 (C-11) ppm. – ^{31}P NMR ($CDCl_3$, 162.0 MHz): δ = + 38.0 (d, *J* = 20.3 Hz), + 39.8 (d, *J* = 19.8 Hz) ppm. – MS (EI) *m/z* (%): 502 [M^++H], 362 (19), 334 (23), 180 (57), 165 (74), 139 (66), 91 (62), 77 (100). – HR-MS (ESI) calcd for: $[M+H]^+$ ($C_{29}H_{29}NO_3P_2$): calcd. 502.1701, found 502.1708. – Anal ($C_{29}H_{29}NO_3P_2$): Calcd: C 69.45, H 5.83, N 2.79; found: C 68.93, H 6.05, N 2.87.

5.3.4 (4*Sp*,5*Rp*)-(-)-Bis-(4*R*,5*S*)-([methyl(phenyl)phosphinyl]-(*N*,3*R*)-diphenylisoxazolidine dioxide (276b)



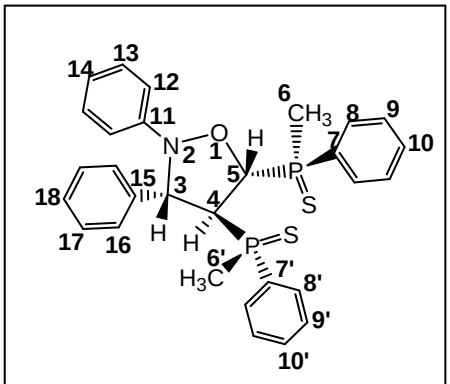
(*Rp*,*Sp*)-**276b**

(*Rp*,*Sp*)-(**276b**)-minor: M. p. = 69 ºC. – $[\alpha]^{D}_{20}$ = – 183.2 (*c* = 0.5, $CHCl_3$). – IR (ATR): $\tilde{\nu}$ = 3047 (w) cm^{-1}, 1597 (w), 1489 (w), 1438 (w), 1297 (w), 1178 (s, P=O), 1115 (s, C-N), 1027 (w), 889 (s), 742 (s), 693 (s). – ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 1.93 (d, $^2J_{PH}$ = 13.1 Hz, 3H, 6-H), 2.07 (d, $^2J_{PH}$ = 13.2 Hz, 3H, 6'-H), 3.2 (m, 1H, 4-H), 4.3 (dd, *J* = 8.8 Hz, $^2J_{PH}$ = 13.2 Hz, 1H, 3-H), 5.3 (dddd, $^2J_{PH}$ = 16.4 Hz, *J* = 9.2 Hz, *J* = 6.8 Hz, *J* = 2.1 Hz, 1H, 5-H), 5.94 (d, *J* = 7.1 Hz, 2H, 16-H), 6.64-7.66 (m, 14H_{Ar}), 7.95 (m, 4H, 8-H + 8H') ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, HMQC, HH-COSY, NOE, $CDCl_3$): δ = 14.5 (d, $^1J_{PC}$ = 69.9

Hz, C-6'), 16.8 (d, $^{1}J_{PC}$ = 71.5 Hz, C-6), 53.8 (dd, $^{1}J_{PC}$ = 70.0 Hz, $^{1}J_{PC}$ = 2.9 Hz, C-4), 71.8 (C-3), 75.4 (d, $^{1}J_{PC}$ = 81.3 Hz, C-5), 118.8 (C-12, C-12'), 124.9 (C-14), 129.0 (C-18), 128.3 (C-10'), 128.42 (C-10), 128.45 (C-16), 128.5 (C-17), 128.6 (C-13), 129.9 (d, $^{1}J_{PC}$ = 9.4 Hz, C-9'), 130.4 (d, $^{1}J_{PC}$ = 9.2 Hz, C-9), 131.2 (d, $^{1}J_{PC}$ = 97.9 Hz, C-7'), 131.7 (d, $^{1}J_{PC}$ = 2.9 Hz, C-8'), 131.9 (d, $^{1}J_{PC}$ = 2.7 Hz, C-8), 132.9 (d, $^{1}J_{PC}$ = 93.2 Hz, C-7), 138.6 (d, $^{3}J_{PC}$ = 2.3 Hz, C-15), 147.9 (C-11) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = + 37.8 (d, J = 16.4 Hz); + 36.1 (d, J = 15.9 Hz) ppm. – MS (EI) *m/z* (%): 502 [M^++H], 362 (19), 334 (23), 180 (57), 165 (74), 139 (66), 91 (62), 77 (100). – HR-MS (ESI) calcd for: $[M+H]^+$ ($C_{29}H_{29}NO_3P_2$): calcd. 502.1701, found 502.1708. – Anal ($C_{29}H_{29}NO_3P_2$): Calcd. C 69.45, H 5.83, N 2.79; found: C 68.96, H 5.91, N 2.80.

5.4 Reduction of New *P*-chiral Diphosphine Dioxides

5.4.1 (4*Sp*,5*Rp*)-(-)-bis-(4*S*,5*R*)-([methyl(phenyl)thiophosphinyl]-(*N*,3*S*)-(diphenyl)isoxazolidine (302a)



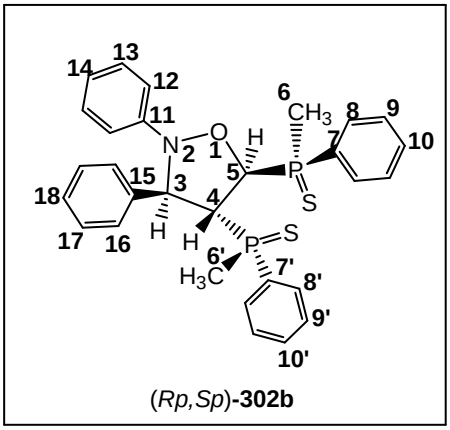
(*Rp,Sp*)-**302a**

To a stirred diphosphine dioxide (*Rp,Sp*)-**276a** (100 mg, 0.2 mmol) in THF (4 mL) was added polymethylhydrosiloxane (PMHS) (0.4 ml) and degassed 2 times. Ti(*i*-OPr)$_4$ (0.2 mL, 0.5988 mmol) was added via syringe and reaction mixture was heated at 66 ºC for 17 h. After cooling to 25 ºC, THF was removed in vacuum. To the residue was added freshly distilled benzene (3 mL) and sulfur (150 mg, 4.7 mmol) was added as a powder and reaction mixture was stirred

at 70 ºC for 2 h. After completed reaction and solvent removal, black residue was purified by column chromatography (SiO_2, 100×4 cm, toluene) to give diphosphine disulfide (*Rp,Sp*)-**302a** 102.2 mg (0.1916 mmol, 96 %) as white viscous oil, which crystallized on a standing in a white solid. M. p. = 71 ºC.

(**302a**): $[\alpha]^{D}_{20}$ = + 91.0 (*c* = 0.5, $CHCl_3$). – IR (ATR): $\tilde{\nu}$ = 3055 (w) cm^{-1}, 1596 (s), 1487 (s), 1454 (w), 1435 (w), 1408 (w), 1310 (w), 1287 (w), 1158 (w), 1105 (s, C-N), 1044 (w), 999 (w), 886 (s), 742 (s), 690 (s, P=S). – ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 1.70 (d, $^2J_{PH}$ = 12.9 Hz, 3H, 6-H), 2.08 (d, $^2J_{PH}$ = 13.7 Hz, 3H, 6-H'), 4.61 (dddd, $^2J_{PH}$ = 20.1 Hz, *J* = 14.0 Hz, *J* = 9.5 Hz, *J* = 3.8 Hz, 1H, 5-H), 4.90 (m, 2H, 3-H, 4-H), 7.03-7.76 (m, 20H_{Ar}) ppm. – ^{13}C NMR ($CDCl_3$, BB, DEPT, HMQC, HMBC, HH-COSY, 100.6 MHz): δ = 17.7 (d, $^1J_{PC}$ = 57.1 Hz, C-6), 20.3 (d, $^1J_{PC}$ = 56.9 Hz, C-6), 54.3 (dd, $^1J_{PC}$ = 51.6 Hz, $^1J_{PC}$ = 7.7 Hz, C-4), 74.4 (d, $^2J_{PC}$ = 4.4 Hz, C-3), 79.9 (dd, $^1J_{PC}$ = 54.8, *J* = 1.9 Hz, C-5), 121.1 (C-12), 126.1 (C-13), 128.3 (d, $^2J_{PC}$ = 2.5 Hz, C-8'), 128.5 (d, $^2J_{PC}$ = 3.1 Hz, C-8), 128.6 (C-14), 128.9 (C-18), 129.0 (C-17), 129.2 (d, $^1J_{PC}$ = 79.7 Hz, C-7'), 129.6 (C-16), 130.2 (d, $^3J_{PC}$ = 10.4 Hz, C-9'), (d, $^4J_{PC}$ = 2.9 Hz, C-10'), 131.5 (d, $^3J_{PC}$ = 10.4 Hz, C-9), 131.8 (d, $^4J_{PC}$ = 2.9 Hz, C-10), 131.9 (d, $^1J_{PC}$ = 73.9 Hz, C-7), 136.9 (d, $^3J_{PC}$ = 1.9 Hz, C-15), 147.3 (C-11) ppm. – ^{31}P NMR ($CDCl_3$, 162.0 MHz): δ = + 46.7 (d, *J* = 29.7 Hz); + 50.93 (d, *J* = 28.7 Hz) ppm. – MS (EI) *m/z* (%): 534 [M^++H], 378 (22), 336 (15), 238 (31), 206 (35), 181 (45), 155 (100), 91 (32), 77 (66). – HR-MS (ESI) calcd for: $[M+H]^+$ ($C_{29}H_{30}NOP_2S_2$): calcd. 534.1246, found 534.1244. – Anal ($C_{29}H_{29}NOS_2P_2$): Calcd: C 65.27, H 5.48, N 2.62; found: C 65.35, H 5.78, N 2.53.

5.4.2 (4*Sp*,5*Rp*)-(-)-bis-(4*R*,5*S*)-([methyl(phenyl)thiophosphinyl]-(*N*,3*R*)-(diphenyl)isoxazolidine (302b)

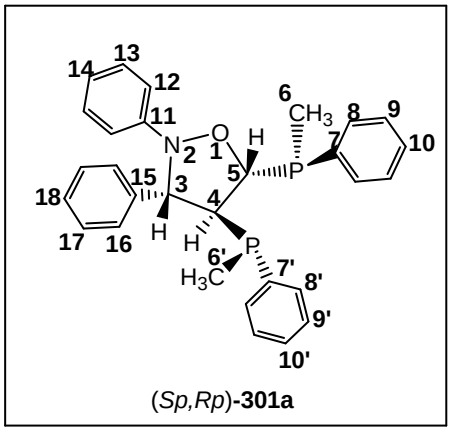


(*Rp,Sp*)-**302b**

(*Rp,Sp*)-**302b** was obtained by the procedure described above for (*Rp,Sp*)-**302a** as a white powder 98.9 mg (0.185 mmol, 93 %). M. p. = 142 ºC. Column chromatography (SiO_2, 100×4 cm, hexane / EtOAc 7:3).

