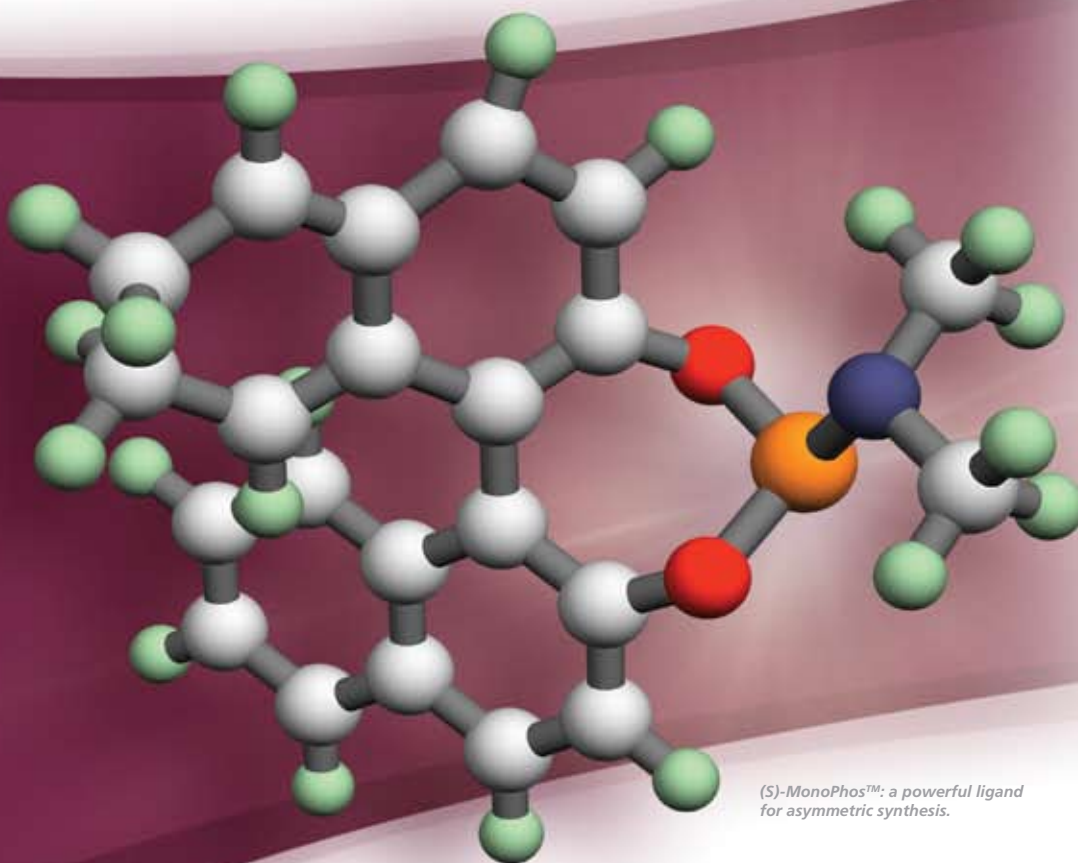


Privileged Ligands



*(S)-MonoPhos™; a powerful ligand
for asymmetric synthesis.*

DUPHOS AND BPE
PHOSPHOLANE
LIGANDS

DSM MONOPHOS™
FAMILY

CHIRALQUEST
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FERROCENYL-BASED
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Introduction

Chemists are continually searching for novel, efficient chiral transition metal catalysts to effect ever more difficult transformations. Highly effective asymmetric catalytic systems offer the possibility of synthesizing either desired enantiomer pure from simple achiral starting materials, with the chiral products then being directly employed in natural product synthesis.¹ Research groups have spent much well-earned effort in designing high performance ligand platforms² that exhibit the following general characteristics: 1) the synthesis should be economically viable and allow for systematic variations in the architecture; 2) most (if not all) members of the ligand family should be readily produced from milligram to kilogram scale; and 3) the ligands should bind strongly to the metal center as well as generate a highly active and selective catalyst system.

Chiral salens,³ bisoxazolines,⁴ tartrate ligands,⁵ and cinchona alkaloids⁶ represent the original "privileged ligands" classes that effect a wide variety of transformations under exceptional enantiocontrol and with high productivity. Impressively, R&D groups have met the challenges and requirements stated above in the design of second-generation "privileged ligands" such as the DuPhos phospholanes,⁷ DSM phosphoramidites,⁸ Solvias Josiphos families,⁹ and ChiralQuest phosphines.¹⁰ These outstanding ligand families have proven their success in industrially useful reaction paradigms such as hydrogenation and hydroformylation, and gained much attention from the synthetic community due to the ready accessibility and modular nature of the design.

Sigma-Aldrich is committed to providing unprecedented accessibility to chiral, state-of-the-art "privileged ligands" used in a wide breadth of C–H, C–C, C–N, and C–O bond-forming transformations. For a complete listing of products related to catalysis, please visit sigma-aldrich.com/catalysis. If you cannot find a product related to your specific research efforts, we welcome your inquiries at amaestri@sial.com and look forward to accelerating your success.

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About Our Cover

The cover image depicts the X-ray structure of the (S)-MonoPhos™ ligand. This ligand fuels highly enantioselective hydrogenation reactions when utilized in combination with Rh(I) pre-catalysts. Note that the base MonoPhos™ ligands can be readily tuned by substituting at nitrogen or via transformations of the BINOL backbone to efficiently mediate other asymmetric processes.

ChemFiles

Vol. 6 No. 8

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DuPhos and BPE Phospholane Ligands

Introduction

Asymmetric hydrogenation reactions represent the ideal process for the commercial manufacture of single-enantiomer compounds, because of the ease by which these robust procedures can be scaled up and because of the low levels of byproducts generated in these asymmetric processes. The most effective hydrogenation systems rely on modifications of the electronic and steric properties of the ligands. Burk and co-workers succeeded in developing a highly effective chiral phospholane class of ligands called DuPhos and BPE that contain 2,5-disubstituted groups allowing for systematic variation of the steric environment around the metal.¹¹ Sigma-Aldrich, in collaboration with Kanata Chemical Technologies, is pleased to now offer a diverse array of DuPhos and BPE phospholane ligands that can be ligated to metal complexes to afford highly active catalysts for asymmetric hydrogenation and other innovative transformations.¹²

The large-scale capacity of these robust catalysts is observed in the efficiency (substrate-to-catalyst (S/C) ratios up to 50,000) and the high activities (TOF > 5000 h⁻¹) in a myriad of enamide and ketone reductions. Under optimized conditions, a (*R,R*)-Me-BPE-Rh complex reduced *N*-acetyl α -arylenamides in >95% ee to yield valuable α -1-arylethylamines (Scheme 1).¹³ It should be noted that Me-DuPhos-Rh complexes were equally effective in asymmetric reductions of prochiral enamides. The general utility of these phospholane ligands is illustrated in the incredible diversity-oriented production of a vast array of chiral compounds (Scheme 2).

Advantages of the DuPhos and BPE Ligands

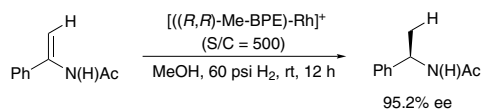
- Superior enantiocontrol in a vast array of catalytic transformations
- High activities at low catalyst loadings
- Exceptional chemoselectivities for specific reaction paradigms
- Asymmetric hydrogenations of numerous unsaturated substrates
- First-to-market exclusivity for selected portfolio ligands
- Screening kit to facilitate tuning selectivities (Fall 2006)

Representative Applications

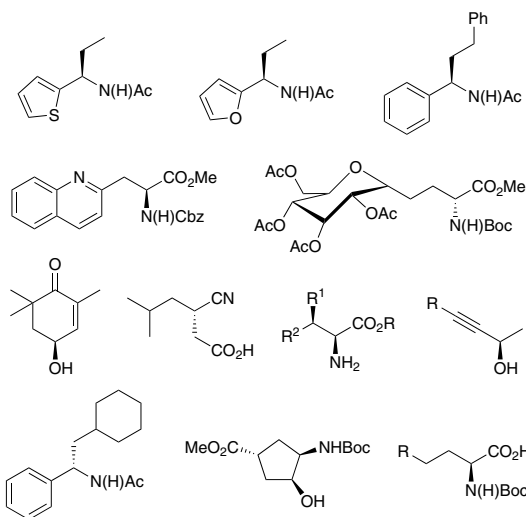
The reactivity profile of these innovative, chiral ligands is covered below and highlights the impressive breadth of valuable transformations mediated by the various portfolio products. In many documented cases, specific ligands have displayed unprecedented selectivities in reactions that form, for instance, chiral centers in heteroatom-functionalized organic building blocks for drug synthesis.

