

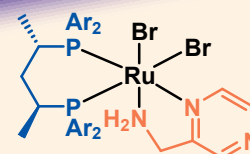
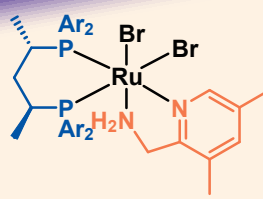
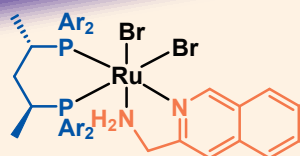
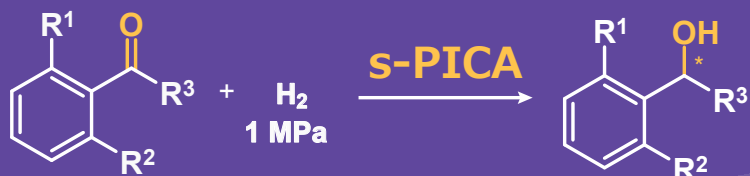
Asymmetric Hydrogenation Catalysts

s-PICA cat.



Kanto Reagents

Optically active alcohols, which couldn't be obtained with previous catalysts, are obtainable with the s-PICA cat.!



s-PICA cat.

2 Diphosphines $\times$ (S,S),(R,R) $\times$ 3 Diamines = 12 type catalysts

Ar = 3,5-*i*Pr₂C₆H₃ [dipskewphos]

Ar = 3,5-Me₂C₆H₃ [xylskewphos]

3-(aminomethyl)isoquinoline [3-AMIQ]

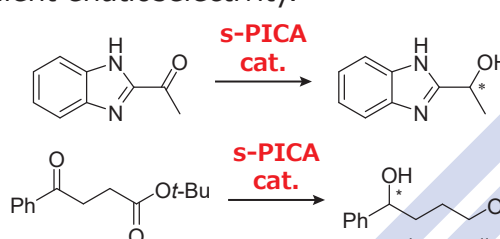
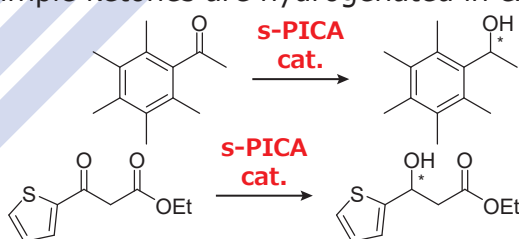
3,5-Dimethyl-2-picolylamine [3,5-DMPICA]

2-Aminomethylpyrazine [AMPZ]

The s-PICA cat. can hydrogenate ketones, which have not been reduced efficiently by the previous catalysts, to afford optically active alcohols in excellent enantiomeric excess. The s-PICA cat. can be applied to industrial scale synthesis.

Improved substrate scope

Polysubstituted acetophenones, acetylbenzimidazole, ketoesters and also simple ketones are hydrogenated in excellent enantioselectivity.

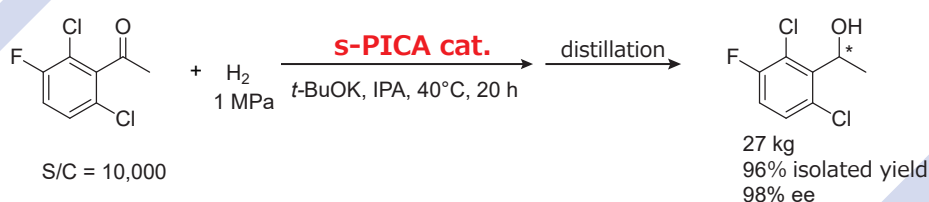


Examples are illustrated at next page.