(*Rp,Sp*)-**302b**: $[\alpha]^{D}_{20}$ = – 205.0 (*c* = 0.5, $CHCl_3$). – IR (ATR): $\tilde{\nu}$ = 3055 (w) cm^{-1}, 1596 (s), 1488 (s), 1454 (w), 1436 (s), 1406 (w), 1310 (w), 1289 (w), 1175 (w), 1157 (w), 1103 (s, C-N), 1072 (w), 1026 (w), 1000 (w), 884 (s), 741 (s), 689 (s, P=S). – ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 2.25 (d, $^2J_{PH}$ = 13.3 Hz, 3H, 6-H), 2.3 (d, $^2J_{PH}$ = 12.9 Hz, 3H, 6-H'), 3.73 (m, 1H, 4-H), 4.15 (dd, *J* = 8.5 Hz, $^2J_{PH}$ = 17.8 Hz, 1H, 3-H), 5.31 (dddd, $^2J_{PH}$ = 20.4 Hz, *J* = 12.3 Hz, *J* = 7.9 Hz, *J* = 4.4 Hz, 1H, 5-H), 5.74 (d, *J* = 7.2 Hz, 2H, 16-H), 6.58-7.64 (m, 16H_{Ar}), 8.19 (m, 2H, 9'-H) ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, HMQC, HMBC, HH-COSY, $CDCl_3$): δ = 18.6 (d, $^1J_{PC}$ = 58.6 Hz, C-6), 22.8 (d, $^1J_{PC}$ = 58.1 Hz, C-6), 53.2 (dd, $^1J_{PC}$ = 51.7 Hz, $^1J_{PC}$ = 7.3 Hz, C-4), 73.7 (d, $^2J_{PC}$ = 4.9 Hz, C-3), 80.5 (dd, $^1J_{PC}$ = 59.2 Hz, $^1J_{PC}$ = 1.0 Hz, C-5), 121.4 (C-12), 125.9 (C-14), 127.2 (C-13), 127.6 (C-17), 127.9 (C-10), 128.0 (C-18), 128.1 (d, $^4J_{PC}$ = 0.8 Hz, C-10'), 128.2 (C-16), 129.0 (dd, $^1J_{PC}$ = 78.4 Hz, *J* = 0.7 Hz, C-7), 129.2 (d, $^1J_{PC}$ = 72.5 Hz, C-7'), 131.2 (d, $^3J_{PC}$ = 10.4 Hz, C-9') 131.5 (d, $^2J_{PC}$ = 2.9 Hz, C-8'), 132.2 (d, $^2J_{PC}$ = 3.1 Hz, C-8), 133.8 (d, $^3J_{PC}$ = 10.2 Hz, C-9), 136.1 (d, $^3J_{PC}$ = 1.5 Hz, C-15), 147.1 (C-11) ppm. – ^{31}P NMR ($CDCl_3$, 162.0 MHz): δ = + 43.3 (d, *J* = 27.2 Hz), + 46.8 (d, *J* = 27.2 Hz) ppm. – MS (EI) m/z (%): 534 [M^++H], 378 (22), 336 (15), 238 (31), 206 (35), 181 (45), 155 (100), 91 (32), 77 (66). – HR-MS (ESI) calcd for: $[M+H]^+$ ($C_{29}H_{30}NOP_2S_2$): calcd. 534.1246, found 534.1244. – Anal ($C_{29}H_{29}NOS_2P_2$): Calcd. C 65.27, H 5.48, N 2.62; found: C 65.38, H 5.84, N 2.58.

5.4.3 (4*Rp*,5*Sp*)-(-)-bis-(4*S*,5*R*)-([methyl(phenyl)phosphinyl]-(*N*,3*S*)-(diphenyl)isoxazolidine (301a)

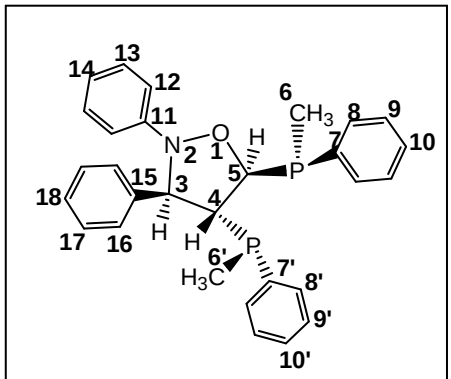


(*Sp,Rp*)-**301a**

In a Schlenk flask diphosphine borane (*Sp,Rp*)-**303a** (50.0 mg, 0.1 mmol) and DABCO (38.6 mg, 0.3 mmol) in toluene (2 mL) were placed. The reaction mixture was stirred at 70 ºC over 3 h. After filtration trough silica gel with toluene (50 mL) as eluent and evaporation in high vacuum, pure diphosphine (*Sp,Rp*)-**301a** was obtained as air-sensitive viscous white solid 43.2 mg (0.1 mmol, 87 %). To avoid oxidation, (*Sp,Rp*)-**301** was stored in a Schlenk flask under argon at – 25 ºC.

(*Sp,Rp*)-**301a**: ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 1.20 (d, $^{2}J_{PH}$ = 4.3 Hz, 3H, 6-H), 1.44 (d, $^{2}J_{PH}$ = 4.3 Hz, 3H, 6'-H), 2.71 (m, 1H, 4-H), 4.13 (dd, J = 9.3 Hz, $^{2}J_{PH}$ = 18.7 Hz, 1H, 5-H), 4.5 (dd, J = 5.7 Hz, $^{3}J_{PH}$ = 10.7 Hz, 1H, 3-H), 6.66 – 7.54 (m, 20H_{Ar}) ppm. – ^{13}C NMR (100.6 MHz BB, DEPT, $CDCl_3$): δ = 7.1 (d, $^{1}J_{PC}$ = 15.0 Hz, C-6'), 10.2 (dd, $^{1}J_{PC}$ = 15.9 Hz, $^{1}J_{PC}$ = 3.5 Hz, C-6), 49.7 (dd, $^{1}J_{PC}$ = 32.9 Hz, $^{1}J_{PC}$ = 8.1 Hz, C-4), 74.4 (d, $^{2}J_{PC}$ = 8.2 Hz, C-3), 77.08 (d, $^{1}J_{PC}$ = 30.5, $^{1}J_{PC}$ = 5.2 Hz, C-5), 114.6 (C-12), 121.7 (C-14), 126.8 (C-13), 127.2 (C-17), 128.3 (d, $^{3}J_{PC}$ = 7.1 Hz, C-9), 128.4 (d, $^{3}J_{PC}$ = 6.7 Hz, C-9'), 128.6 (C-16), 128.8 (C-18), 129.0 (C-10), 129.1 (C-10'), 132.1 (d, $^{1}J_{PC}$ = 18.6 Hz, C-7'), 132.1 (d, $^{1}J_{PC}$ = 19.2 Hz, C-7), 135.7 (d, $^{2}J_{PC}$ = 15.0 Hz, C-8'), 136.4 (d, $^{2}J_{PC}$ = 11.9 Hz, C-8), 142.6 (d, $^{3}J_{PC}$ = 2.5 Hz, C-15), 150.6 (C-11) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = – 28.8 (d, J = 10.9 Hz), – 30.6 (d, J = 10.9 Hz) ppm.

5.4.4 (4*Rp*,5*Sp*)-(-)-Bis-(4*R*,5*S*)-([methyl(phenyl)phosphinyl]-(*N*,3*R*)-(diphenyl)isoxazolidine (301b)

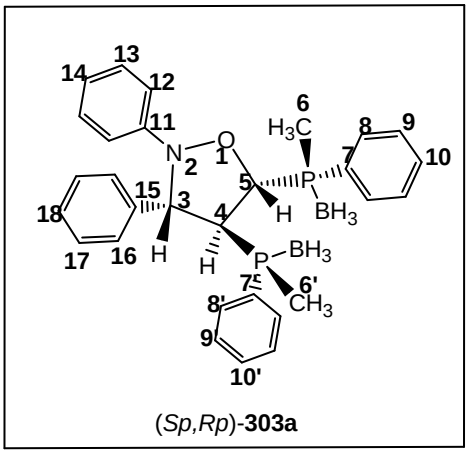


(*Sp,Rp*)-**301a**

(*Sp,Rp*)-**302b** was obtained by the procedure described above for (*Sp,Rp*)-**302a** as air-sensitive viscous white solid 43.7 mg (0.1 mmol, 88 %). To avoid oxidation, (*Sp,Rp*)-**302b** was stored in a Schlenk flask under argon at – 25 °C.

(*Sp,Rp*)-**302b**: ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 1.44 (d, $^{2}J_{PH}$ = 4.3 Hz, 3H, 6-H), 1.62 (d, $^{2}J_{PH}$ = 4.3 Hz, 3H, 6'-H), 2.52 (dddd, *J* = 5.2 Hz, *J* = 9.3 Hz, *J* = 12.6 Hz, $^{2}J_{PH}$ = 27.3 Hz, 1H, 4-H), 4.31 (dd, *J* = 5.7 Hz, $^{3}J_{PH}$ = 12.2 Hz, 1H, 3-H), 4.42 (ddd, *J* = 9.4 Hz, *J* = 14.2 Hz, $^{2}J_{PH}$ = 23.6 Hz, 1H, 5-H), 6.53 – 7.74 (m, 20H_{Ar}) ppm. – ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 7.1 (d, $^{1}J_{PC}$ = 11.1 Hz, C-6'), 10.2 (dd, $^{1}J_{PC}$ = 7.7 Hz, $^{1}J_{PC}$ = 14.3 Hz, C-6), 56.5 (dd, $^{1}J_{PC}$ = 27.6 Hz, $^{1}J_{PC}$ = 9.8 Hz, C-4), 74.9 (dd, $^{2}J_{PC}$ = 19.4 Hz, $^{2}J_{PC}$ = 4.2 Hz, C-3), 77.08 (dd, $^{1}J_{PC}$ = 49.3 Hz, $^{1}J_{PC}$ = 23.2 Hz, C-5), 114.3 (C-12), 121.5 (C-14), 126.5 (C-13), 126.6 (C-17), 128.0 (d, $^{3}J_{PC}$ = 7.7 Hz, C-9), 128.2 (C-10), 128.4 (d, $^{3}J_{PC}$ = 7.5 Hz, C-9'), 128.8 (C-16), 129.0 (C-10'), 129.5 (C-18), 129.6 (C-18), 132.7 (d, $^{1}J_{PC}$ = 20.0 Hz, C-7'), 134.5 (d, $^{1}J_{PC}$ = 20.1 Hz, C-7), 136.5 (d, $^{2}J_{PC}$ = 13.6 Hz, C-8'), 142.6 (d, $^{3}J_{PC}$ = 3.3 Hz, C-15), 150.8 (C-11) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = – 27.5 (d, *J* = 7.6 Hz), – 30.2 (d, *J* = 7.6 Hz) ppm.

5.4.5 (4*Rp*,5*Sp*)-(-)-Bis-(4*S*,5*R*)-boranato([methyl(phenyl)phosphino]-(*N*,3*S*)-(diphenyl) isoxazolidine (303a)

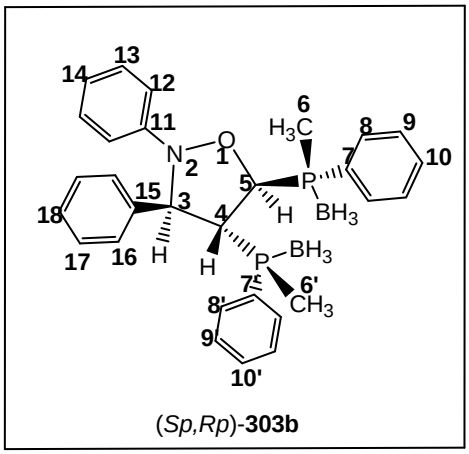


(*Sp,Rp*)-**303a**

To a stirred diphosphine dioxide (*Rp,Sp*)-**276a** (200 mg, 0.3992 mmol) in THF (7 mL) was added polymethylhydrosiloxane (PMHS) 0.8 ml (excess) and degassed 2 times. Ti(*i*-OPr)$_4$ (3 equiv., 0.35 mL, 1.2 mmol) was added via syringe and reaction mixture was heated at 66 ºC for 17 h. After cooling to 25 ºC, reaction mixture was filtered trough silica gel under argon with THF (60 mL), which thereafter was evaporated. To the residue was again added THF (10 mL) and cooled to 0 ºC. Borane-THF complex (1.0 M in THF) (0.172 g, 2 mL, 0.002 mol) was dropped during 3 min. and reaction mixture was allowed to reach 25 ºC. After 0.5 h water was carefully added and well extracted with EtOAc (4×20). Extracts were dried over $MgSO_4$. The chromatography (SiO_2, 4×50, hexane / EtOAc 9:1) as eluent leads to desired diphosphine borane (*Sp,Rp*)-**303a** as white solid 160.7 mg (0.32 mmol, 81%). M.p. = 74 ºC.