Asymmetric Hydrogenation of the C=N Group

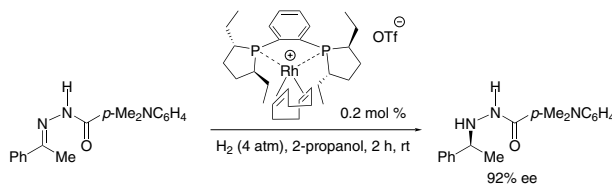
Burk and co-workers exploited the high activity of the Ethyl-DuPhos ligand via a powerful catalytic reductive amination process.¹⁴ The procedure exhibits general applicability in the reduction of a wide variety of *N*-arylhydrazones, yielding enantioselectivities for most substrates >90% (Scheme 3). Additionally, this Et-DuPhos-Rh catalyzed system displays exceptionally high chemoselectivities, yielding little or no reduction of unfunctionalized alkenes, alkynes, ketones, aldehydes, and imines in competition experiments. The synthetic utility of these asymmetric hydrazone reductions is enhanced by their facile reaction at ambient temperature with samarium diiodide to afford the corresponding chiral amines, which proceeds with no observable loss of optical purity.



Scheme 1



Scheme 2



Scheme 3

Monthly Chemistry E-Newsletter

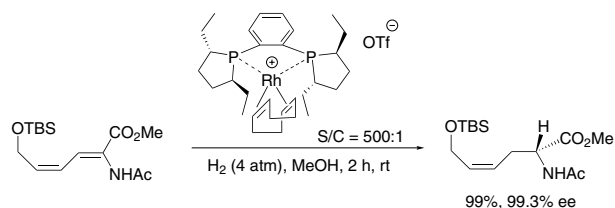
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Catalytic Hydrogenation of Enamides

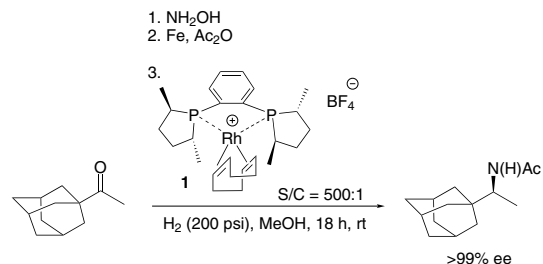
Burk also pioneered the asymmetric hydrogenation of various enamido olefins affording highly enantiopure δ,γ -unsaturated amino acid products.¹⁵ The (*S,S*)-Et-DuPhos-Rh catalyst system controls the reactivity of conjugated substrates with high regioselectivities as well. Under the standard hydrogenation conditions (S/C = 500, H₂ pressures ranging from 60 to 90 psi, and 0.5–3 h), this catalyst gave less than 2% overreduction with all products isolated in better than 95% yield. The authors elaborated upon this outstanding catalyst reactivity by demonstrating a concise and highly selective synthesis of the natural product (–)-bulgocinine, preceeded by formation of the key chiral intermediate in 99% yield with 99.3% ee (**Scheme 4**).



Scheme 4

Highly Asymmetric Reductive Amidation

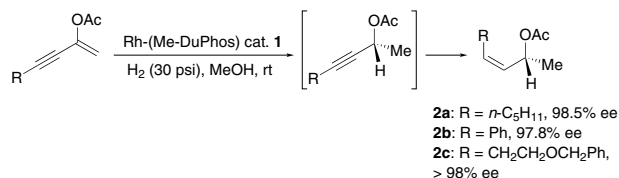
Burk and co-workers have also illustrated a rapid three-step process for reductive amidation, converting various ketones to the respective chiral amines with high enantioselectivity.¹⁶ Note that the transformation shown involves reacting the ketone with hydroxylamine followed by subsequent reduction with iron metal. This methodology benefits from the utilization of crude enamides isolated as crystalline solids in the direct asymmetric catalytic hydrogenation without prior purification. The conversion of 1-acetyladamantane to the novel amine compound occurs with >99% ee and in high yield via use of cationic Rh(I) catalyst **1** (**Scheme 5**).



Scheme 5

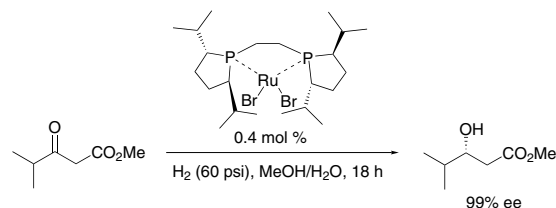
Preparation of Chiral Organics with C–O Stereogenic Centers

Neil Boaz utilized rhodium(I)-(*R,R*)-Me-DuPhos catalyst **1** to produce chiral alcohols via the asymmetric hydrogenation of enol esters (**Scheme 6**). Allylic alcohol derivatives are desirable organic building blocks in diversity-oriented synthesis, because the olefin can be further functionalized after the stereochemistry has been set in the hydrogenation.¹⁷ Under asymmetric hydrogenation conditions, the initially formed propargylic acetate was subsequently reduced to yield the *Z*-allylic acetate. Impressively, the enantioselectivity observed in this reaction was very high among the general substrate class **2a-c**.



Scheme 6

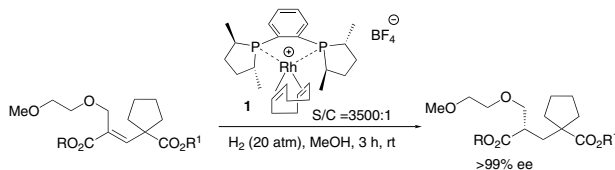
Burk and co-workers have also designed highly effective catalysts for the asymmetric reduction of C=O bonds under hydrogenation conditions.¹⁸ In the case shown, the methodology proceeded via use of a chiral [Ru(II)Br₂-(*i*-Pr-BPE)] complex, which was prepared by reacting [(cod)Ru(2-methylallyl)₂] with the BPE ligand followed by treatment with methanolic HBr. A variety of esters were rapidly hydrogenated as mediated by this catalyst to the hydroxyl esters with very high enantioselectivities (>98%) ee for the alkyl-substituted substrates (**Scheme 7**).



Scheme 7

Preparation of Chiral Organics with C–C Stereogenic Centers

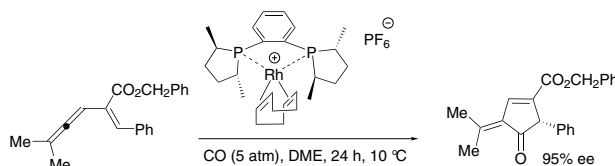
As a complement to the C–O bond-forming asymmetric synthesis, Burk and co-workers have performed highly enantioselective hydrogenations of unique substrates that are precursors to natural products. This methodology is highlighted by enantioselectivities approaching 100% and high efficiencies (S/C > 2500), and has allowed this research team to surmount the problems associated with the asymmetric synthesis of the drug Candoxitil (**Scheme 8**).¹⁹



Scheme 8

Novel Asymmetric [4+1] Cycloadditions

These highly practical enantioselective reactions have been accomplished by the Murkami research group, thus expanding the synthetic utility of these powerful chiral ligands.²⁰ The [4+1] cycloaddition between vinylallenes and carbon monoxide affords complex cyclopentenone derivatives in a single step and with enantiopurities up to 95% (**Scheme 9**).



Scheme 9

Palladium-Catalyzed Asymmetric Phosphination

Glueck and co-workers have successfully developed a catalytic asymmetric phosphination reaction utilized in the production of P-chirogenic phosphines (**Scheme 10**).²¹ The fast conversions, moderate catalyst loadings, and superb enantioselectivities allow for the expeditious construction of enantioenriched phosphine building blocks. Metal-catalyzed routes to these valuable P-chiral ligands are rare making this methodology attractive as a viable route to synthesize other phosphine ligands.

Catalytic Asymmetric Alkylation of *N*-Diphenylphosphinoylimines

Recently Charette has published a facile asymmetric synthesis of various α -chiral amines via the enantioselective addition of dialkylzinc reagents to *N*-phosphinoylimines.²² (*R,R*)-Me-DuPhos, in conjunction with a Cu(OTf)₂ source, yielded exceptional enantiomeric excess for this reaction above 90% for all aromatic substrates (**Scheme 11**). The mild reaction conditions, reasonable temperatures, and use of various dialkylzinc reagents all contribute to the attractiveness of this methodology.