Industrial scale production

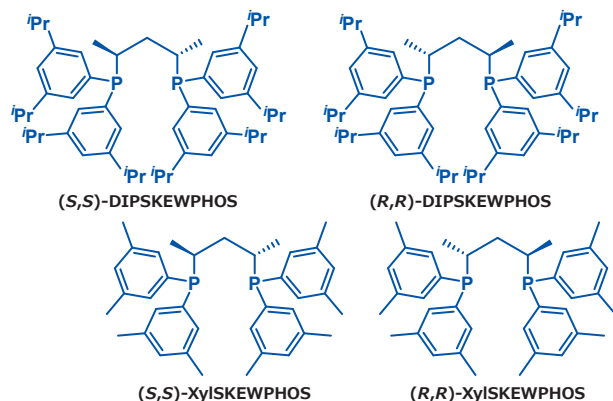
Multi kg-scale synthesis has been achieved.

The reaction proceeds at a substrate-to-catalyst molar ratio(S/C) of >10,000.

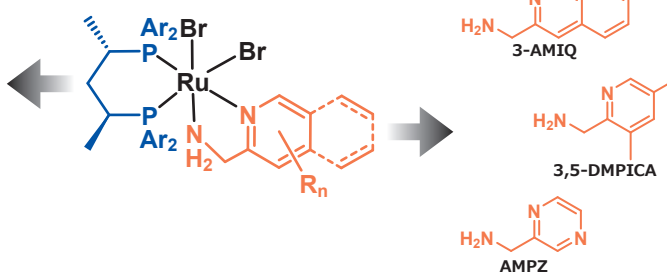


Kanto Chemical Co., Inc.

s-PICA cat.: The Feature of Ligands



s-PICA Cat.



Diphosphine ligands

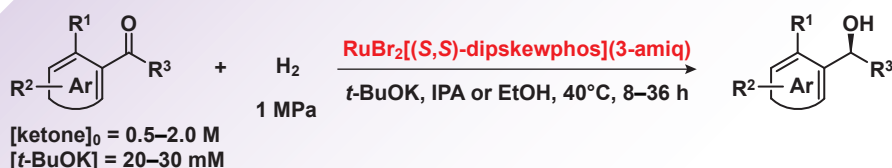
ligands	feature
DIPSKEWPHOS	better enantioselectivity
XylSKEWPHOS	better reactivity

Diamine ligands

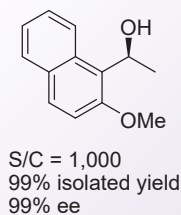
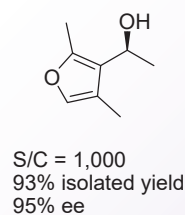
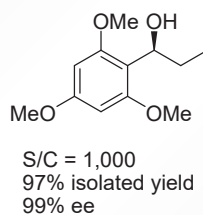
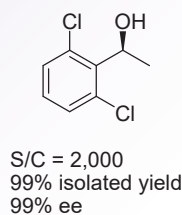
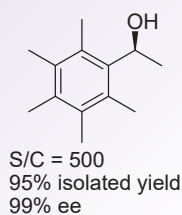
ligands	feature
3-AMIQ	better enantioselectivity
3,5-DMPICA	good enantioselectivity and reactivity
AMPZ	suitable at higher temp.(60–70°C) suitable for heteroarenes

Examples of reaction

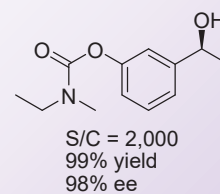
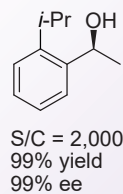
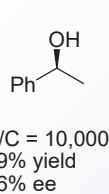
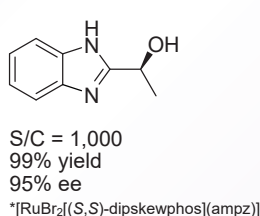
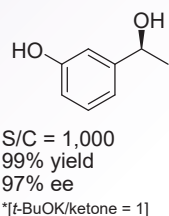
Asymmetric hydrogenation of polysubstituted aromatic ketones¹⁾ and other aromatic ketones