(*Sp,Rp*)-**303a**: $[\alpha]^{D}_{20}$ = + 125.8 (*c* = 0.5, $CHCl_3$). – IR (ATR): $\tilde{\nu}$ = 2991 (w) cm^{-1}, 2375 (br, B-H), 2169 (w), 1596 (w), 1488 (s), 1454 (w), 1436 (w), 1412 (w), 1260 (w), 1180 (w), 1111 (w), 1060 (s, C-N), 888 (s), 742 (s), 690 (s). – ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 0.5-1.2 (br, 6H, BH_3), 1.42 (d, $^2J_{PH}$ = 10.2 Hz, 3H, 6-H'), 1.67 (d, $^2J_{PH}$ = 10.2 Hz, 3H, 6-H), 3.95-4.03 (m, 1H, 5-H), 4.64 (dddd, $^2J_{PH}$ = 16.6 Hz, *J* = 8.3 Hz, *J* = 4.8 Hz, *J* = 3.4 Hz, 1H, 4-H), 4.72 (dd, $^3J_{PH}$ = 14.7 Hz, *J* = 7.8 Hz; 1H, 3-H), 6.95-7.57 (m, 20H$_{Ar}$) ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, $CDCl_3$,): δ = 7.8 (d, $^1J_{PC}$ = 39.1 Hz, C-6'), 10.2 (d, $^1J_{PC}$ = 38.7 Hz, C-6), 51.5 (dd, $^1J_{PC}$ = 31.3 Hz, $^1J_{PC}$ = 10.2 Hz, C-4), 74.3 (d, $^2J_{PC}$ = 7.3 Hz, C-3), 76.5 (d, $^1J_{PC}$ = 32.8, $^1J_{PC}$ = 3.3 Hz, C-5), 120.2 (C-12), 125.3 (C-14), 125.7 (C-13), 126.3 (d, $^1J_{PC}$ = 54.3 Hz, C-7), 128.2 (C-16), 128.7 (C-17), 128.75 (C-10'), 128.8 (d, $^1J_{PC}$ = 53.1 Hz, C-7'), 128.9 (C-10), 131.3 (d, $^4J_{PC}$ = 2.5 Hz, C-10'), 131.6 (d, $^2J_{PC}$ = 8.8 Hz, C-8'), 131.9 (d, $^4J_{PC}$ = 2.5 Hz, C-10), 132.4 (d, $^2J_{PC}$ = 9.0 Hz, C-8), 137.1 (d, $^3J_{PC}$ = 2.3 Hz, C-15), 147.3 (C-11) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = + 17.7 (d, *J* = 41.6 Hz), +24.6 (d, *J* = 45.5 Hz). – MS (EI) *m/z* (rel. intensity): 77 (100), 91 (80), 123 (97), 180 (46), 206 (25), 246 (41), 346 (43), 358 (23), 494 [M$^+$-3H]. – Anal ($C_{29}H_{35}NOB_2P_2$): Calcd. C 70.06, H 7.10, N 2.82; found: C 69.57, H 7.16, N 2.76.

5.4.6 (4*Rp*,5*Sp*)-(-)-Bis-(4*R*,5*S*)-boranato([methyl(phenyl)phosphino]-(*N*,3*R*)-(diphenyl) isoxazolidine (303b)



(*Sp,Rp*)-**303b**

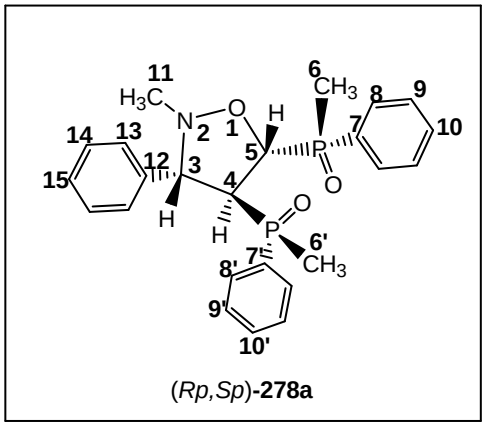
(*Sp,Rp*)-**303b** was obtained by the procedure described above for (*Sp,Rp*)-**303a** as a white powder 166.7 mg (0.33 mmol, 84 %). M. p. = 115-116 ºC. Column chromatography (SiO_2, 4×50, toluene).

(*Sp,Rp*)-**303b**: $[\alpha]^{D}_{20}$ = – 269.0 (*c* = 0.5, $CHCl_3$). – IR (ATR): $\tilde{\nu}$ = 2924 (w) cm^{-1}, 2363 (br, B-H), 1593 (w), 1485 (s), 1454 (w), 1436 (w), 1412 (w), 1293 (w), 1260 (s), 1224 (w), 1188 (w), 1063 (s, C-N), 1023 (s), 891 (s), 794 (s), 743 (s), 691 (s). – ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 0.5-1.2 (br, 6H, B*H*$_3$), 1.81 (d, $^{2}J_{PH}$ = 9.9 Hz, 3H, 6-H), 1.92 (d, $^{2}J_{PH}$ = 9.9 Hz, 3H, 6'-H), 3.41-3.51 (m, 1H, 5-H), 4.07 (dd, $^{3}J_{PH}$ = 15.4 Hz, *J* = 8.5 Hz, 1H, 3-H), 5.02 (dddd, $^{2}J_{PH}$ = 16.1 Hz, *J* = 10.9 Hz, *J* = 6.5 Hz, *J* = 4.4 Hz, 1H, 4-H), 5.76 (d, *J* = 7.2 Hz, 2H, 16-H), 6.95-7.57 (m, 18H$_{Ar}$) ppm. – ^{13}C NMR (100.6 MHz BB, DEPT, HMQC, $CDCl_3$): δ = 9.2 (d, $^{1}J_{PC}$ = 42.9 Hz, C-6'), 13.2 (d, $^{1}J_{PC}$ = 38.7 Hz, C-6), 49.7 (dd, $^{1}J_{PC}$ = 32.9 Hz, $^{1}J_{PC}$ = 8.05 Hz, C-4), 74.4 (d, $^{2}J_{PC}$ = 8.24 Hz, C-3), 77.1 (d, $^{1}J_{PC}$ = 30.48, $^{1}J_{PC}$ = 5.18 Hz, C-5), 121.0 (C-12), 125.2 (C-14), 125.8 (C-13), 126.0 (d, $^{1}J_{PC}$ = 51.4 Hz, C-7'), 126.4 (dd, $^{1}J_{PC}$ = 53.7 Hz, $^{1}J_{PC}$ = 0.8 Hz, C-7'), 127.7 (C-17), 128.2 (d, $^{3}J_{PC}$ = 10.16 Hz, C-9'), 128.3 (d, $^{3}J_{PC}$ = 10.16 Hz, C-9), 128.4 (C-18), 128.9 (C-16), 131.6 (d, $^{4}J_{PC}$ = 2.49 Hz, C-10'), 132.1 (d, $^{2}J_{PC}$ = 9.39 Hz, C-8'), 132.2 (d, $^{4}J_{PC}$ = 2.5 Hz, C-10), 134.7 (d, $^{2}J_{PC}$ = 9.4 Hz, C-8), 135.9 (d, $^{3}J_{PC}$ = 1.34 Hz, C-15), 147.1 (C-11) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = + 17.1 (d, *J* = 45.7 Hz), + 19.7 (d, *J* = 44.6 Hz) ppm. – MS (EI) *m/z* (%): 494 [M^{+}-3H], 358 (23), 346 (43), 246 (41), 206 (25), 180 (46), 123 (97), 91 (80), 77 (100). – Anal ($C_{29}H_{35}NOB_2P_2$): Calcd: C 70.06, H 7.10, N 2.82; found: C 69.49, H 7.37, N 2.70.

Crystal Structure Analysis of (*Sp,Rp*)-**303b**: Crystals were obtained by slow evaporation from toluene at 20 ºC. Empirical formula $C_{29}H_{35}B_2NOP_2$, formula weight 497.16 g/mol, crystal system monoclinic, space group P 1211, unit cell dimensions *a* = 16.449(4), *b* = 11.291(14), *c*

= 17.171(4) Å, α = 90º, β = 112.64(2)º, γ = 90º, V = 2943.3 (13)(4) Å^3, Z = 1, $d_{Calc.}$ = 1.126 g/cm^3, μ = 0.169 mm^{-1}, crystal size 0.09 x 0.20 x 0.25 mm, F (000) = 1040, refinement method full-matrix least-squares on F^2, STOE IPDS one-axis diffractometer with imaging plate detector, T = 293(2) K, $Mo_{K\alpha}$ radiation (λ= 0.71073 Å), θ-range 2.19 to 26.30º, reflections collected / unique 11421 / 2917 [R(int) = 0.1711], completeness of data θ = 26.30 (95.2%), index ranges –20≤ h ≤ 20, -14≤ k ≤ 14, -21 ≤ l ≤ 21, direct methods, full-matrix least-squares refinement on F^2, goodness-of-fit on F^2 = 0.618, R_1 = 0.0626 ($I > 2\sigma_I$), wR_2 = 0.1365, R-indices [all data] R_1 = 0.2163 , wR_2 = 0.1922, final difference electron density map 0.350 and –0.270 eÅ^{-3}.

5.4.7 (4*Sp*,5*Rp*)-(-)-Bis-(4*R*,5*S*)-(methyl(phenyl)phosphinyl)-*N*-methyl-(3*R*)-(phenyl) isoxazolidine dioxide (278a)



(*Rp,Sp*)-**278a**

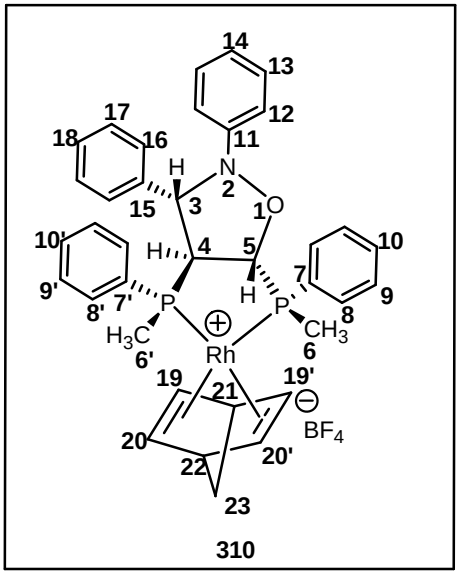
In a 80-mL microwave tube were placed (*Sp,Sp*)-**155** (40 mg, 0.13 mmol) and *C*-phenyl-*N*-methyl-nitrone **277** (25.5 mg, 0.26 mmol) in toluene (2 mL). Reaction mixture was heated for 40 min at 130 ºC (130 μW). After reaction, toluene was removed at reduced pressure, and black-brownish residue was separated at the column (SiO_2, MeOH / CH_2Cl_2 (30:1) to give 47.2 mg (0.107 mmol, 81%) of the (*Rp,Sp*)-**278a** as white viscous liquid, which after addition of petroleum ether crystallized in white solid. Ratio of diastereoisomers 6:1 (^{31}P NMR). Second (minor) diastereomer was not isolated.

(*Rp,Sp*)-**278a**-major: $[\alpha]^{D}_{20}$ = + 60.9 (c = 1.05, $CHCl_3$). – IR (ATR): $\tilde{\nu}$ = 2221 (w) cm^{-1}, 1496 (w), 1456 (w), 1438 (w), 1295 (w), 1176 (s, P=O), 1115 (s), 1042 (w), 882 (s), 739 (s), 696 (s). – ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 1.40 (d, $^2J_{PH}$ = 12.9 Hz, 3H, 6-H), 1.80 (d, $^2J_{PH}$ = 13.3 Hz, 3H, 6'-H), 2.62 (s, 3H, 11-H), 3.98 (m, 2H, 4-H, 3-H), 4.42 (m, 1H, 5-H), 7.15-7.44 (m, 15H$_{Ar}$) ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, HMQC, HH-COSY, $CDCl_3$): δ = 12.7

(d, $^{1}J_{PC}$ = 71.1 Hz, C-6), 15.6 (d, $^{1}J_{PC}$ = 69.8 Hz, C-6'), 41.9 (C-11), 52.1 (dd, $^{1}J_{PC}$ = 68.6 Hz, J = 3.3 Hz, C-4), 73.2 (C-3), 76.4 (d, $^{1}J_{PC}$ = 76.3 Hz, C-5), 128.3 (C-10'), 128.4 (C-10), 128.5 (C-15), 128.9 (C-14), 129.1 (C-13), 129.6 (d, $^{3}J_{PC}$ = 9.2 Hz, C-9'), 130.1 (d, $^{3}J_{PC}$ = 9.4 Hz, C-9), 130.6 (d, $^{1}J_{PC}$ = 98.7 Hz, C-7'), 131.3 (d, $^{2}J_{PC}$ = 2.7 Hz, C-8'), 131.8 (d, $^{2}J_{PC}$ = 2.7 Hz, C-8), 132.2 (d, $^{1}J_{PC}$ = 90.7 Hz, C-7), 136.7 (d, $^{3}J_{PC}$ = 1.0 Hz, C-12) ppm. – ^{31}P NMR ($CDCl_3$, 162.0 MHz): δ = + 37.6 (d, J = 23.8 Hz), + 40.6 (d, J = 23.8 Hz) ppm. – MS (EI) *m/z* (rel. intensity): 300 (25), 289 (17), 272 (36), 166 (11), 165 (100), 139 (56), 118 (34), 91 (20), 77 (53) 51 (20). – HR-MS (ESI) calcd for: $[M+H]^+$ ($C_{24}H_{27}NO_3P_2$): calcd. 440.1544, found 440.1546.