Enantioselective Hydrogenation of Alkenes and Imines

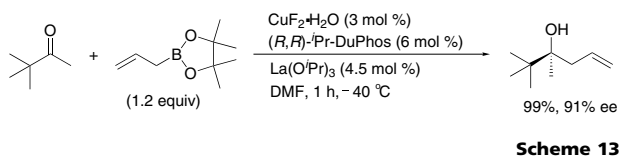
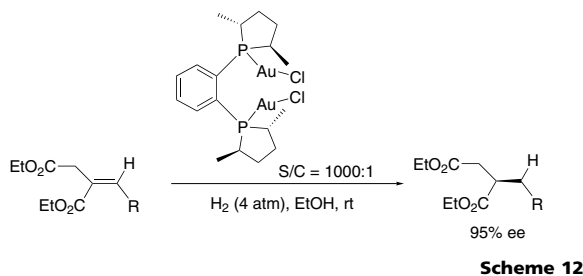
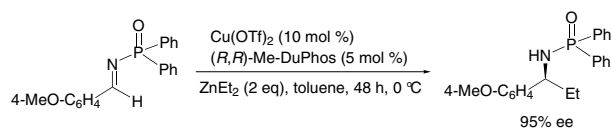
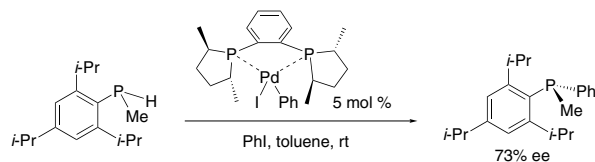
The use of gold complexes to effect catalytic transformations is on the rise, with numerous reports of catalytically active gold species.²³ Sanchez and co-workers have now reported the first example of a gold hydrogenation catalyst utilized in asymmetric transformations.²⁴ The authors found that the bulkiest substrate, which incorporates a diethyl 2-naphthylidene succinate group, proceeds under the reaction conditions to afford the highest enantioselectivities due to reactant control (**Scheme 12**). Future plans in gold-mediated asymmetric hydrogenation involve substantial modifications to the ligand structure to provide higher levels of enantiocontrol.

The First Catalytic Enantioselective Allylboration of Ketones

The Shibasaki research group has also championed use of the DuPhos ligand system for asymmetric catalysis.²⁵ They have now reported the first general catalytic, enantioselective allylation reaction with ketones, which employs copper salts and a rare-earth lanthanide additive. Impressively, a diverse array of aromatic, heteroaromatic, α,β -unsaturated, and aliphatic ketones are rapidly allylated at ambient temperature and under low catalyst loadings (**Scheme 13**). The enantioselectivities range from 67 to 92%, however, the reaction appears to be quite general for both the allylation and crotylboration reactions.

Conclusion

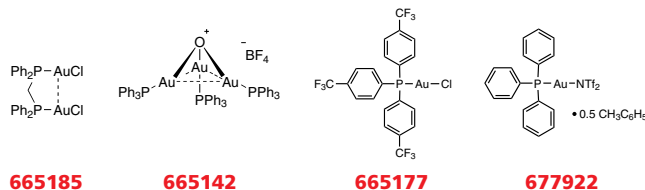
The modular nature of these chiral phospholane ligands has allowed variation of the electronics and sterics around the metal upon complexation. These bidentate ligands perform highly enantioselective reactions to produce a wide array of compounds containing C–C, C–O, and C–N stereogenic centers. Sigma-Aldrich is your dedicated source for a broad spectrum of chiral building blocks that provide essential starting materials in the synthesis of complex organic molecules. Our growing portfolio of catalysis products, supplemented by the DuPhos/BPE family, strongly complements the existing Sigma-Aldrich chemical line and will accelerate your research success. For comprehensive information on our most recent product launches, please visit sigma-aldrich.com/duphos.



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(1)(a) Gorin, D. J. et al. *J. Am. Chem. Soc.* **2005**, *127*, 11260. (b) Kennedy-Smith et al. *J. Am. Chem. Soc.* **2004**, *126*, 4526. (c) Mézailles, N. et al. *Org. Lett.* **2005**, *7*, 4133.

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(+)-1,2-Bis[(2*S*,5*S*)-2,5-dimethylphospholano]benzene NEW

$C_{18}H_{28}P_2$
FW: 306.36
[136735-95-0]



665266-100MG	100 mg
665266-500MG	500 mg
665266-2G	2 g

(-)-1,2-Bis[(2*R*,5*R*)-2,5-dimethylphospholano]benzene NEW

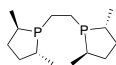
$C_{18}H_{28}P_2$
FW: 306.36
[147253-67-6]



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665258-500MG	500 mg
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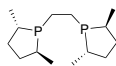
$C_{14}H_{24}P_2$
FW: 258.32
[129648-07-3]



665231-100MG	100 mg
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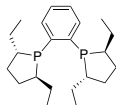
$C_{14}H_{24}P_2$
FW: 258.32
[136779-26-5]



665207-100MG	100 mg
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665207-2G	2 g

(+)-1,2-Bis[(2*S*,5*S*)-2,5-diethylphospholano]benzene NEW

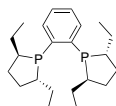
$C_{22}H_{36}P_2$
FW: 362.47
[136779-28-7]



668486-100MG	100 mg
668486-500MG	500 mg
668486-2G	2 g

(-)-1,2-Bis[(2*R*,5*R*)-2,5-diethylphospholano]benzene NEW

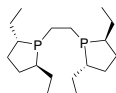
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FW: 362.47
[136705-64-1]



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668494-2G	2 g

(-)-1,2-Bis[(2*S*,5*S*)-2,5-diethylphospholano]ethane NEW

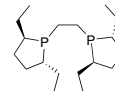
$C_{18}H_{36}P_2$
FW: 314.43
[136779-27-6]



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(+)-1,2-Bis[(2*R*,5*R*)-2,5-diethylphospholano]ethane NEW

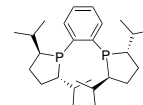
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FW: 314.43
[136705-62-9]



668478-100MG	100 mg
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(-)-1,2-Bis[(2*S*,5*S*)-2,5-diisopropylphospholano]benzene NEW

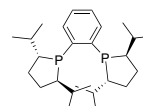
$C_{26}H_{44}P_2$
FW: 418.57
[147253698]



668176-100MG	100 mg
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668176-2G	2 g

(+)-1,2-Bis[(2*R*,5*R*)-2,5-diisopropylphospholano]benzene NEW

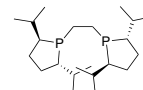
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FW: 418.57
[136705652]



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668524-2G	2 g

1,2-Bis[(2*S*,5*S*)-2,5-diisopropylphospholano]ethane NEW

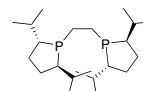
$C_{22}H_{44}P_2$
FW: 370.53



668435-100MG	100 mg
668435-500MG	500 mg
668435-2G	2 g

1,2-Bis[(2*R*,5*R*)-2,5-diisopropylphospholano]ethane NEW

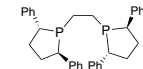
$C_{22}H_{44}P_2$
FW: 370.53



668443-100MG	100 mg
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668443-2G	2 g

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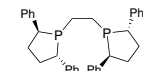
$C_{34}H_{36}P_2$
FW: 258.32
[528565799]



667811-100MG	100 mg
667811-500MG	500 mg
667811-2G	2 g

(+)-1,2-Bis[(2*S*,5*S*)-2,5-diphenylphospholano]ethane NEW

$C_{34}H_{36}P_2$
FW: 258.32
[824395677]



667854-100MG	100 mg
667854-500MG	500 mg
667854-2G	2 g

DSM MonoPhos™ Family

Introduction

Sigma-Aldrich, in collaboration with DSM, is pleased to offer a range of MonoPhos™ ligands for the research market.[†] Feringa and co-workers have invented a diverse array of these chiral, monodentate phosphoramidites based on the privileged BINOL platform.²⁶ The MonoPhos™ family has exhibited high levels of enantiocontrol in synthetic transformations ranging from metal-catalyzed asymmetric 1,4-additions of organometallic reagents to allylic alkylations to desymmetrization of *meso*-cycloalkene oxides.²⁷

Advantages of the MonoPhos™ Ligands

- Superior enantiocontrol in numerous transformations
- High activities at low catalyst loadings
- Hydrogenations under low-pressure conditions
- Applied in tandem reactions to yield valuable chiral organics
- First-to-market exclusivity for selected portfolio ligands

Representative Applications

The reactivity profile of these innovative chiral ligands is covered below and highlights the impressive breadth of valuable transformations mediated by the various portfolio products. In many documented cases, specific ligands have displayed unprecedented selectivities in reactions that form, for instance, chiral quaternary centers that cannot be readily generated via alternative methodologies.

Asymmetric 1,4-additions of Organometallic Reagents

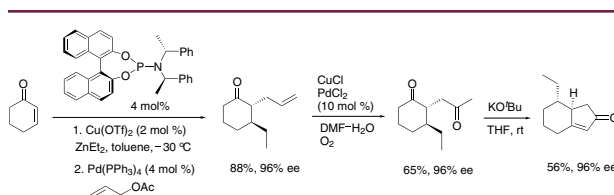
Feringa and co-workers exploited the high activity of the (*S,R,R*)-phosphoramidite ligand shown in **Scheme 14** in copper-catalyzed 1,4-additions of organozinc reagents to cyclohexenones.²⁶ Interestingly, the *in situ* formed zinc species originating from the cyclohexenone is readily trapped via a palladium-catalyzed allylation. The Feringa group then completed a formal annulation process through a palladium-catalyzed Wacker oxidation, followed by an aldol cyclization. The high (96%) enantioselectivity of this methodology is completely retained throughout this synthetic strategy (**Scheme 14**).