Examples : Reaction of polysubstituted aromatic ketones

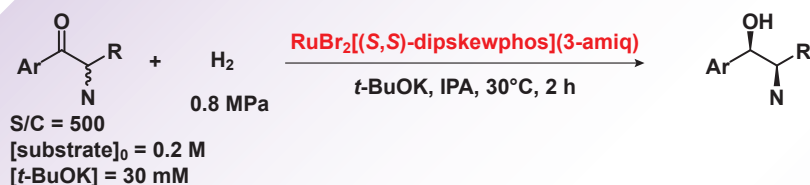
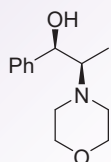


Examples : Reaction of other aromatic ketones

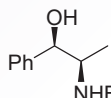


Comparison of catalysts for the hydrogenation of polysubstituted acetophenone

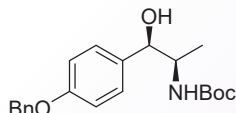
	Ru cat.	S/C	yield (%)	ee (%)
s-PICA cat.	RuBr ₂ [(<i>S,S</i>)-xylskewphos](3,5-dmpica)	20,000	99	98
	RuBr ₂ [(<i>S,S</i>)-dipskewphos](3-amiq)	1,000	99	99
	RuCl ₂ [(<i>R</i>)-binap][(R,R)-dpen]	1,000	21	15

Asymmetric hydrogenation of α -aminoketones with DKRExamples : Reaction of α -aminoketones

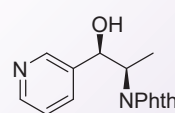
97% isolated yield
syn:anti = 96:4
99% ee



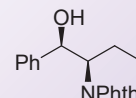
95% isolated yield
syn:anti = 87:13
97% ee



80% isolated yield
syn:anti = 85:15
97% ee

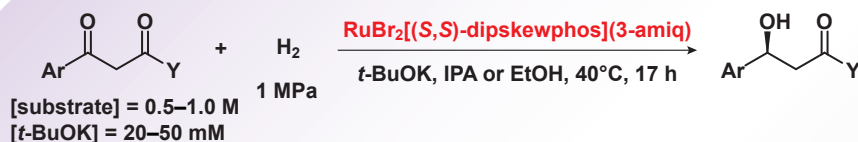
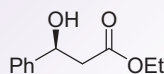


82% isolated yield
syn:anti = 99:1
>99% ee

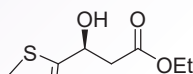


82% isolated yield
syn:anti = 99:1
99% ee

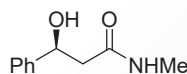
*[RuBr₂[(S,S)-dipskewphos](ampz)]

Asymmetric hydrogenation of β -ketoesters, amides and analoguesExamples : Reaction of β -ketoesters, amides and analogues

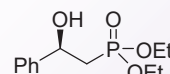
S/C = 5,000
97% yield
99% ee



S/C = 1,000
95% yield
97% ee

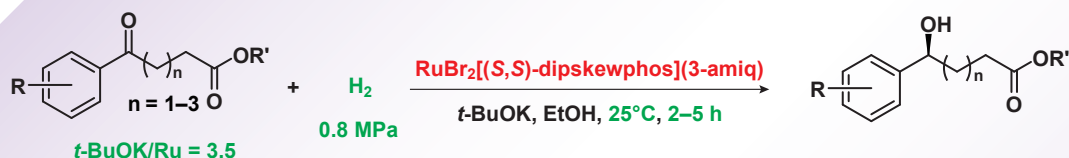
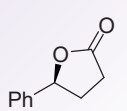


S/C = 500
97% yield
96% ee

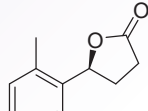


S/C = 500
98% yield
98% ee

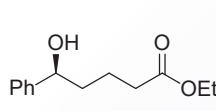
*[60°C]
*[RuBr₂[(S,S)-dipskewphos](ampz)]