5.5 Synthesis of Rhodium Complex 310

5.5.1 {(4*Sp*,5*Rp*)-(-)[(*N*,3*S*)-Diphenyl--bis-4,5-[methyl(phenyl)phosphinyl] isoxazolidine](bicyclo[2.2.1]hepta-2,5-diene)}rhodium (I) tetrafluroborate (310)



310

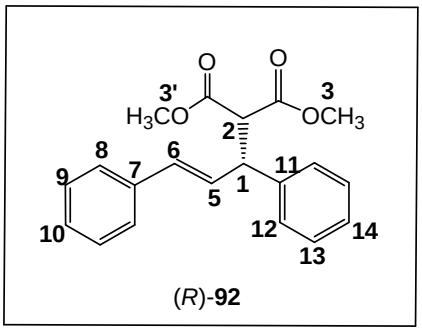
To a stirred at –30 ºC solution of diphosphine (*Sp,Rp*)-**301a** (65 mg, 0.1 mmol) in THF (5 mL) was added $Rh(nbd)_2BF_4$ (39.5 mg, 0.106 mmol) as a solid under argon. After stirring for 30 min at –20 ºC, the orange clear solution was filtered trough silicagel with THF as eluent. After evaporation, the orange powder was washed 3 times with hexane (3×2 mL) to give after solvent removal rhodium complex **301** as an air-sensitive orange powder 64.6 mg (0.08 mmol, 78 %).

(**310**): ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 1.61 (br.s 2H, 23-H), 1.99 (d, $^{2}J_{PH}$ = 8.4 Hz, 3H, 6-H'), 2.06 (d, $^{2}J_{PH}$ = 8.3 Hz, 3H, 6-H), 3.77 (m, 1H, 4-H), 4.13 (br, 2H, 19, 20-H), 4.42 (dd, $^{3}J_{PH}$ = 16.1 Hz, $^{2}J_{HH}$ = 7.0 Hz, 1H, 3-H), 4.88 (br.s, 2H, 21,22-H), 5.15 (m, 1H, 5-H), 5.48

(br.s, 2H, 19', 20'-H), 6.71-7.72 (m, 20H_{Ar}) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = – 3.8 (dd, $^1J_{RhP}$ = 151.5 Hz, $^2J_{PP}$ = 38.1 Hz), + 12.3 (dd, $^1J_{RhP}$ = 155.8 Hz, $^2J_{PP}$ = 38.1 Hz) ppm.

5.6 Palladium Catalyzed Asymmetric Allylic Substitution

5.6.1 (*R*)-Methyl-2-carbomethoxy-3,5-diphenylpent-4-enoate (92)[174]



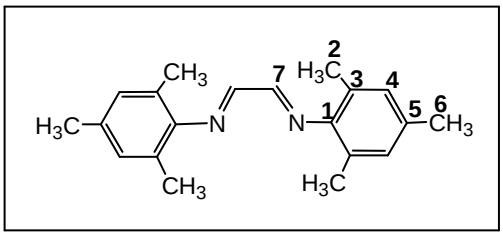
(*R*)-**92**

To a 10 mL flask containing a magnetic stirrer bar was added *rac*-1,3-diphenyl-2-propenyl acetate (252 mg, 1 mmol), THF (1 mL), dimethyl malonate (264.23 mg, 2 mmol), *N*,*O*-bis(trimethylsilyl)acetamide (470 µL, 2 mmol) and K_2CO_3 (14 mg, 0.1 mmol) in this order under argon. To this solution was added $[Pd(\pi\text{-}C_3H_5)Cl]_2$ (1.8 mg, 0.005 mmol), and *P*-chiral diphosphine ligand (*Sp*,*Rp*)-**301a** (5.63 mg, 0.012 mmol) in THF (450 µL). The mixture was stirred at 25 ºC with occasional monitoring by TLC (EtOAc / hexane 1:7) for 18 h. Thereafter the reaction mixture was diluted with the minimum amount of ethyl acetate and purified by flash chromatography on silica gel (SiO_2, 25×2, EtOAc / hexane 1:7) to give the pure product 308 mg (0.95 mmol, 97%) as white crystals. $[\alpha]^D_{20}$ = + 8.55 (*c* = 1.8, EtOH). According the literature the absolute configuration of the product is *R*.[167] The enantiomeric excess was determined by chiral dirhodium method[174], and found to be 81 % *ee*.

R-(**92**): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.53 (s, 3H, 3-H), 3.70 (s, 3H, 3'-H), 3.96 (d, *J* = 11.0 Hz, 2-H), 4.28 (dd, *J* = 8.8 Hz, *J* = 11.0 Hz, 1-H), 6.33 (dd, *J* = 8.5 Hz, *J* = 15.7, 6-H), 6.48 (d, *J* = 15.8 Hz, 5-H), 7.15-7.42 (m, 10H_{Ar}) ppm.

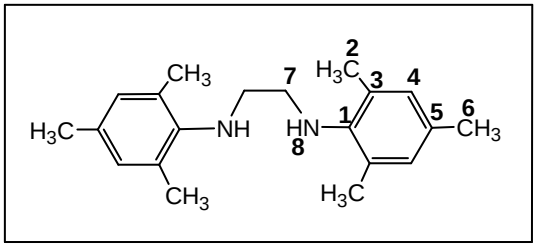
5.7 Alkene Metathesis: Synthesis of Ruthenium Precatalysts

5.7.1 *N*,*N*-Bis(2,4,6-trimethylphenyl)-1,2-ethanediimine[65]



To a stirred solution of glyoxal (18.7 mL of a 40 % in water) in methanol (1500 mL) was added dropwise 2,4,6-trimethylaniline (39.6 g, 0.3 mol) over 15 min. The mixture was stirred for 12 h at 22 °C as a bright yellow precipitate slowly formed. The mixture was diluted with CH_2Cl_2, dissolving the solid. The resulting yellow solution was dried over $MgSO_4$, filtered, and concentrated to a yellow-orange solid residue. The unpurified product was recrystallized from methanol. After slow cooling to 22 °C followed by subsequent storage of the sample at –20 °C for 12 h, long canary yellow crystals formed. The product was recovered by vacuum filtration, washed with pentane, and dried under high vacuum 27.0 g (0.1 mol, 63 %).
^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 2.23 (s, 12H, 2-H), 2.34 (s, 6H, 6-H), 6.95 (s, 4H, 4-H), 8.12 (s, 2H, 7-H) ppm.

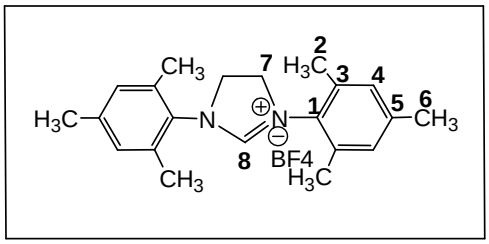
5.7.2 *N*,*N*-Bis(2,4,6-trimethylphenyl)-1,2-ethanediamine[65]



The bis(imine) (27.0 g, 0.1 mol) was suspended in MeOH (700 mL) and several crystals of bromocresol green were added as a pH indicator, and the mixture was cooled to 0 °C. $NaCNBH_3$ (37.3 g, 0.6 mol) was added to the reaction mixture in one portion as a solid. Vigorous bubbling was observed, and the reaction mixture turned a deep blue-green color (alkaline pH). After 10 min, concentrated HCl was added dropwise to the mixture, restoring its original yellow colour. Additional reduction slowly occurred, causing the mixture to again become basic. The acidification process was repeated (typically two more times) until the yellow color persisted. The reaction mixture was warmed to 22 °C and stirred for 1 h. A solution of 2M.KOH was added dropwise until the mixture was weakly alkaline (pH = 8-9). The mixture was then diluted with water (600 mL), transferred to a separatory funnel, and washed three times with TBME (3×300 mL). The combined organic layers were washed with brine (700 mL), dried over MgSO4, filtered, and concentrated to an yellow oil. Silica gel chromatography (SiO_2, 50×4, cyclohexane / EtOAc 9:1) afforded the product as a colourless oil 14.1 g (0.05 mol, 54 %).

^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 2.31 (s, 6H, 6-H), 2.37 (s, 12H, 2-H), 3.24 (s, 4H, 7-H), 6.94 (s, 4H, 4-H) ppm.

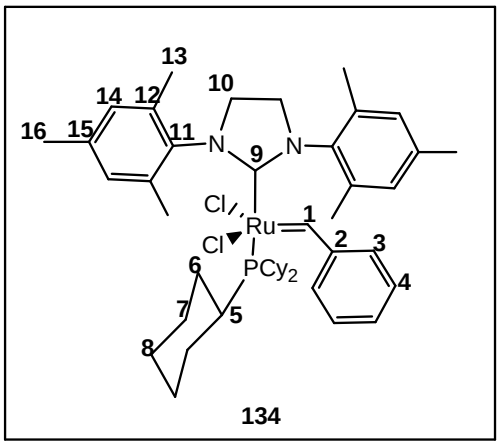
5.7.3 1,3-Bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazolium tetrafluoroborate[65]



A 50 mL roundbottom flask was charged with (14.0 g, 0.05 mol) and ammonium tetrafluoroborate (5.0 g, 0.05 mol). Triethylorthoformate (6.9 g, 0.05 mol) was added by syringe. The flask was equipped with a reflux condenser and submerged into a preheated oil bath at 120 °C. The mixture was refluxed for 3 h and cooled to 22 °C. A tan-colored solid precipitated, leaving a cloudy suspension. This mixture was recrystallized from hot ethanol. The resulting bright white crystals of product were recovered by vacuum filtration, washed with cold hexane, and dried under high vacuum 9.5 g (0.03 mol, 54 %). Additional product could be obtained by further recrystallization of the mother liquor.

^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 2.33 (s, 6H, 6-H), 2.38 (s, 12H, 2-H), 4.44 (s, 4H, 7-H), 7.10 (s, 4H, 4-H), 8.15 (s, 1H, 8-H) ppm.

5.7.4 [1,3-Bis(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(phenylmethylene) (tricyclohexylphosphine)]ruthenium (134)[64]



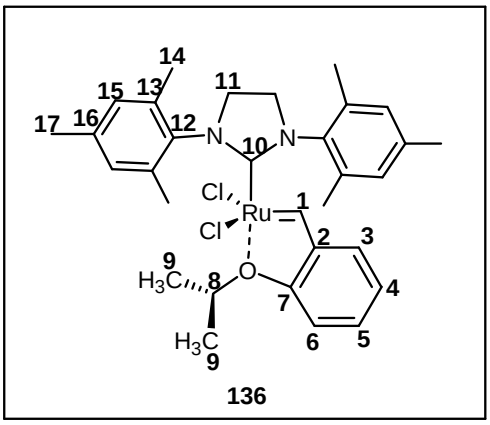
134

A solution potassium *tert*-amylate (2 mL, 3 mmol, 1.7 M in toluene) was added under argon to a suspension of 1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazolium tetrafluoroborate (1.2 g, 0.003 mol) in *n*-hexane (50 mL) and the resultant slightly turbid, yellow solution was stirred at room temperature for 1 h. Grubbs catalyst **133** (2.06 g, 2.4 mmol) was then added to the flask as a solid and the reaction mixture was heated to reflux for 1 h. followed by TLC (hexane / EtOAc 7:3). The brown-pink reaction mixture was cooled to 25 ºC and the solvent was removed in vacuum. The brown residue was purified by column chromatography (SiO_2, 50×4, hexane / EtOAc 7:3) to give **134** as brown-pink powder 1.75 g (0.002 mol, 69 %).
(**134**): ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 0.20-2.65 (m, 51H, P*Cy*$_3$, 13-H, 16-H), 3.91 (s, 4H, 10-H), 4.44 (s, 4H, 7-H), 7.02-7.41 (m, 9H, 10-H, 2-H, 3-H, 4-H), 19.17 (s, 1H, 1-H) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = + 32.1 ppm.

General procedure for the synthesis Hoveyda-Grubbs precatalysts

In a Schlenk flask were placed Grubbs catalyst **134** (500 mg, 0.59 mmol) and CuCl (58 mg, 0.59 mmol) and degassed 3 times and dichloromethane (30 mL) was added. After stirring for 5 min. appropriate isopropoxystyrene (0.59 mmol) was added and the reaction mixture was stirred at reflux for 1 h. After completed reaction, the solvent was removed at reduced pressure and the residue was purified by column chromatography on silica gel.