High potential also exists for the use of organoaluminum reagents in asymmetric conjugate addition reactions, because of their commercial availability and proof of concept in carboalumination reactions. Woodward and co-workers have now pioneered the enantioselective phosphoramidite-catalyzed 1,4-additions of organoaluminum reagents to enones.²⁸ This methodology provides facile access to chiral ketones with excellent enantioselectivities and in good yields (**Scheme 15**).

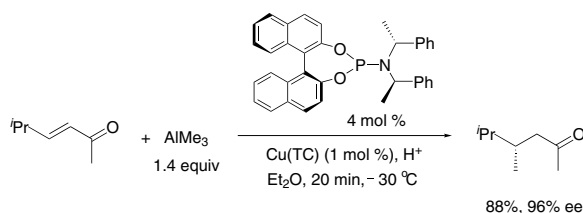
Highly Asymmetric Rhodium-Catalyzed Hydrogenation

Feringa has also gone to great lengths to develop structurally varied MonoPhos™ ligands in industrially useful transformations such as asymmetric hydrogenation.²⁹ Impressively, the (*S*)-*N*-benzyl-*N*-methyl-MonoPhos™ derivative shown below has been utilized in highly selective hydrogenations of (*E*)-*N*-acylated dehydro- β -amino acid esters, affording the corresponding enantiopure β -amino acid derivatives (**Scheme 16**).^{29a} The authors found that this ligand, after being screened versus related chiral phosphoramidites, afforded the highest enantiocontrol in hydrogenations albeit at slightly longer reaction times.

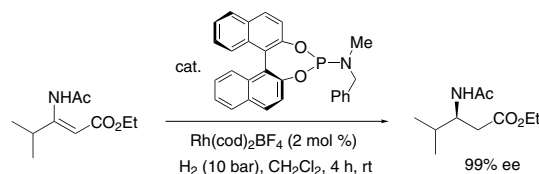
The Feringa research group has broadened the substrate scope of the asymmetric hydrogenation reaction by generating another chiral center on the amine moiety of the phosphoramidite ligand. Amazingly, this fine ligand tuning produces a very active and productive catalyst, which efficiently hydrogenates a wide range



Scheme 14



Scheme 15



Scheme 16

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of acetamido derivatives in less time than the corresponding Me-DuPhos analogs.^{29a} Note that the chiral (*S,R*)-phosphoramidite ligand below is the only ligand known to afford enantioselectivities for the substrate shown greater than 90% (**Scheme 17**).

Recently, Feringa's research group prepared additional structurally varied phosphoramidite ligands for rhodium-catalyzed asymmetric hydrogenations. The aptly named PipPhos and MorfPhos ligands (**Scheme 18**) contain piperidiny and morpholinyl subunits, respectively, and are examples of easily synthesized chiral ligands for highly effective enantioselective transformations. Under mild reaction conditions including low H₂ pressure, this catalyst system yields unprecedented enantioselectivities for several substrates such as dimethyl itaconate and α -dehydroamino ester derivatives (**Scheme 19**).³⁰

Asymmetric Regioselective Allylic Aminations

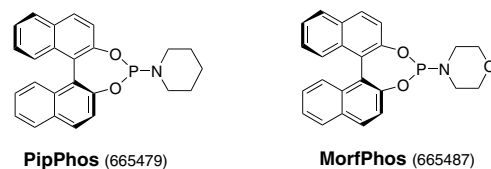
Hartwig and co-workers have succeeded in developing highly selective iridium catalysts with (*R,R,R*)-phosphoramidite L*.^{27g} The allylic aminations of a wide variety of achiral allylic esters proceeded with total conversion and superb regioselectivity in many cases. The reaction shown clearly illustrates the power of this methodology, wherein cinnamyl acetate was converted to the allylic benzyl amine **3** in excellent yield and enantiopurity (**Scheme 20**). The authors mentioned that these valuable amination reactions were mediated by air-stable Ir complexes at ambient temperatures, which should lead to wide acceptance of this catalyst in bench-top organic synthesis.

As a complement to the Hartwig chemistry, Helmchen and co-workers have performed highly enantioselective iridium-catalyzed intra- and intermolecular aminations with *N*-nucleophiles.^{31a} Impressively, dicarbonate **5** reacts smoothly under the reaction conditions to afford the pyrrolidine products **6a** and **6b** in moderate yield but with excellent selectivity (**Scheme 21**).

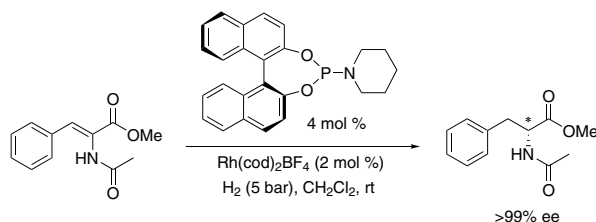
Asymmetric Hydrovinylation – An Efficient Route to All-Carbon Quaternary Centers

These highly practical enantioselective reactions have been accomplished by RajanBabu's research group at Ohio State University.³² The generation of all-carbon quaternary centers is extremely attractive to drug discovery groups, as evidenced in the example shown. Note that the asymmetric hydrovinylation of substituted vinylarenes offers an attractive, general method for creating an asymmetric center (**Scheme 22**). The low ligand loadings, excellent yields, and superb enantioselectivities ensure that this methodology can be utilized in the production of chiral building blocks and directly applied to the synthesis of natural products such as Lyngbyatoxin A.³³

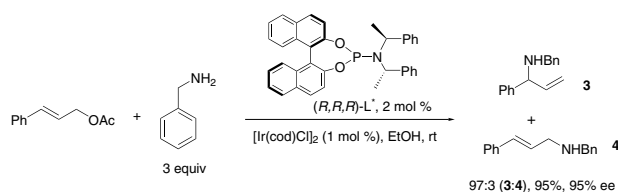
Zhang and RajanBabu have also extended this methodology to the asymmetric hydrovinylation of 1,3-dienes. 1,3-dienes were found to be less reactive than the vinylarene derivatives, thus higher temperatures were applied to drive adequate conversions. Under these conditions, the hydrovinylation of conjugated 1,3-diene **7** with the (*S,R,R*)-phosphoramidite ligand gave exquisite regio- and enantioselectivities (**Scheme 23**).³⁴



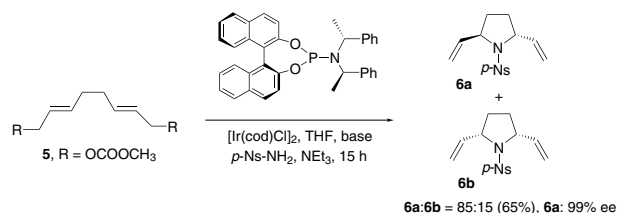
Scheme 18



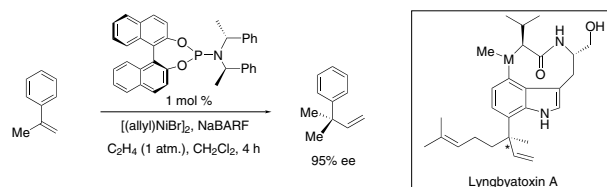
Scheme 19



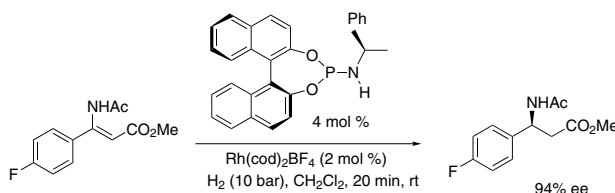
Scheme 20



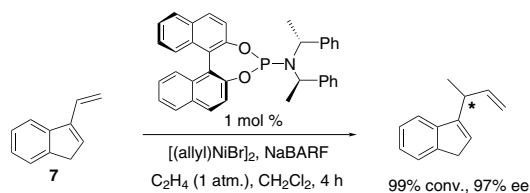
Scheme 21



Scheme 22



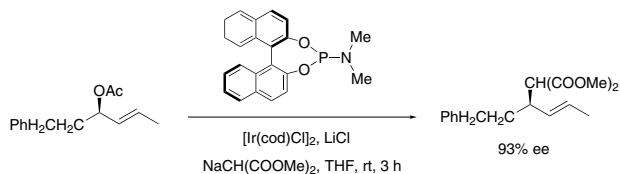
Scheme 17



Scheme 23

Asymmetric Allylic Substitution Reactions

The (*R*)-MonoPhos™ ligand has been effectively utilized in the enantioselective, iridium-catalyzed allylic substitution reaction.³⁵ Simply mixing an iridium precatalyst and the ligand in THF in the presence of LiCl creates a highly active catalyst, which generates a stereogenic C–C bond center in good to excellent enantioselectivities (**Scheme 24**). The high product yields and short reaction times further accentuate this methodology for application to the expedient construction of chiral building blocks.