Asymmetric hydrogenation of γ -, δ - and ϵ -ketoesters²⁾Examples : Reaction of γ -, δ - and ϵ -ketoesters

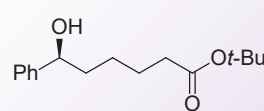
S/C = 5,000
97% isolated yield
97% ee



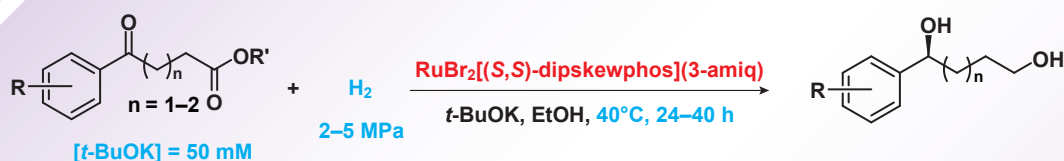
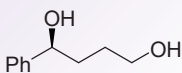
S/C = 5,000
97% isolated yield
99% ee



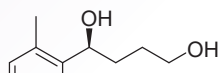
S/C = 500
99% yield
>99% ee



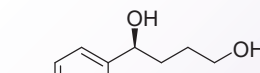
S/C = 500
99% yield
99% ee

Asymmetric hydrogenation of γ - and δ -ketoesters to diols²⁾Examples : Reaction of γ - and δ -ketoesters to diols