5.7.5 [1,3-Bis(2,4,6-trimethylphenyl)-2-imidazolinylidene]dichloro[(2-isopropoxyphenyl)methylene]ruthenium (136)[65]

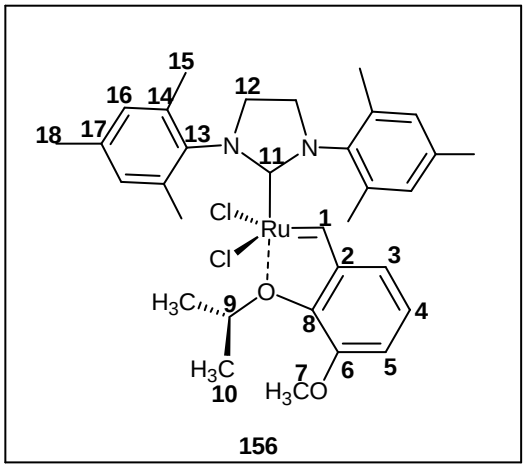


136

136 was obtained in 77 % yield as a green solid after purification (SiO_2, 25×2, CH_2Cl_2 / hexane 1:1).

(**136**): ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 1.26 (d, J = 5.9 Hz, 6H, 9-H), 2.42 (s, 6H, 17-H), 2.49 (s, 12H, 14-H), 4.19 (s, 4H, 11-H), 4.91 (sept, J = 6.3 Hz, 8-H), 6.80 (d, J = 8.6 Hz, 1H, H_{Ar}), 6.87 (dd, J = 7.4 Hz, J = 7.0 Hz, 1H, H_{Ar}), 6.95 (dd, J = 7.4 Hz, J = 1.6 Hz, 1H, H_{Ar}), 7.08 (s, 4H, 15-H), 7.49 (m, 1H, H_{Ar}), 16.56 (s, 1H, 1-H).

5.7.6 [1,3-Bis(2,4,6-trimethylphenyl)-2-imidazolinylidene]dichloro[(2-isopropoxy-3-methoxyphenyl)methylene]ruthenium (156)[85]

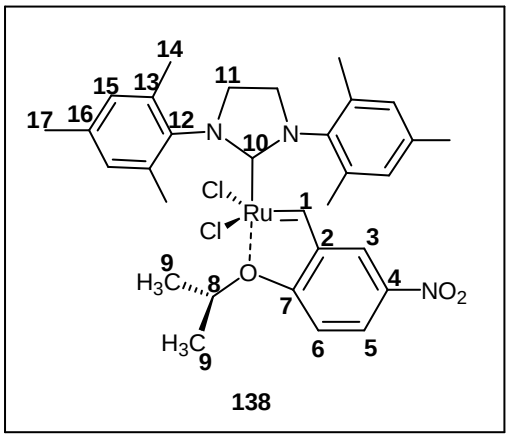


156

156 was obtained in 72 % yield as a green solid after purification (SiO_2, 25×2, TBME / hexane 1:2).

(**156**): ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 1.21 (d, J = 6.2 Hz, 6H, 10-H), 2.46 (br.s, 18H, 15-H+18-H), 3.82 (s, 3H, 7-H), 4.15 (s, 4H, 12-H), 5.69 (sept, J = 6.2 Hz, 9-H), 6.58 (d, J = 7.5 Hz, 1H, H_{Ar}), 6.91 (dd, J = 8.0 Hz, J = 7.5 Hz, 1H, H_{Ar}), 7.09 (s, 4H, 16-H), 7.49 (d, J = 8.0 Hz, 1H, H_{Ar}) 16.51 (s, 1H, 1-H) ppm.

5.7.7 [1,3-Bis(2,4,6-trimethylphenyl)-2-imidazolinylidene]dichloro[(2-isopropoxy-5-nitrophenyl)methylene]ruthenium (138)[67, 109]

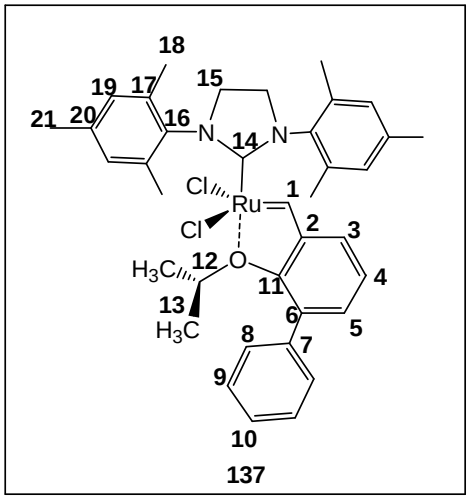


138

138 was obtained in 83 % yield as a green solid after purification (SiO_2, 25×2, EtOAc / cyclohexane 2:5).

(**138**): ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 1.31 (d, J = 6.1 Hz, 6H, 9-H), 2.46 (br.s, 18H, 14-H+17-H), 4.20 (s, 4H, 11-H), 4.98 (sept, J = 6.1 Hz, 8-H), 6.88 (d, J = 9.1 Hz, 1H, H_{Ar}), 7.09 (s, 4H, 15-H), 7.80 (d, J = 2.5 Hz, 1H, H_{Ar}), 6.91 (dd, J = 9.1 Hz, J = 2.5 Hz, 1H, H_{Ar}), 16.47 (s, 1H, 1-H) ppm.

5.7.8 [1,3-Bis(2,4,6-trimethylphenyl)-2-imidazolinylidene]dichloro[(2-isopropoxy-biphenyl)methylene]ruthenium (137)[66]

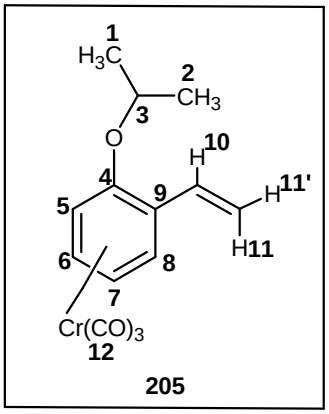


137 was obtained in 59 % yield as a green solid after purification (SiO_2, 25×2, EtOAc / cyclohexane 1:9).

(**137**): ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ = 0.87 (d, J = 6.3 Hz, 6H, 13-H), 2.15-2.58 (br.s, 18H, 18-H+21-H), 4.19 (s, 4H, 15-H), 4.38 (sept, J = 6.2 Hz, 12-H), 6.87-6.92 (m, 2H, H_{Ar}), 7.06 (s, 4H, 15-H), 7.28-7.37 (m, 6H, H_{Ar}), 16.62 (s, 1H, 1-H) ppm.

5.8 Synthesis of New, Highly Active Bimetallic Precatalyst for Alkene Metathesis

5.8.1 *rac*-Tricarbonyl(2-isopropoxystyrene)chromium (0) (205)

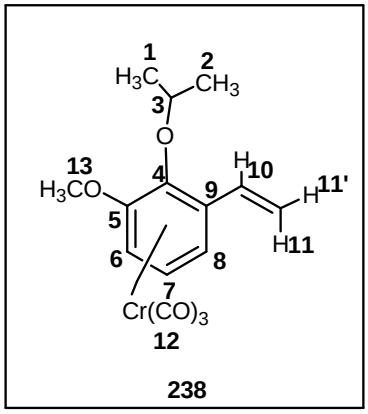


205

2-Isopropoxystyrene[65] (**199**), (1.000 g, 6.2 mmol) in 3 THF (3 mL) was added to $Cr(CO)_6$ (1.76 g, 8.0 mmol) in Bu_2O / THF (10:1) (440 mL) and heated at reflux. In the first 2 hours the color of the reaction mixture turned to orange. After 42 h in all, the reaction mixture was cooled to 25 °C and filtered under argon through the silica gel. Solvent evaporation at reduced pressure gave an orange residue, which was purified by column chromatography (SiO_2, PE / TBME 2:1), R_f = 0.42 to give 1.050 g (3.5 mmol, 59 %) of **205** as a yellow powder. M. p. = 63.5 - 64.0 ºC.

(**205**): IR (ATR): $\tilde{\nu}$ = 2981 (w) cm $^{-1}$, 1941(s, $Cr(CO)_3$), 1837 (s), 1626 (w), 1532 (w), 1461 (s), 1424 (s), 1375 (w), 1335 (w), 1280 (w), 1249 (s), 1157 (w), 1107 (s), 993 (w), 949 (w), 918 (s), 816 (w), 667(s), 625 (s). – ^{1}H NMR (400 MHz, HH-COSY, NOE, C_6D_6): δ = 0.77 (d, *J* = 6.02 Hz, 3H, 1-H), 1.09 (d, *J* = 6.2 Hz, 3H, 2-H), 3.71 (sept, *J* = 6.1 Hz, 1H, 3-H), 4.14 (t, *J* = 6.3 Hz, 1H, 7-H), 4.22 (d, *J* = 6.8 Hz, 1H, 5-H), 4.75-4.78 (t, *J* = 7.0 Hz, 1H, 6-H), 4.92 (d, *J* = 11.1 Hz, 1H, 11'-H), 5.27 (dd, *J* = 6.6 Hz, *J* = 1.2 Hz, 1H, 8-H), 5.32 (d, *J* = 17.6 Hz, 1H, 11-H), 6.64-6.71 (dd, *J* = 17.6 Hz, *J* = 11.1 Hz, 1H, 10-H) ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, HMQC, HMBC, C_6D_6): δ = 21.5 (C-2), 22.1 (C-1), 72.0 (C-3), 75.8 (C-5), 84.8 (C-7), 92.7 (C-8), 93.8 (C-6), 94.7 (C-9), 114.9 (C-11), 129.7 (C-10), 139.9 (C-4), 233.8 (C-12) ppm. – MS (EI) *m/z* (%): 298 (42) [M^+], 242 (19) [M^+ – 2CO)], 215 (28), 214 (89) [M^+ – 3CO)], 173 (8), 172 (29), 171 (98), 162 (6), 145 (7), 143 (22), 120 (20), 91 (14), 52 (100) [Cr^+]. – HR-MS (IE) calcd. for ($C_{14}H_{14}O_4$ ^{52}Cr) 298.0297; found: 298.0297. – Anal ($C_{14}H_{14}O_4Cr$): Calcd. C 56.38, H 4.73; found: 56.43, 4.61.

5.8.2 *rac*-Tricarbonyl (2-isopropoxy-3-methoxystyrene)chromium (0) (238)

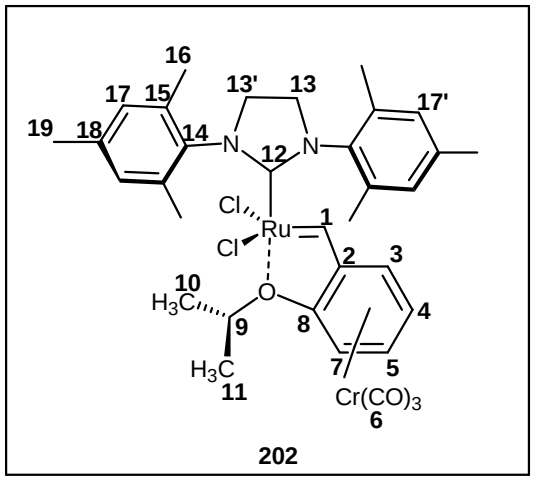


238

2-Isopropoxy-3-methoxystyrene[104] (0.470 g, 2.446 mmol) in THF (3 mL) was added to $Cr(CO)_6$ (0.59 g, 2.7 mmol, 1.1 equiv.) in Bu_2O / THF (10:1) (175 mL) and heated at reflux for 42 h. In the first 2 hours the color of the reaction mixture turned to orange. The reaction mixture was cooled to 25 °C and filtered under argon through the silica gel. Solvent evaporation at reduced pressure gave a yellow residue, which was purified by column chromatography (SiO_2, PE / TBME 2:1) to give 0.46 g (1.25 mmol, 51 %) of **238** as a light yellow powder. M. p. = 99 ºC.