Scheme 24

Conclusion

A powerful family of monodentate phosphine ligands has been developed on the well known BINOL backbone, which demonstrates both higher activities and higher enantioselectivities in asymmetric transformations when compared to the majority of bidentate chiral phosphines. These phosphoramidite ligands are accessible in a concise, linear fashion and display robust stability when combined with rhodium precatalysts. We have a range of phosphoramidite ligands commercially available that differ in the amine functionality of the ligand architecture, allowing for rapid optimization of catalyst performance.

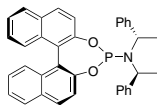
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(*S,S,S*)-(+)-(3,5-Dioxa-4-phospha-cyclohepta [2,1-a;3,4-a']dinaphthalen-4-yl)bis(1-phenylethyl)amine NEW

C₃₆H₃₀NO₂P

FW: 539.6

[380230-02-4]

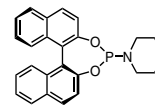


665290-100MG	100 mg
665290-500MG	500 mg
665290-2G	2 g

(*S*)-(+)-(3,5-Dioxa-4-phospha-cyclohepta [2,1-a;3,4-a']dinaphthalen-4-yl)piperidine NEW

C₂₅H₂₂NO₂P

FW: 399.42



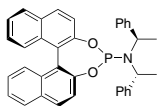
665479-100MG	100 mg
665479-500MG	500 mg
665479-2G	2 g

(*S,R,R*)-(+)-(3,5-Dioxa-4-phospha-cyclohepta [2,1-a;3,4-a']dinaphthalen-4-yl)bis(1-phenylethyl)amine NEW

C₃₆H₃₀NO₂P

FW: 539.6

[415918-91-1]

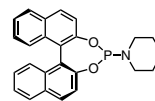


665363-100MG	100 mg
665363-500MG	500 mg
665363-2G	2 g

(*S*)-(+)-(3,5-Dioxa-4-phospha-cyclohepta [2,1-a;3,4-a']dinaphthalen-4-yl)morpholine NEW

C₂₄H₂₀NO₃P

FW: 401.39



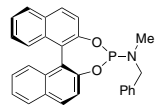
665487-100MG	100 mg
665487-500MG	500 mg
665487-2G	2 g

(*S*)-(+)-Benzyl(3,5-dioxa-4-phospha-cyclohepta [2,1-a;3,4-a']dinaphthalen-4-yl)methylamine NEW

C₂₈H₂₂NO₂P

FW: 435.45

[490023-37-5]



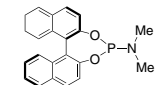
665355-100MG	100 mg
665355-500MG	500 mg
665355-2G	2 g

(*R*)-(-)-(3,5-Dioxa-4-phospha-cyclohepta [2,1-a;3,4-a']dinaphthalen-4-yl)dimethylamine NEW

C₂₂H₂₀NO₂P

FW: 361.37

[157488-65-8]



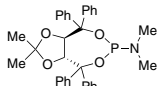
668206-1G	1 g
668206-5G	5 g

(3*aR*,8*aR*)-(-)-(2,2-Dimethyl-4,4,8,8-tetraphenyl-tetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepin-6-yl)dimethylamine NEW

C₃₃H₃₄NO₄P

FW: 539.6

[213843-90-4]



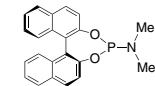
665460-100MG	100 mg
665460-500MG	500 mg

(*S*)-(+)-(3,5-Dioxa-4-phospha-cyclohepta [2,1-a;3,4-a']dinaphthalen-4-yl)dimethylamine NEW

C₂₂H₂₀NO₂P

FW: 361.37

[185449-80-3]



668192-1G	1 g
668192-5G	5 g

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Introduction

One of the most efficient methods for constructing chiral compounds is asymmetric hydrogenation. Catalytic asymmetric hydrogenations are among the most widely used industrial catalytic processes, due to their high turnover rates, atom economy, and inexpensive material costs. Transition metal complexes associated with chiral phosphine ligands are the dominant choice of catalysts for asymmetric hydrogenation, in large part due to the Nobel prize-winning, pioneering work of Noyori and Knowles. The requirement of an electron-rich chiral phosphine ligand is at the core of this transformation.

Professor Xumu Zhang at Penn State has made remarkable advances by creating a toolbox of chiral phosphines which can be used on a variety of substrates, some of which have been historically resistant to hydrogenation. Furthermore, an additional benefit in some reductions is reduced catalyst loading, due to increased turnover numbers (TON). Sigma-Aldrich is pleased to announce an agreement with ChiralQuest to distribute research quantities of a series of Zhang's chiral phosphines for catalytic asymmetric hydrogenations.

Representative Ligands and Applications

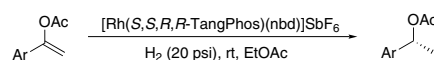
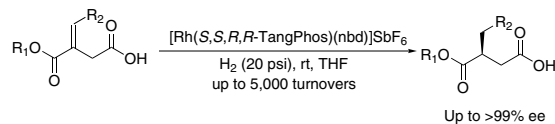
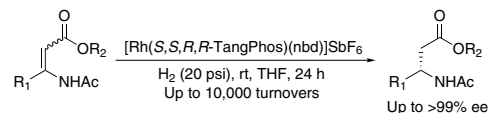
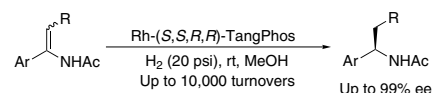
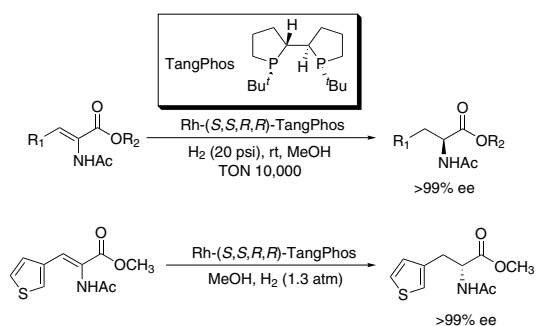
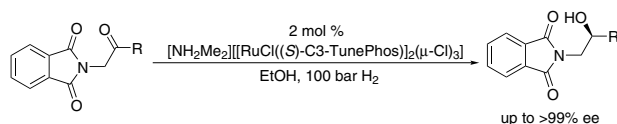
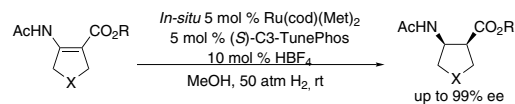
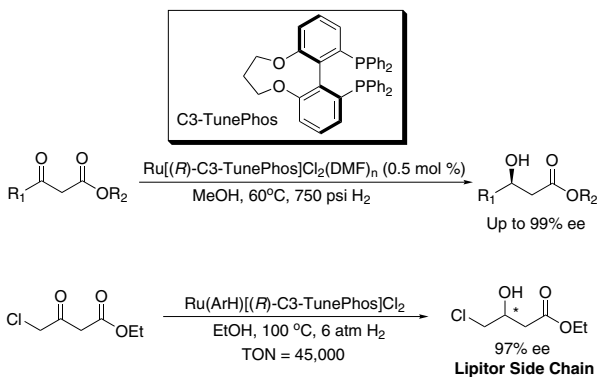
(S)-C₃-TunePhos

C₃-TunePhos, a member of the atropisomeric aryl bisphosphine ligand family with tunable dihedral angles, provides comparable or superior enantioselectivities and catalytic abilities to BINAP in Ru-catalyzed asymmetric hydrogenation of β -keto esters (**Scheme 25**),³⁶ cyclic β -(acylamino) acrylates (**Scheme 26**),³⁷ and α -phthalimide ketones (**Scheme 27**).³⁸

(1S,1S',2R,2R')-TangPhos

A highly electron-donating, low molecular weight, and rigid P-chiral bisphospholane ligand, TangPhos proves incredibly efficient in the rhodium-catalyzed hydrogenation of a variety of functionalized olefins such as α -dehydroamino acids (**Scheme 28**),³⁹ α -arylenamides (**Scheme 29**),³⁹ β -(acylamino)acrylates (**Scheme 30**),⁴⁰ itaconic acids (**Scheme 31**),⁴¹ and enol acetates (**Scheme 32**).⁴¹

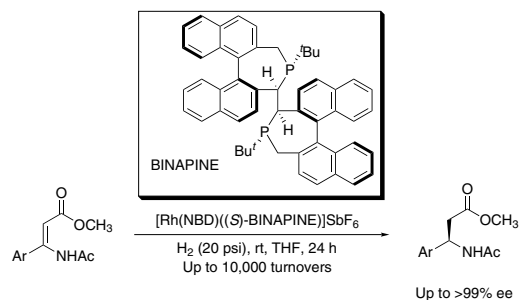
This P-chiral phosphorus ligand represents a superior ligand for asymmetric catalysis including hydrogenation because of its ability to force the chiral environment to encompass the substrate in close proximity to the reactive metal center. TangPhos exhibits substantial conformational rigidity allowing for high enantioselectivities in the hydrogenation of a wide variety of densely functionalized prochiral olefins, with some reaction examples approaching 100% ee.