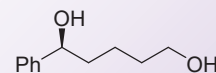
S/C = 5,000
97% isolated yield
96% ee



S/C = 5,000
97% isolated yield
98% ee



S/C = 500
96% isolated yield
95% ee



S/C = 500
96% isolated yield
98% ee

Product list

Product Name	Product No.	Package
Dibromo[(S,S)-DIPSKEWPHOS](3-AMIQ)ruthenium(II) Dibromo[(2S,4S)-2,4-bis[bis(3,5-diisopropylphenyl)phosphino]pentane] (3-aminomethylisoquinoline)ruthenium(II) CAS : 2170985-21-2 FW : 1196.24	 Ar = 3,5- <i>i</i> -Pr ₂ C ₆ H ₃	10163-68 100 mg
Dibromo[(R,R)-DIPSKEWPHOS](3-AMIQ)ruthenium(II) Dibromo[(2R,4R)-2,4-bis[bis(3,5-diisopropylphenyl)phosphino]pentane] (3-aminomethylisoquinoline)ruthenium(II) CAS : - FW : 1196.24	 Ar = 3,5- <i>i</i> -Pr ₂ C ₆ H ₃	10164-68 100 mg
Dibromo[(S,S)-DIPSKEWPHOS](3,5-DMPICA)ruthenium(II) Dibromo[(2S,4S)-2,4-bis[bis(3,5-diisopropylphenyl)phosphino]pentane] (2-aminomethyl-3,5-dimethylpyridine)ruthenium(II) CAS : 2241509-73-7 FW : 1174.23	 Ar = 3,5- <i>i</i> -Pr ₂ C ₆ H ₃	10173-68 100 mg
Dibromo[(R,R)-DIPSKEWPHOS](3,5-DMPICA)ruthenium(II) Dibromo[(2R,4R)-2,4-bis[bis(3,5-diisopropylphenyl)phosphino]pentane] (2-aminomethyl-3,5-dimethylpyridine)ruthenium(II) CAS : - FW : 1174.23	 Ar = 3,5- <i>i</i> -Pr ₂ C ₆ H ₃	10181-68 100 mg
Dibromo[(S,S)-DIPSKEWPHOS](AMPZ)ruthenium(II) Dibromo[(2S,4S)-2,4-bis[bis(3,5-diisopropylphenyl)phosphino]pentane] (2-aminomethylpyrazine)ruthenium(II) CAS : - FW : 1147.16	 Ar = 3,5- <i>i</i> -Pr ₂ C ₆ H ₃	10165-68 100 mg
Dibromo[(R,R)-DIPSKEWPHOS](AMPZ)ruthenium(II) Dibromo[(2R,4R)-2,4-bis[bis(3,5-diisopropylphenyl)phosphino]pentane] (2-aminomethylpyrazine)ruthenium(II) CAS : - FW : 1147.16	 Ar = 3,5- <i>i</i> -Pr ₂ C ₆ H ₃	10166-68 100 mg
Dibromo[(S,S)-XyLSKEWPHOS](3-AMIQ)ruthenium(II) Dibromo[(2S,4S)-2,4-bis[di(3,5-xylyl)phosphino]pentane] (3-aminomethylisoquinoline)ruthenium(II) CAS : 1646350-83-5 FW : 971.80	 Ar = 3,5-Me ₂ C ₆ H ₃	11214-68 100 mg
Dibromo[(R,R)-XyLSKEWPHOS](3-AMIQ)ruthenium(II) Dibromo[(2R,4R)-2,4-bis[di(3,5-xylyl)phosphino]pentane] (3-aminomethylisoquinoline)ruthenium(II) CAS : - FW : 971.80	 Ar = 3,5-Me ₂ C ₆ H ₃	11215-68 100 mg
Dibromo[(S,S)-XyLSKEWPHOS](3,5-DMPICA)ruthenium(II) Dibromo[(2S,4S)-2,4-bis[di(3,5-xylyl)phosphino]pentane] (2-aminomethyl-3,5-dimethylpyridine)ruthenium(II) CAS : 1646350-81-3 FW : 949.80	 Ar = 3,5-Me ₂ C ₆ H ₃	11218-68 100 mg
Dibromo[(R,R)-XyLSKEWPHOS](3,5-DMPICA)ruthenium(II) Dibromo[(2R,4R)-2,4-bis[di(3,5-xylyl)phosphino]pentane] (2-aminomethyl-3,5-dimethylpyridine)ruthenium(II) CAS : - FW : 949.80	 Ar = 3,5-Me ₂ C ₆ H ₃	11219-68 100 mg
Dibromo[(S,S)-XyLSKEWPHOS](AMPZ)ruthenium(II) Dibromo[(2S,4S)-2,4-bis[di(3,5-xylyl)phosphino]pentane] (2-aminomethylpyrazine)ruthenium(II) CAS : 1646350-84-6 FW : 922.73	 Ar = 3,5-Me ₂ C ₆ H ₃	11216-68 100 mg
Dibromo[(R,R)-XyLSKEWPHOS](AMPZ)ruthenium(II) Dibromo[(2R,4R)-2,4-bis[di(3,5-xylyl)phosphino]pentane] (2-aminomethylpyrazine)ruthenium(II) CAS : - FW : 922.73	 Ar = 3,5-Me ₂ C ₆ H ₃	11217-68 100 mg

We can supply other catalysts for asymmetric hydrogenation or asymmetric transfer hydrogenation, and optically active alcohols that are produced by these asymmetric catalysts.
 The ligands such as DIPSKEWPHOS, XyLSKEWPHOS and SKEWPHOS are also suppliable.
 Please contact us for more information.

Reference

- 1) *ChemCatChem* **2018**, 10, 1.
- 2) *Angew. Chem. Int. Ed.* **2018**, 57, 1386

- Please use the products listed in the catalog as reagents (chemicals used for testing or research purpose).
- Product information is subject to change without notice. For the latest information, please have a look at our website "Cica-Web".

 **KANTO CHEMICAL CO., INC.**
REAGENT DIVISION

2-1, Nihonbashi Muromachi 2-chome, Chuo-ku, Tokyo, 103-0022, Japan
 TEL : +81-0-6214-1092
 E-mail : kanto-61@kanto.co.jp
 Website: <https://www.kanto.co.jp>

OEA-07(201910)