(**238**): IR (ATR): $\tilde{\nu}$ = 2978 (w) cm $^{-1}$, 1950 (s, $Cr(CO)_3$), 1869 (s), 1844 (s), 1518 (w), 1411 (w), 1376 (w), 1276 (w), 1205 (w), 1097 (w), 1047 (w), 996 (w), 916 (w), 855 (w), 797 (w), 735 (w), 708 (w), 665 (w), 628 (s). – ^{1}H NMR (400 MHz, C_6D_6): δ = 1.09 (d, *J* = 6.2 Hz, 3H, 1-H), 1.23 (d, *J* = 6.1 Hz, 3H, 2-H), 2.97 (s, 3H, 13-H), 4.11 (m, 1H, 6-H), 4.28 (sept, *J* = 6.1 Hz, 1H, 3-H), 4.51 (m, 2H, 7-H; 8-H), 5.08 (d, *J* = 11.0 Hz, 1H, 11'-H), 5.29 (d, *J* = 17.8 Hz, 1H, 11-H), 6.52-6.78 (dd, *J* = 17.8 Hz, *J* = 11.0 Hz, 1H, 10-H) ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, HMQC, HMBC, C_6D_6): δ = 22.5 (C-2), 22.3 (C-1), 55.9 (C-13), 74.2 (C-6), 79.6 (C-3), 81.9 (C-8), 90.2 (C-7), 104.5 (C-9), 117.4 (C-11), 127.1 (C-5), 130.4 (C-10), 136.8 (C-4), 234.3 (C-12) ppm. – MS (EI) *m/z* (%): 328 (31) [M^+], 272 (12), 244 (92), 216 (26), 202 (82), 186 (82), 150 (11). – Anal ($C_{15}H_{16}O_5Cr$) Calcd. C 54.88, H 4.91; found: C: 54.81, H: 5.21.

5.8.3 [1,3-bis(2,4,6-trimethylphenyl)-2-imidazolinylidene]dichloro [(2-isopropoxyphenyl) methylene] tricarbonylchromium ruthenium (202)



202

205 (88 mg, 0.3 mmol) in dichloromethane (3 mL) was added dropwise *via* syringe to benzylidene complex **134** (250 mg, 0.3 mmol) and CuCl (30 mg, 0.3 mmol) in dichloromethane (5 mL). The mixture was heated at reflux for 1 h the reaction progress being monitored by TLC (R_f = 0.13, hexane/EtOAc 5:2). After solvent removal at reduced pressure the residue was dissolved in benzene (35 mL) and carefully filtered under argon through silica gel to remove residual **205**. Subsequent elution with hexane / TBME (2:1) gave 168 mg (0.2 mmol, 74 %) of **202** as an air stable dark red solid. M. p. >176 ^{o}C (dec).

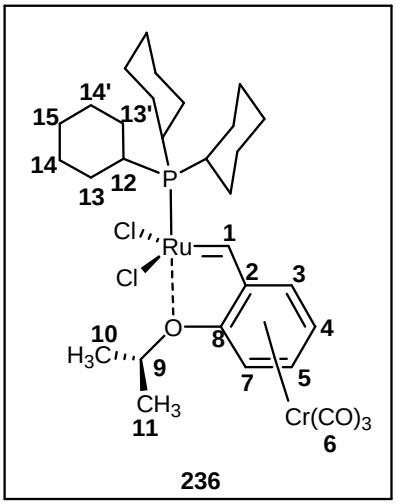
(**202**): IR (ATR): $\tilde{\nu}$ = 2925 (w) cm^{-1} 2847 (w), 2052 (w), 1963 (s, $Cr(CO)_3$), 1903 (s), 1867 (s), 1739 (w), 1605 (w), 1484 (w), 1448 (w), 1382 (w), 1296 (w), 1260 (s), 1208 (w), 1098 (w), 1016 (b), 928 (w), 854 (w), 822 (w), 674 (w), 661 (w), 620 (w). – ^{1}H NMR (400 MHz, C_6D_6): δ = 1.08 (d, J = 6.04 Hz, 3H, 11-H), 1.21 (d, J = 6.2 Hz, 3H, 10-H), 2.25 (s, 6H, 19-H), 2.54 (bs, 12H, 16-H), 3.36 (s, 4H, 13, 13'-H), 3.74 (t, J = 6.2 Hz, 1H, 4-H); 4.01 (sept, J = 6.2 Hz, 1H, 9-H); 4.10 (d, J = 6.9 Hz, 1H, 7-H); 4.68 (dt, J = 7.0 Hz, 1H, J = 1.2 Hz, 5-H); 4.97 (dd, J = 6.5 Hz, 1H, J = 1.2 Hz, 3-H); 6.88 (s, 2H, 17'-H); 7.00 (s, 2H, 17-H), 15.57 (s, 1H, 1-H) ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, HMQC, HMBC, HH-COSY, C_6D_6): δ = 17.9 (C-19), 21.1 (C-16), 21.4 (C-11), 21.6 (C-10), 51.2 (br, C-13; C-13'), 76.1 (C-7), 77.3 (C-9), 83.8 (C-4), 91.5 (C-3), 91.6 (C-5), 107.3 (C-2), 129.5 (C-18), 129.9 (C-17; C-17'), 135.5 (C-18), 137.2 (C-15), 138.4 (C-14), 138.6 (C-8), 210.7 (C-12), 233.0 (C-6), 283.5 (C-1) ppm. – ^{1}H NMR (500 MHz, CD_2Cl_2): δ = 1.14 (d, J = 6.04 Hz, 3H, 11-H), 1.26 (d, J = 6.2 Hz, 3H, 10-H), 2.37 (br, 18H, 16-H+19-H), 4.15 (s, 4H, 13-H, 13'-H), 4.62 (sept, J = 6.2 Hz, 1H, 9-H), 4.79 (t, J = 6.2 Hz, 1H, 4-H), 5.18 (dd, J = 6.45 Hz, J = 1.2 Hz, 1H, 3-H), 5.23 (d, J = 6.9 Hz, 1H, 7-H), 5.65 (t, J = 7.0 Hz, 1H, 5-H), 7.03 (br, 4H, 17-H+17'-H), 15.49 (s, 1H, 1-H). –

^{13}CNMR (125 MHz, CD_2Cl_2) : δ = 21.0 (br, C-16 + C-19), 21.4 (C-11), 21.4 (C-10), 51.5 (br, C-13, C-13'), 77.05 (C-7), 77.7 (C-9), 85.2 (C-4), 92.2 (C-3), 92.3 (C-5), 107.2 (C-2), 128.5 (C-18), 129.3 (br, C-17; C-17'), 136.8 (C-15), 138.6 (C-14), 138.7 (C-8), 208.8 (C-12), 232.7 (C-6), 285.4 (C-1). – HRMS (in CH_3CN) $C_{36}H_{41}ClCrN_3O_4Ru$ $[M\text{-}Cl + CH_3CN]^+$ Calcd. 768.1234. found: 768.1250.

Crystal Structure Analysis of **202**: Crystals were obtained by slow evaporation from hexane: TBME (2:1) at 25 °C under argon. Empirical formula $C_{34}H_{38}Cl_2CrN_2O_4Ru$, formula weight 762.63 g/mol, crystal system monoclinic, space group P 2_1/c (14), unit cell dimensions a = 9.996(4), b = 23.873(8), c = 15.218(6) Å, β = 99.64(5)°, V = 3580(2) Å^3, Z = 4, $d_{Calc.}$ = 1.415 g/cm^3, μ = 0.912 mm^{-1}, crystal size 0.33 x 0.07 x 0.07 m^3, STOE IPDS one-axis diffractometer with imaging plate detector, T = 298 K, $Mo_{K\alpha}$ radiation (λ = 0.71073 Å), θ_{max} = 26.19°, 51478 (6823) measured (unique) reflections, R(int) = 0.076, direct methods, full-matrix least-squares refinement on F^2 including all data (SHELXL-97), H atoms geometrically placed and allowed to ride on the respective C atoms, the trimethylphenyl group attached to N2 treated as two-fold positionally disordered rigid group, the methyl groups of all trimethylphenyl groups treated two-fold rotationally disordered, anisotropic displacement parameters for all non-H atoms with the exception of the C atoms of the disordered mesityl group for which isotropic displacement parameters were used, 348 (8) parameters (restraints) in final refinement, $R1$ = 0.040 ($I > 2\sigma_I$, 2595 reflections), w$R2$ = 0.064 (all reflections), largest peak (hole) in final difference electron density map 0.36 (–0.50) eÅ^{-3}.

One-Pot Synthesis of 202 from Grubbs I (133): At 25 °C 0.23 ml (0.39 mmol, 1.7 M in toluene) of potassium *tert*-amylate was added to 158 mg (0.4 mmol) of 1,3-dimesitylimidazolinium tetrafluoroborate in 7 ml of hexane and stirred for 1h. 300 mg (0.36 mmol) of Grubbs first **133** generation catalyst was added as a solid, and the reaction mixture was heated at reflux for 40 min being monitored by TLC (hexane/EtOAc 9:1). Thereafter the reaction mixture was cooled to 25 °C, and 37 mg (0.38 mmol) of CuCl and 113.3 mg (0.37 mmol) of **205** in 7 ml of dichloromethane were added. After stirring the reaction mixture at reflux for 1h, solvents were removed at reduced pressure and the residue purified as described previously. Yield 161 mg (0.21 mmol, 59%) of **202**.

5.8.4 [Tricyclohexylphosphine]dichloro[(2-isopropoxyphenyl)methylene] tricarbonylchromium ruthenium (236)

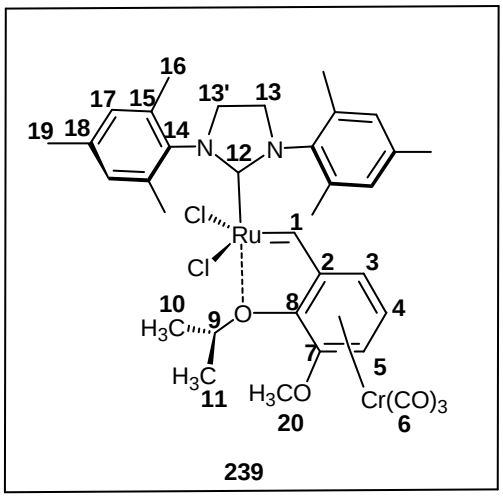


236

Tricarbonyl(2-isopropoxystyrene)chromium(0) (**205**) (145.0 mg, 0.49 mmol) in dichloromethane (6 mL) was added *via* syringe to benzylidene complex **133** (200 mg, 0.25 mmol) and CuCl (24.1 mg, 0.24 mmol) in dichloromethane (12 mL). The reaction mixture was heated at 40º C for 1 h the reaction progress being monitored by TLC (R_f = 0.13, hexane / TBME 15:1). After solvent removal at reduced pressure the residue was purified by column chromatography under argon leading to **236** as brown-red powder 85.6 mg, (0.112 mmol, 48 %).

(**236**): IR (ATR): $\tilde{\nu}$ = 2922 (w) cm $^{-1}$, 2849 (w), 1957 (s, ($Cr(CO)_3$), 1882 (s), 1518 (w), 1444 (w), 1261 (w), 1102 (w), 949 (w), 801 (w), 725 (w), 658 (w), 622 (w). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.7-2.24 (m, 33H, PCy_3; d, J = 6.0 Hz, 3H, 10-H; d, J = 6.0 Hz, 3H, 11-H), 4.90 (t, J = 6.1 Hz, 1H, 4-H), 5.02 (sept, J = 6.0 Hz, 1H, 9-H), 5.47 (d, J = 6.9 Hz, 1H, 7-H), 5.74 (dt, J = 6.9 Hz, J = 1.0 Hz, 1H, 5-H), 5.97 (dd, J = 6.5 Hz, J = 1.2 Hz, 1H, 3-H), 16.58 (d, J = 4.2 Hz, 1H, 1-H) ppm. – ^{13}C NMR (100.6 MHz, BB, DEPT, $CDCl_3$): δ = 21.9 (C-10), 22.7 (C-11), 26.2 (C-15), 27.6 (d, $^2J_{PC}$ = 12.3 Hz, C-13), 29.9 (d, $^1J_{PC}$ = 31.1 Hz, C-12), 35.6 (d, $^3J_{PC}$ = 25.6 Hz, C-14), 77.2 (C-7), 77.8 (C-9), 84.3 (C-4), 91.8 (C-3), 91.9 (C-5), 105.7 (C-2), 137.5 (C-8), 232.2 (C-6), 274.01 (C-1) ppm. – ^{31}P NMR ($CDCl_3$, 161 MHz): δ = + 64.1 ppm

5.8.5 [1,3-Bis(2,4,6-trimethylphenyl)-2-imidazolinylidene]dichloro[(2-isopropoxy-3-methoxyphenyl)methylene]tricarbonylchromium ruthenium (239)



239

Tricarbonyl(2-isopropoxy-3-metoxystyrene)chromium(0) (**238**) (38.6 mg, 0.12 mmol) in in dichloromethane (2 mL) was added *via* syringe to benzylidene complex **134** (100 mg, 0.1177 mmol) and CuCl (11.6 mg, 0.1177 mmol) in dichloromethane (5 mL). The reaction mixture was heated at 40 ºC for 1 h. After solvent removal at reduced pressure the residue was dissolved in benzene (10 mL) and carefully filtered under argon through silica gel to remove residual **238**. Subsequent elution with diethyl ether afforded 40.1 mg (0.05 mmol, 43 %) of **239** as purple solid. M. p. = 109-110 ºC.