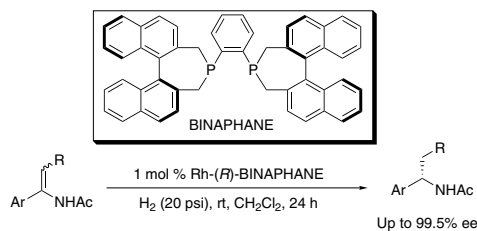
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(S)-BINAPINE

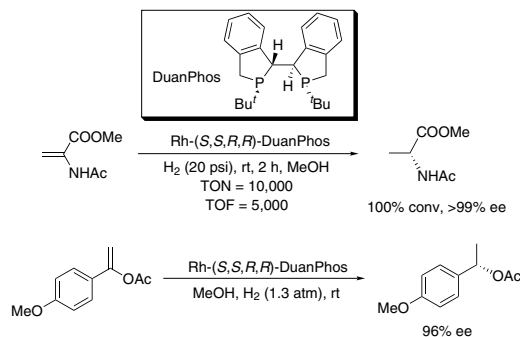
BINAPINE, a highly electron-donating rigid ligand, demonstrates excellent enantioselectivity and reactivity, with TON up to 10,000 for the asymmetric hydrogenation of *Z*- β -aryl(β -acylamino) acrylates (**Scheme 33**).⁴² Interestingly, BINAPINE is a rare example of a bisbinaphthophosphine ligand with *P*-chiral phosphine atoms. High enantioselectivities have been obtained with substrates that contain diverse substituents ranging from electron-rich and electron-poor aryl groups to heteroaryl components. This catalyst system illustrates the incredible effects of rigidity on stereocontrol in the hydrogenation reaction.

**(R)-BINAPHANE**

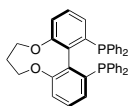
(*R*)-BINAPHANE shows excellent enantioselectivity (up to >99% ee) for hydrogenation of *E/Z*-isomeric mixtures of β -substituted arylenamides (**Scheme 34**).⁴³ This ligand incorporates a bisphosphinite backbone that displays restricted orientation of the aromatic groups proximate to the phosphines. Zhang and co-workers can tune BINAPHANE by modifying the groups on the aromatic and/or the phosphine, thus creating a general catalytic system useful for obtaining high enantioselectivities in the asymmetric hydrogenation reaction.

**(1*R*,1'*R*,2*S*,2'*S*)-DuanPhos**

DuanPhos is more rigid than the related TangPhos ligand, due to the fused phenyl rings on the phospholane architecture. This self-imposed conformational stability improves the enantioselectivity in the hydrogenations of a diverse array of functionalized olefins. Furthermore, Zhang and co-workers have successfully synthesized both enantiomers of this electron-rich ligand through a trivial resolution process. Even highly electron-rich prochiral olefins are readily hydrogenated with exceptional stereocontrol by this productive Rh-catalyst system (**Scheme 35**).

**(R)-C₃-TunePhos**

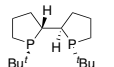
C₃₉H₃₂O₂P₂
FW: 594.62
[301847-89-2]



650862-100MG	100 mg
650862-500MG	500 mg

(S,S',R,R')-TangPhos

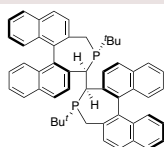
C₁₆H₃₂P₂
FW: 286.37
[470480-32-1]



650889-100MG	100 mg
650889-500MG	500 mg

(S)-Binapine

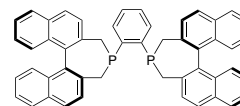
C₅₂H₄₈P₂
FW: 734.89
[610304-81-9]



650870-100MG	100 mg
650870-500MG	500 mg

(R)-Binaphane

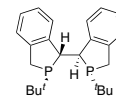
C₅₀H₃₆P₂
FW: 698.77
[253311-88-5]



650854-100MG	100 mg
650854-500MG	500 mg

(1*R*,1'*R*,2*S*,2'*S*)-DuanPhos

C₂₄H₃₂P₂
FW: 382.46
[528814-26-8]



657697-100MG	100 mg
657697-500MG	500 mg

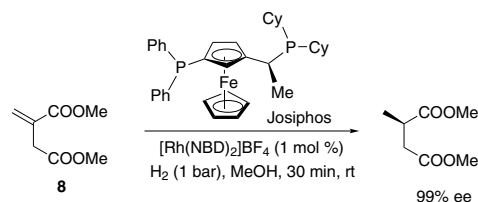
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Solvias Ferrocenyl-Based Ligands

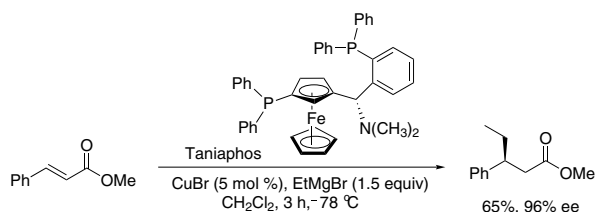
Solvias AG has demonstrated the incredible utility of chiral ferrocenyl diphosphine ligands in a wide range of reaction paradigms ranging from hydrogenation⁹ to the aldol reaction⁴⁵ to hydroboration.⁴⁶ For years, BINAP was considered the only ligand platform that could perform at a high-level in a wide variety of reactions. The ferrocenyl architecture in the Solvias portfolio serves as the superstructure for a unique group of chiral ligands that can be fine tuned electronically and/or sterically for asymmetric synthesis optimization. The Solvias ligands can be combined with metal precursors to form exceptionally active catalysts that exhibit high levels of enantiocontrol in industrially useful processes such as hydrogenation (Scheme 36).⁹ This example illustrates the high enantioselective control exerted by the Josiphos ligand on dimethyl itaconate derivative **8**. The dimethyl (*S*)-2-methylsuccinate product was isolated in quantitative yield and with an optical purity of 99%. Also of interest to synthetic chemists is the high substrate to catalyst ratio (1000:1), while the low hydrogen pressure and fast conversion times further improve the attractiveness of this system.

Feringa and co-workers have pioneered the use of the Solvias ligand family in the copper-catalyzed asymmetric conjugate addition of Grignard reagents to unsaturated carbonyl compounds.⁴⁷ Prior to this group's research, only meager selectivities had been observed in the conjugate addition of Grignard reagents, which stands in stark contrast to the success seen with the related addition of dialkylzinc reagents.⁴⁸ The Feringa group utilized the Taniaphos-type ligand in conjunction with Cu(I) salts to create a highly effective catalyst system. For instance, the conjugate addition of EtMgBr to methyl cinnamate affords 96% enantiopure product at a modest 65% conversion (Scheme 37). The lower conversions in this chemistry are most likely due to the necessity of running the reaction at -78 °C.

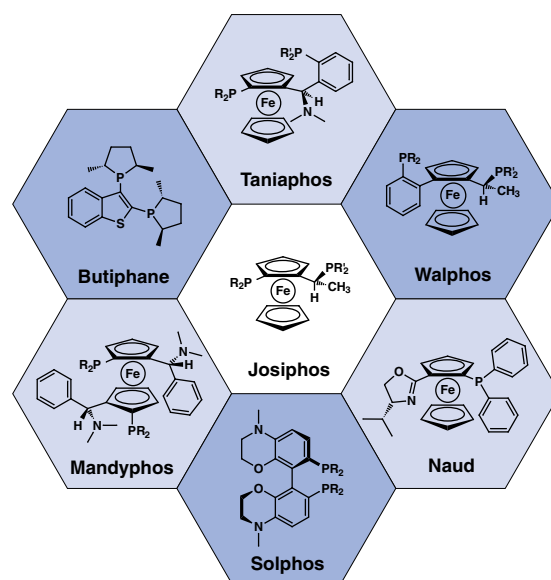
Sigma-Aldrich, in collaboration with Solvias AG, is pleased to offer a diverse array of chiral ligands that can be ligated to metal complexes to afford highly active catalysts for asymmetric hydrogenation and other innovative transformations.⁴⁹ We are excited to offer 40 different ligands and catalysts in 100 mg sample sizes in both enantiomeric forms giving you access to a total of 80 products all in one convenient kit! This kit will allow rapid screening of your asymmetric synthesis plans. Each individual ligand from the unique families below can also be ordered as individual units (Scheme 38). For complete product ordering information on our solvias ligand portfolio, please visit sigma-aldrich.com/solvias.