IR (ATR): $\tilde{\nu}$ = 2924 (w) cm $^{-1}$, 2845 (w), 2363 (w), 2052 (w), 1955 (s, $Cr(CO)_3$), 1874 (s), 1479 (w), 1443 (w), 1262 (s), 1173 (w), 1099 (w), 887 (w), 851 (w), 806 (w), 674 (w), 657 (w). – ^{1}H NMR (400 MHz, C_6D_6): 1.35 (d, *J* = 6.0 Hz, 6H, 11-H, 10-H), 2.71 (br, 18H, 16-H, 19-H), 3.42 (sept, 1H, 9-H), 2.79 (s, 3H, 20-H), 3.68 (s, 4H, 13-H), 3.88 (t, 1H), 4.25 (d, 1H), 4.69 (d, 1H), 7.05 (s, 4H, 17-H), 15.72 (s, 1H, 1-H) ppm.

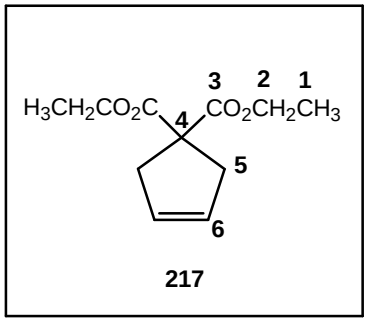
5.9 General procedures for alkene metathesis reactions catalyzed by 202

5.9.1 General Procedure for RCM and enyne metathesis (Entries 1-9, Table 3)

The solution of **202** in dichloromethane [0.00050 mmol (0.1%), 0.00500 mmol (1%) or 0.02500 mmol (5%)] is added to a solution of the substrate (0.5 mmol) (0.02 M) in dichloromethane at 0 °C or at 25 °C. The mixture is stirred at this temperature, and the reaction is monitored by TLC (hexane / ethyl acetate). After completed reaction cold vinyl ethyl ether (0.5 mL, 2 M in CH_2Cl_2) was added to the reaction mixture. The solvent is

removed at reduced pressure, and the product is isolated by column chromatography (SiO_2, hexane / ethyl acetate).

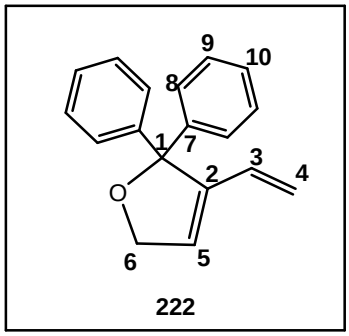
5.9.2 Cyclopenten-3-ene-1,1-dicarboxylic acid diethyl ester (217)[109]



217

(**217**): ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.23 (t, J = 7.1 Hz, 6H, 1-H), 2.98 (s, 4H, 5-H), 4.16 (q, 4H, J = 7.1 Hz, 2-H), 5.60 (s, 2H, 6-H) ppm. – ^{13}CNMR ($CDCl_3$, 50 MHz): δ = 13.9 (C-1), 40.8 (C-5), 58.8 (C-4), 61.6 (C-2), 127.8 (C-6), 172.1 (C-3) ppm.

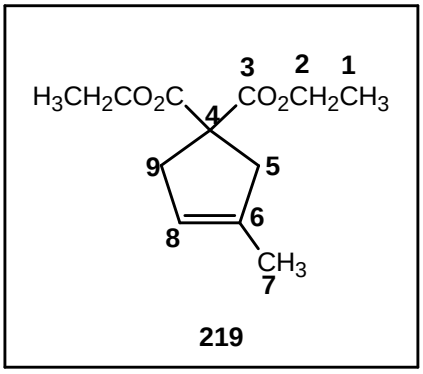
5.9.3 2,2-Diphenyl-3-vinyl-2,5-dihydrofuran (222)[109, 110a]



222

(**222**): ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 4.77 (s, 2H, 6-H), 5.09 (d, J = 11.2 Hz, 1H, 4-H_{cis}), 5.31 (d, J = 17.8 Hz, 1H, 4-H_{trans}), 6.16 (m, 1H, 5-H), 6.23 (dd, J = 17.8, J = 11.2 Hz, 1H, 3-H), 7.35-7.22 (m, 10H_{Ar}) ppm. – ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 73.2 (C-6), 94.5 (C-1), 117.5 (C-4), 124.9 (C-5), 127.4 (C-10), 127.9 (C-8), 129.8 (C-9), 142.2 (C-2), 143.3 (C-3), 143.7 (C-7) ppm.

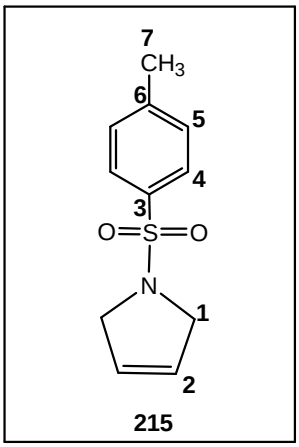
5.9.4 3-Methyl-cyclopent-3-en-1,1-dicarboxylic acid diethylester (219)[109]



219

(**219**): ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.21 (t, J = 7.1 Hz, 6H, 1-H), 1.72 (s, 3H, 7-H), 2.87 (m, 2H, 5-H), 2.93 (m, 2H, 9-H), 4.16 (q, J = 7.1 Hz, 4H, 2-H), 5.15 (s, 1H, 8-H) ppm. – ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.1(C-1), 16.2 (C-7), 40.8 (C-9), 44.5 (C-5), 59.4 (C-4), 61.4 (C-2), 121.2 (C-8), 137.4 (C-6), 172.4 (C-3) ppm.

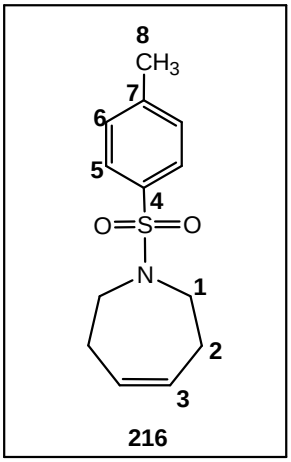
5.9.5 2,5-dihydro-1*H*-pyrrole-1-toluenesulfonate (215)[109]



215

(**215**): ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.41 (s, 3H, 7-H), 4.10 (s, 4H, 1-H), 5.63 (s, 2H, 2-H), 7.29 (d, 2H, 5-H), 7.70 (d, 2H, 4-H) ppm. – ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.9 (C-7), 55.2 (C-1), 125.8 (C-4), 127.8 (C-2), 130.1 (C-5), 134.7 (C-3), 143.8 (C-6) ppm.

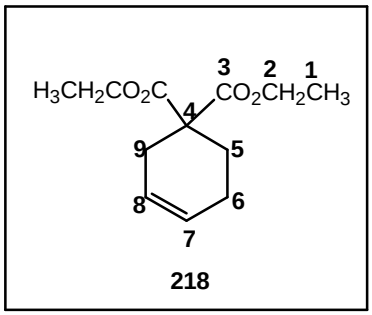
5.9.6 2,3,6,7--tetrahydro-1*H*-azepine-1-toluenesulfonate (216)[109]



216

(**216**): ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.28 (m, 4H, 2-H), 2.39 (s, 3H, 8-H), 3.25 (m, 4H, 1-H), 5.72 (m, 2H, 3-H), 7.25 (d, 2H, J = 8.2 Hz, 6-H), 7.64 (d, 2H, J = 8.2 Hz, 5-H) ppm. – ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.5 (C-8), 29.9 (C-2), 48.2 (C-1), 126.9 (C-5), 129.5 (C-3), 130.1 (C-6), 136.2 (C-4), 142.9 (C-7) ppm.

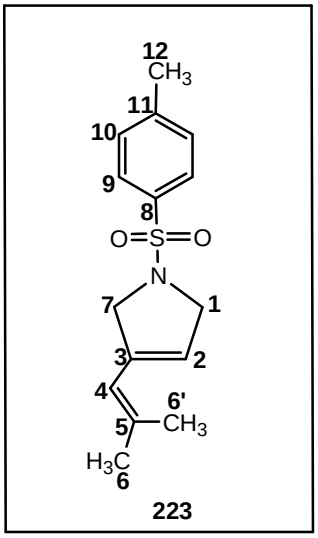
5.9.7 Cyclohex-3-ene-1,1-dicarboxylic acid diethylester (218)[66]



218

(**218**): ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.22 (t, J = 7.1 Hz, 6H, 1-H), 2.05 (m, 2H, 6-H), 2.15 (m, 2H, 5-H), 2.45 (m, 2H, 9-H), 4.15 (q, J = 7.1 Hz, 4H, 2-H), 5.65 (s, 2H, 7-H, 8-H) ppm. – ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 13.9 (C-1), 22.4 (C-6), 27.4 (C-9), 30.4 (C-5), 52.9 (C-4), 61.3 (C-2), 124.1 (C-7), 126.1 (C-8), 171.5 (C-3) ppm.

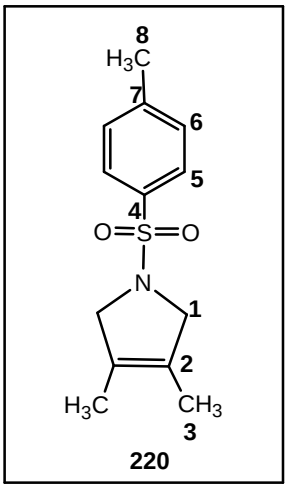
5.9.8 3-(2-methyl-1-propenyl)-2,5-dihydro-1*H*-pyrrole-1-toluenesulfonate (223)[110a, 84]



223

(**223**): ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.74 (d, J = 6.4 Hz, 6H, 6-H), 2.41 (s, 3H, 12-H), 4.12 (bs, 2H, 1-H), 4.22 (d, J = 3.3 Hz, 2H, 7-H), 5.37 (bs, 1H, 2-H), 5.60 (bs, 1H, 4-H), 7.31 (d, J = 7.9 Hz, 2H, 10-H), 7.71 (d, J = 8.2 Hz, 2H, 9-H) ppm. – ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 19.9 (C-6'), 21.6 (C-12), 27.3 (C-6), 54.5 (C-1), 56.3 (C-7), 117.2 (C-2), 120.8 (C-4), 127.4 (C-9), 129.7 (C-10), 136.2 (C-5), 137.8 (C-8), 143.3, (C-11) ppm.

5.9.9 3,4-dimethyl-2,5-dihydro-1*H*-pyrrole-1-toluenesulfonate (220)[109]



220

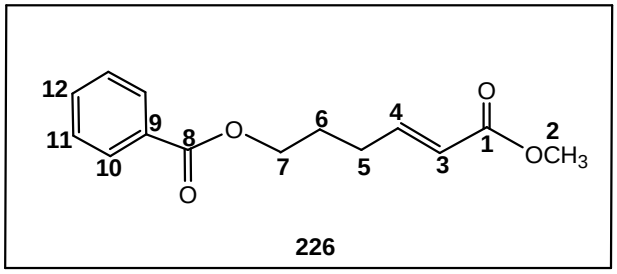
(**220**): ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.53 (s, 6H, 3-H), 2.42 (s, 3H, 8-H), 3.96 (s, 4H, 1-H), 7.31 (d, J = 8.1 Hz, 2H, 6-H), 7.71 (d, J = 8.1 Hz, 2H, 5-H) ppm. – ^{13}CNMR ($CDCl_3$, 50 MHz): δ = 11.1 (C-3), 21.5 (C-8), 58.8 (C-1), 126.2 (C-2), 127.5 (C-5), 129.7 (C-6), 134.3 (C-4), 143.2 (C-7) ppm.

5.9.10 Cross-metathesis and homo-metathesis

General Procedure for CM (Entries 1-8, Table 4)

202 in dichloromethane [(0.00500 mmol (1%), 0.0125 mmol (2.5%) or 0.02500 mmol (5%)] is added to the substrate (0.5 mmol) (0.125 M or 0.2 M) at 25 °C. The mixture is stirred at this temperature or at 40 °C, and the reaction is monitored by TLC (hexane / ethyl acetate). After completed reaction cold vinyl ethyl ether (0.5 mL, 1 M in CH_2Cl_2 is added. The solvent is removed at reduced pressure, and the product is isolated by column chromatography (SiO_2, hexane / ethyl acetate).

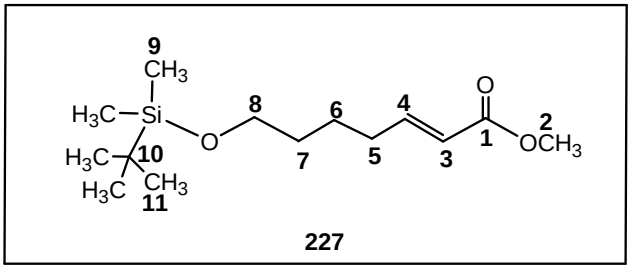
5.9.11 (*E*)-5-methoxycarbonyl-pent-4-enyl-benzoate (226)[66]



226

(**226**): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.94 (dt, *J* = 6.6 Hz, 2H, 6-H), 2.38 (q, *J* = 7.1 Hz, 2H, 5-H), 3.71 (s, 3H, 2-H), 4.94 (t, *J* = 6.0 Hz, 2H, 7-H), 5.88 (dt, *J* = 16.0 Hz, 1H, 3-H), 7.00 (dt, *J* = 16.7 Hz, 1H, 4-H), 7.43 (t, *J* = 7.0 Hz, 2H, 11-H), 8.03 (d, *J* = 7.0 Hz, 2H, 10-H), 7.55 (t, *J* = 7.0 Hz, 1H, 12-H) ppm. – ^{13}C NMR ($CDCl_3$, 100.6 Hz): δ = 27.2 (C-5), 28.9 (C-6), 51.5 (C-2), 64.0 (C-7), 121.7 (C-3), 128.4 (C-11), 129.6 (C-10), 130.2 (C-9), 133.1 (C-12), 147.8 (C-4), 166.5 (C-1), 166.9 (C-8) ppm.

5.9.12 Methyl-7-[1-(*tert*-butyl)-1,1-dimethyl-silyl]oxy-2-heptenoate (227)[109]

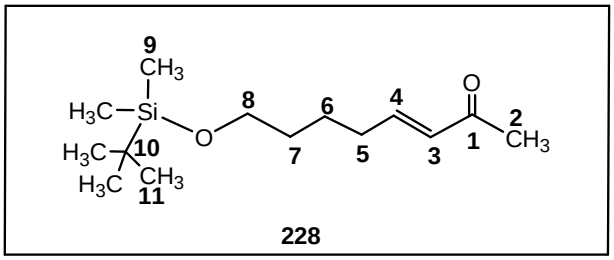


227

(**227**): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.03 (s, 6H, 9-H), 0.88 (s, 9H, 11-H), 1.46-1.57 (m, 4H, 6-H, 7-H), 2.17-2.25 (m, 2H, 5-H), 3.61 (t, *J* = 5.9 Hz, 2H, 8-H), 3.71 (s, 3H, 2-H), 5.81

(dt, *J* = 15.7 Hz, 1.6 Hz, 1H, 3-H), 6.96 (dt, *J* = 15.7 Hz, 7.0 Hz, 1H, 4-H) ppm. – ^{13}C NMR ($CDCl_3$, 100.6 Hz): δ = – 5.3 (C-9), 18.3 (C-10), 24.4 (C-11), 25.9 (C-6), 31.9 (C-5), 32.2 (C-7), 51.3 (C-2), 62.7 (C-8), 121.1 (C-3), 149.6 (C-4), 167.2 (C-1) ppm.

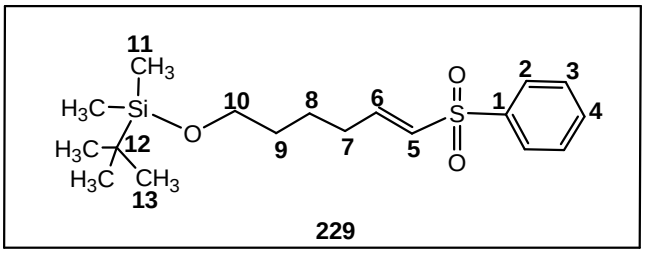
5.9.13 8-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-3-*E*-octen-2-one (228)[109]



228

(**228**): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.04 (s, 6H, 9-H), 0.88 (s, 9H, 11-H), 1.50 (m, 4H, 6-H, 7-H), 2.22 (s, 3H, 2-H), 2.21 (m, 2H, 5-H), 3.58 (m, 2H, 8-H), 6.07 (dt, *J* = 15.9 Hz, 1.4 Hz, 1H, 3-H), 6.79 (dt, *J* = 15.9 Hz, 6.9 Hz, 1H, 4-H) ppm. – ^{13}C NMR ($CDCl_3$, 100.6 Hz): δ = – 5.3 (C-9), 18.3 (C-10), 24.6 (C-11), 25.9 (C-6), 26.8 (C-2), 32.1 (C-5), 32.3 (C-7), 62.9 (C-8), 131.4 (C-3), 148.2 (C-4), 198.6 (C-1) ppm.

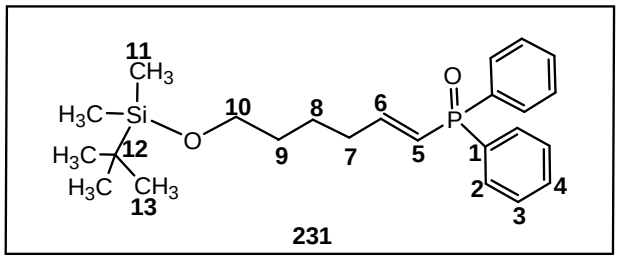
5.9.14 (*E*)-6-[1-(*tert*-butyl)-1,1-dimethylsilyl]-oxy-1-hexenyl phenyl sulfone (229)[109]



229

(**229**): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.03 (s, 6H, 11-H), 0.88 (s, 9H, 13-H), 1.40-1.60 (m, 4H, 8-H, 9-H), 2.20 (m, 2H, 7-H), 3.53 (m, 2H, 10-H), 6.32 (dt, *J* = 15.1 Hz, 1.5 Hz, 1H, 5-H), 7.00 (dt, *J* = 15.1 Hz, 6.8 Hz, 1H, 6-H), 7.47-7.93 (m, 5H$_{Ar}$) ppm. – ^{13}C NMR ($CDCl_3$, 100.6 Hz): δ = –5.4 (C-11), 18.3 (C-12), 24.1 (C-13), 25.9 (C-8), 31.2 (C-7), 32.0 (C-9), 62.5 (C-10), 127.5 (C-2), 127.7 (C-3), 129.2 (C-4), 130.4 (C-1), 133.2 (C-5), 140.7 (C-6) ppm.

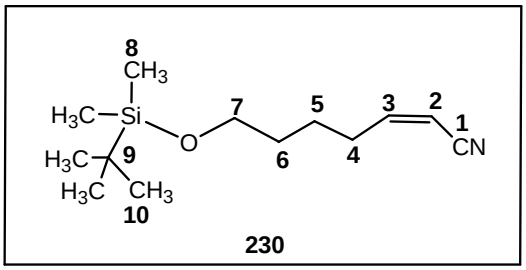
5.9.15 (*E*)-6-[1-(*tert*-butyl)-1,1-dimethylsilyl]-oxy-1-hexenyl(diphenyl)phosphine oxide (231)[83]



231

(**231**): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.01 (s, 6H, 11-H), 0.86 (s, 9H, 13-H), 1.51 (m, 4H, 8-H, 9-H), 2.34 (m, 2H, 7-H), 3.59 (m, 2H, 10-H), 6.22 (ddt, *J* = 24.5 Hz, 17.0 Hz, 1.5 Hz, 1H, 5-H), 6.71 (ddt, *J* = 19.5 Hz, 17.0 Hz, 6.5 Hz, 1H, 6-H), 7.40-7.61 (m, 6H$_{Ar}$), 7.64-7.71 (m, 4H$_{Ar}$) ppm – ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = – 5.4 (C-11), 18.3 (C-12), 24.3 (d, *J* = 1.2 Hz, C-8), 25.9 (C-13), 32.1 (C-9), 34.1 (d, *J* = 16.9 Hz, C-7), 62.7 (C-10), 122.3 (d, *J* = 103.3 Hz, C-1), 128.4 (d, *J* = 12.1 Hz, C-3), 131.2 (d, *J* = 9.8 Hz, C-2), 131.5 (d, *J* = 2.6 Hz, C-4), 133.0 (d, *J* = 105.0 Hz, C-5), 152.5 (d, *J* = 1.9 Hz, C-6) ppm. – ^{31}P NMR ($CDCl_3$, 162 MHz): δ = + 24.9 ppm.

5.9.16 7-*tert*-butyl-dimethylsiloxy-hept-2-enenitrile (230)[109]



230

(**230**): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.04 (s, 6H, 8-H), 0.88 (s, 9H, 10-H), 1.54 (m, 4H, 5-H, 6-H), 2.43 (q, *J* = 7.5 Hz, 2H, 4-H), 3.60 (t, *J* = 5.8 Hz, 2H, 7-H), 5.32 (d, *J* = 10.9 Hz, 1H, 2-H), 6.46 (dt, *J* = 10.9 Hz, 1H, 3-H) ppm. – ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = –5.4 (C-8), 18.3 (C-9), 24.7 (C-5), 25.9 (C-10), 31.6 (C-4), 32.1 (C-6), 62.5 (C-7), 99.6 (C-2), 116.0 (C-1), 155.0 (C-3) ppm.

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Lebenslauf

n Persönliche Daten

Vorname/Name	Nikolai Vinokurov
Geburtstag-/ort	10.03.1980 in Krasnodar, Russland
Familienstand	ledig

n Schulische Ausbildung

1987 – 1997	Schule № 82, Krasnodar

n Hochschulausbildung

09.1997 - 06.2002	Chemie (Diplom) Kuban State University (KubSU), Krasnodar Diplomarbeit (ausgezeichnet) Thema: „Untersuchungen zu Umsetzungen Organoaminosilanen mit 1 – Alkinen in Gegenwart von $ZnCl_2$. Eine neue Methode zur Herstellung der silylierten Akinen.”
10.2002 - 07.2003	Wissenschaftlicher Mitarbeiter am Institut für Organische Chemie, KubSU Thema: „Die direkte Germylierung von 1 - Alkinen mit Germaniumtetrachlorid und Organogermylaminen in Gegenwart von $ZnCl_2$.” AK Prof. A.A. Andreev.

n Promotion

06. 2003	Verleihung eines Promotionsstipendiums von der Gottlieb Daimler- und Karl Benz Stiftung

09. 2003-07.2007	Anfertigung der Dissertation unter der Anleitung von Herrn Prof. Dr. Holger Butenschön Thema: "Synthese von *P* - chiralen zweizähnigen Diphosphanliganden für die Asymmetrische Katalyse." am Institut für Organische Chemie, Leibniz Universität Hannover Note: "Mit Auszeichnung" (summa cum laude)
06.2005-12.2007	wissenschaftlicher Mitarbeiter im Rahmen eines von der Deutschen Forschungsgemeinschaft geförderten Projektes. Thema: "*P* - chirale Diphosphinoethan-Liganden für die Asymmetrische Katalyse." Projektnummer: BU 814/12-1

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1. N. Vinokurov, A. Michrowska, A. Szmigielska, Z. Drzazga, G. Wójciuk, O. Demchuk, K. Grela, K. M. Pietrusiewicz, H. Butenschön, "**Homo and Cross-Olefin Metathesis Coupling of Vinylphosphane Oxides and Electron Poor Alkenes: Access to *P*-Stereogenic Dienophiles"**, *Adv. Synth. Catal*. **2006,** 348**,** 931-938**.**
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n Stipendien/Preise

1.09.2003-28.02.2005	Promotionsstipendium - Stipendiat der Gottlieb Daimler- und Karl Benz Stiftung. Projektnummer: 02-07/03.
Posterpreis	"Synthesis of *P*-Chiral Bidentate Phosphorus Ligands via Olefin Cross - Metathesis" JCF-Frühjahrsymposium, 3. April 2004, Heidelberg
Roche Grant	Roche Continents Youth! Arts! Science! 5 - 11 August 2007, Salzburg