Scheme 36



Scheme 37

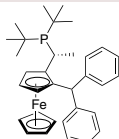


Scheme 38

(*R*)-1-[(1*S*)-2-(Diphenylphosphino)ferrocenyl]-ethyldi-*tert*-butylphosphine

NEW

C₃₂H₄₀FeP₂
FW: 542.45
[155830-69-6]

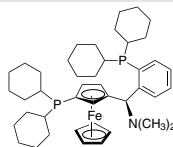


88719-100MG 100 mg
88719-500MG 500 mg

(*S*)-1-Dicyclohexylphosphino-2-[(*R*)- α -(dimethylamino)-2-(dicyclohexylphosphino)benzyl]ferrocene

NEW

C₄₃H₆₃FeNP₂
FW: 711.76
[494227-38-2]

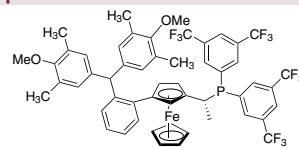


07541-100MG 100 mg
07541-500MG 500 mg

(*R*)-1-[(*R*)-2-[2-[Bis(4-methoxy-3,5-dimethylphenyl)-phosphino]phenyl]ferrocenyl]ethylbis[3,5-bis-(trifluoromethyl)phenyl]phosphine

NEW

C₅₂H₄₄F₁₂FeO₂P₂
FW: 1046.68
[494227-30-4]



65677-100MG 100 mg
65677-500MG 500 mg
65677-1G 1 g
65677-5G 5 g

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References

- (1) (a) Noyori, R., Ed. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994.
(b) Beller, M.; Bolm, C., Eds. *Transition Metals for Organic Synthesis*; 2nd ed.; Wiley-VCH: Weinheim, 2004.
(c) Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds. *Comprehensive Asymmetric Catalysis*, Springer: Berlin, 1999.
- (2) (a) Yoon, T. P.; Jacobsen, E. N. *Science* **2003**, 299, 1691.
(b) Gladysz, J. A. *Pure Appl. Chem.* **2001**, 73, 1319.
- (3) (a) Jacobsen, E. N. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley-VCH: New York, 1993; Chapter 4.2.
(b) Katsuki, T. In *Catalytic Asymmetric Synthesis*, 2nd ed.; Ojima, I., Ed.; Wiley-VCH: New York, 2000; pp 287–325.
(c) Katsuki, T. *Adv. Synth. Catal.* **2002**, 344, 131.
- (4) (a) Ghosh, A. K. et al. *Tetrahedron: Asymmetry* **1998**, 8, 1.
(b) Jorgensen, K. A. et al. *Acc. Chem. Res.* **1999**, 32, 605.
- (5) (a) Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley-VCH: New York, 1993; Chapter 4.1.
(b) Katsuki, T.; Martin, V. S. *Org. React.* **1996**, 48, 1.
(c) Seebach, D.; Beck, A. K.; Heckel, A. *Angew. Chem., Int. Ed.* **2001**, 1, 92.
- (6) (a) Kolb, H. C.; Van Nieuwenzhe, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, 94, 2483.
(b) Bolm, C. Jacobsen, E. N. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley-VCH: New York, 2000; pp 399–428.
- (7) (a) Burk, M. J. et al. *J. Am. Chem. Soc.* **1991**, 113, 8518.
(b) Burk, M. J., *Handbook of Chiral Chemicals*, Abel, Ager, D.J., Ed.; Marcel Dekker: New York, 1999; Ch. 18, p 339.
- (8) Feringa, B. L. et al. *Adv. Synth. Catal.* **2002**, 344, 1003.
- (9) Togni, A. et al. *J. Am. Chem. Soc.* **1994**, 116, 4062.
- (10) Zhang, Z. et al. *Org. Lett.* **2002**, 4, 4495.
- (11) Burk, M. J. *Acc. Chem. Res.* **2000**, 33, 363.
- (12) DuPhos and BPE ligands are sold in collaboration with Kanata Chemical Technologies and licensed from E. I. Dupont for the research market only.
- (13) Burk, M. J. et al. *J. Am. Chem. Soc.* **1996**, 118, 5142.
- (14) Burk, M. J. et al. *J. Am. Chem. Soc.* **1992**, 114, 6266.
- (15) Burk, M. J. et al. *J. Am. Chem. Soc.* **1998**, 120, 657.
- (16) Burk, M. J. et al. *J. Org. Chem.* **1998**, 63, 6084.
- (17) Boaz, N. W. *Tetrahedron Lett.* **1998**, 39, 5505.
- (18) Burk, M. J. et al. *J. Am. Chem. Soc.* **1995**, 117, 4423.
- (19) Burk, M. J. et al. *J. Org. Chem.* **1999**, 64, 3290.
- (20) Murakami, M. et al. *J. Am. Chem. Soc.* **1995**, 121, 4130.
- (21) Moncarz, J. R. et al. *J. Am. Chem. Soc.* **2002**, 124, 13356.
- (22) Charette, A. B. et al. *J. Am. Chem. Soc.* **2003**, 125, 1692.
- (23) Dyker, G. *Angew. Chem. Int. Ed.* **2000**, 39, 4237.
- (24) Sanchez, F. et al. *Chem. Commun.* **2005**, 3451.
- (25) Shibasaki, M. et al. *J. Am. Chem. Soc.* **2004**, 126, 8910.
- (26) Feringa, B. L. *Acc. Chem. Res.* **2000**, 33, 346.
- (27) (a) Feringa, B. L. et al. *Angew. Chem. Int. Ed. Engl.* **1997**, 36, 2620.
(b) Martina, S. L. X. et al. *Tetrahedron Lett.* **2005**, 46, 7159.
(c) Malda, H. et al. *Org. Lett.* **2001**, 3, 1169.
(d) Alexakis, A. et al. *Chem. Commun.* **2005**, 2843.
(e) Streiff, S. et al. *Chem. Commun.* **2005**, 2957.
(f) Bertozzi, F. et al. *Org. Lett.* **2000**, 2, 933.
(g) Hartwig, J. F. et al. *J. Am. Chem. Soc.* **2002**, 124, 15164.
- (28) Alexakis, A.; Albrow, V.; Biswas, K.; Augustin, M.; Prieto, O.; Woodward, S. *Chem. Commun.*, **2005**, 2843.
- (29) (a) Pena, D. et al. *J. Am. Chem. Soc.* **2002**, 124, 14552.
(b) Van den Berg, M. et al. *Adv. Synth. Catal.* **2003**, 345, 308.
- (30) Bernsmann, H. et al. *J. Org. Chem.* **2005**, 70, 943.
- (31) (a) Helmchen, G. et al. *Chem. Commun.* **2005**, 3541.
(b) Helmchen, G. et al. *Chem. Commun.* **2005**, 2957.
- (32) RajanBabu, T. V. et al. *J. Am. Chem. Soc.* **2006**, 128, 5620.
- (33) Gerwick, W. H. et al. *J. Am. Chem. Soc.* **2004**, 126, 11432.
- (34) RajanBabu, T. V. et al. *J. Am. Chem. Soc.* **2005**, 127, 54.
- (35) Helmchen, G. et al. *Chem. Commun.* **1999**, 741.
- (36) Zhang, Z. et al. *J. Org. Chem.* **2000**, 65, 6223.
- (37) Tang, W. et al. *J. Am. Chem. Soc.* **2003**, 125, 9570.
- (38) Lei, A. et al. *J. Am. Chem. Soc.* **2004**, 126, 1626.
- (39) Tang, W.; Zhang, X. *Angew. Chem. Int. Ed. Engl.* **2002**, 41, 1612.
- (40) Tang, W.; Zhang, X. *Org. Lett.* **2002**, 4, 4159.
- (41) Tang, W. et al. *Org. Lett.* **2003**, 5, 205.
- (42) Tang, W. et al. *Angew. Chem. Int. Ed. Engl.* **2003**, 42, 3509.
- (43) Xiao, D. et al. *Org. Lett.* **1999**, 1, 1679.
- (44) Liu, D.; Zhang, X. *Eur. J. Org. Chem.* **2005**, 646.
- (45) Togni, A. et al. *J. Org. Chem.* **1990**, 55, 1649.
- (46) Togni, A. et al. *Organometallics* **1997**, 16, 255.
- (47) Feringa, B. L. et al. *J. Am. Chem. Soc.* **2006**, 128, 9103.
- (48) (a) Lippard, S. J. et al. *J. Am. Chem. Soc.* **1988**, 110, 3175.
(b) Lippard, S. J. et al. *Organometallics* **1990**, 9, 3178.
(c) van Koten, G. et al. *J. Am. Chem. Soc.* **1992**, 114, 3400.
(d) Pfaltz, A. et al. *Tetrahedron* **1994**, 50, 4467.
(e) Seebach, D. et al. *Angew. Chem., Int. Ed.* **2000**, 39, 153.
(f) Tomioka, K. et al. *Tetrahedron Lett.* **1998**, 54, 10295.
(g) Sammakia, T. et al. *Tetrahedron* **1997**, 53, 16503.
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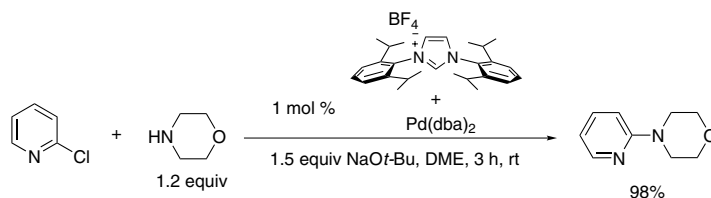
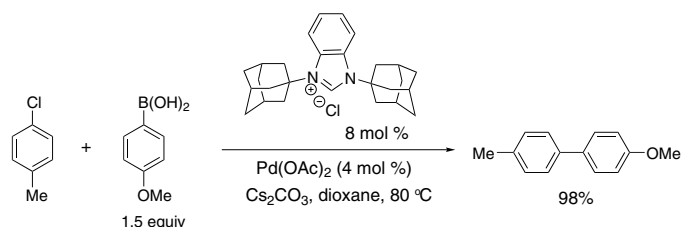
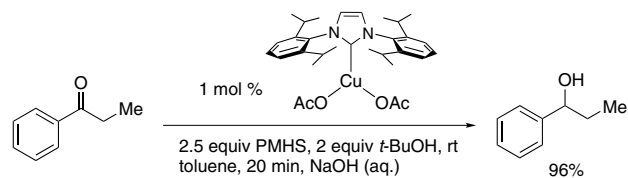
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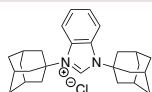
(1) Herrmann, W. A. *Angew. Chem. Int. Ed. Engl.* **2002**, *41*, 1290. (2) (a) Herrmann, W. A. et al. *Chem. Ber.* **1992**, *125*, 1795; (b) Ofele, K. et al. *J. Organomet. Chem.* **1993**, *459*, 177; (c) Herrmann, W. A. et al. *J. Organomet. Chem.* **1994**, *480*, C7. (3) Hartwig, J. F. et al. *Org. Lett.* **2000**, *2*, 1423. (4) Organ, M. G. et al. *Org. Lett.* **2005**, *7*, 1991. (5) Yun, J. et al. *Chem. Commun.* **2005**, 5181.



1,3-Bis(1-adamantyl)benzimidazolium chloride

NEW

C₂₇H₃₅ClN₂
FW: 423.03



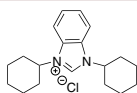
673188-500MG

500 mg

1,3-Dicyclohexylbenzimidazolium chloride

NEW

C₁₉H₂₇ClN₂
FW: 318.88



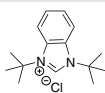
673404-500MG

500 mg

1,3-Di-*tert*-butylbenzimidazolium chloride

NEW

C₁₅H₂₃ClN₂
FW: 266.81

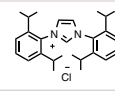


673390-500MG

500 mg

1,3-Bis(2,6-diisopropylphenyl)imidazolium chloride

C₂₇H₃₇ClN₂
FW: 425.05
[250285-32-6]



574074-500MG

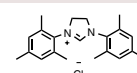
500 mg

574074-2G

2 g

1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride

C₂₁H₂₇ClN₂
FW: 342.91
[173035-10-4]



656631-1G

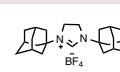
1 g

656631-5G

5 g

1,3-Bis(1-adamantyl)imidazolium tetrafluoroborate

C₂₃H₃₃BF₄N₂
FW: 424.33
[286014-42-4]



660035-1G

1 g

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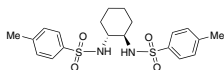
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(1*R*,2*R*)-(+)-*N,N'*-Di-*p*-tosyl-1,2-cyclohexanediamine

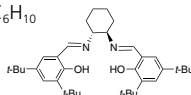
$(\text{C}_3\text{C}_6\text{H}_4\text{SO}_2\text{NH})_2\text{C}_6\text{H}_{10}$
FW: 422.56
[143585-47-1]



482757-1G 1 g
482757-5G 5 g

(*R,R*)-(-)-*N,N'*-Bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamine

$[(\text{C}_6\text{H}_3\text{C}_2\text{Me}_2)_2\text{C}_6\text{H}_2\text{-2-(OH)CH=N}]_2\text{C}_6\text{H}_{10}$
FW: 546.83
[135616-40-9]

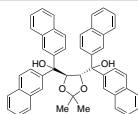


404411-1G 1 g
404411-5G 5 g

TADDOLS

(4*R*,5*R*)-2,2-Dimethyl- $\alpha,\alpha,\alpha',\alpha'$ -tetra(2-naphthyl)dioxolane-4,5-dimethanol

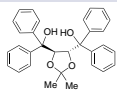
$\text{C}_{47}\text{H}_{38}\text{O}_4$
FW: 666.8
[137365-09-4]



393754-250MG 250 mg
393754-1G 1 g

(4*R*,5*R*)-2,2-Dimethyl- $\alpha,\alpha,\alpha',\alpha'$ -tetraphenyldioxolane-4,5-dimethanol

$\text{C}_{31}\text{H}_{30}\text{O}_4$
FW: 466.57
[93379-48-7]

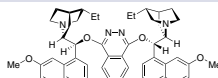


265004-250MG 250 mg
265004-1G 1 g

Cinchona Alkaloids

Hydroquinidine 1,4-phthalazinediyl diether

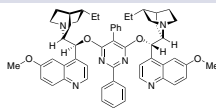
$\text{C}_{48}\text{H}_{54}\text{N}_6\text{O}_4$
FW: 778.98
[140853-10-7]



53954-1G 1 g

Hydroquinidine 2,5-diphenyl-4,6-pyrimidinediyl diether

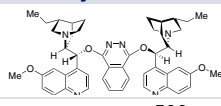
$\text{C}_{56}\text{H}_{60}\text{N}_6\text{O}_4$
FW: 881.11
[149725-81-5]



53951-250MG 250 mg
53951-1G 1 g

Hydroquinine 1,4-phthalazinediyl diether

$\text{C}_{48}\text{H}_{54}\text{N}_6\text{O}_4$
FW: 778.98
[140924-50-1]

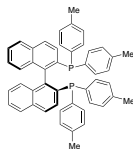


53959-500MG 500 mg

BINAPS

(*S*)-(-)-2,2'-Bis(di-*p*-tolylphosphino)-1,1'-binaphthyl

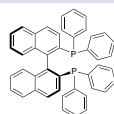
$\text{C}_{48}\text{H}_{40}\text{P}_2$
FW: 678.78
[100165-88-6]



668974-250MG 250 mg
668974-1G 1 g

(*S*)-(-)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthalene

$[(\text{C}_6\text{H}_5)_2\text{PC}_{10}\text{H}_6\text{-}]_2$
FW: 622.67
[76189-56-5]



295825-250MG 250 mg
295825-1G 1 g

BINOLS

(*S*)-(-)-5,5',6,6',7,7',8,8'-Octahydro(1,1'-binaphthalene)-2,2'-diol

$\text{C}_{20}\text{H}_{22}\text{O}_2$
FW: 294.39
[65355-00-2]



540579-1G 1 g

(*S*)-(-)-3,3'-Dibromo-1,1'-bi-2-naphthol

$\text{C}_{20}\text{H}_{12}\text{Br}_2\text{O}_2$
FW: 444.12
[119707-74-3]



595837-250MG 250 mg
595837-1G 1 g

BIPHEPS

(*R*)-(+)-2,2'-Bis(diphenylphosphino)-6,6'-dimethoxy-1,1'-biphenyl

$\text{C}_{38}\text{H}_{32}\text{O}_2\text{P}_2$
FW: 582.61
[133545-16-1]



95536-250MG 250 mg
95536-1G 1 g

(*R*)-(-)-5,5'-Dichloro-2,2'-bis(diphenylphosphino)-6,6'-dimethoxy-1,1'-biphenyl

$\text{C}_{38}\text{H}_{30}\text{Cl}_2\text{O}_2\text{P}_2$
FW: 651.5
[185913-98-8]

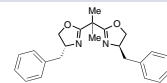


76854-250MG-F 250 mg
76854-1G-F 1 g

BOX

(+)-2,2'-Isopropylidenebis[(4*R*)-4-benzyl-2-oxazoline]

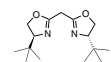
$\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_2$
FW: 362.46
[141362-77-8]



495301-250MG 250 mg
495301-1G 1 g

2,2'-Methylenebis[(4*S*)-4-*tert*-butyl-2-oxazoline]

$\text{C}_{15}\text{H}_{26}\text{N}_2\text{O}_2$
FW: 266.38
[132098-54-5]



405965-100MG 100 mg
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