

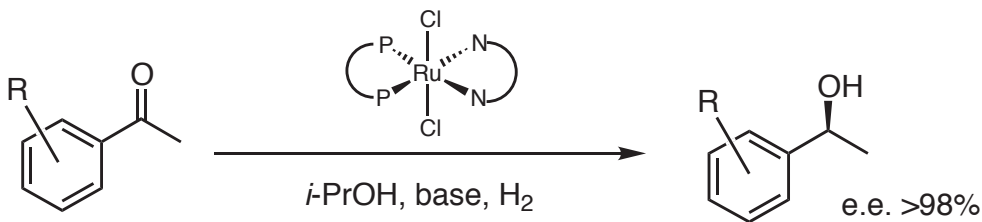


Johnson Matthey Catalysts

Catalysis & Chiral Technologies

Noyori Technology for the Synthesis of Chiral Alcohols

Homogeneous asymmetric hydrogenation of ketones is one of the core technologies that Johnson Matthey Catalysts offers to the pharmaceutical and fine chemical industries.^{1,2}



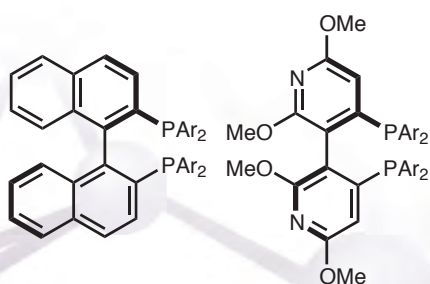
Licensed to Johnson Matthey Catalysts by the Japan Science and Technology Corporation (JST), this reaction system provides a very cost-effective process for the asymmetric reduction of aromatic, heteroaromatic, cyclic and unsaturated ketones.

Since 2003 Johnson Matthey's expertise has been successfully applied to further develop and optimize this technology.

Whether you are searching for a customized catalyst kit for internal screening, a comprehensive research proposal, or catalyst supply on lab, kilo or commercial scale, you can be confident that our team of professionals will deliver a high performance, economical catalytic solution.

Core Catalyst Technology

Phosphine:

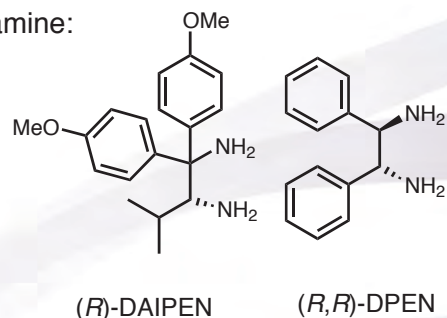


Ar = Ph
(*R*)-P-Phos
(*R*)-Binap

Ar = *p*-CH₃-C₆H₄
(*R*)-Tol-P-Phos
(*R*)-Tol-Binap

Ar = 3,5-(CH₃)₂-C₆H₃
(*R*)-Xylyl-P-Phos

Diamine:



With the catalysts' modular design, the phosphine and the diamine ligands in the [phosphine RuCl₂ diamine] Noyori complexes can be varied to improve reactivity and enantioselectivity

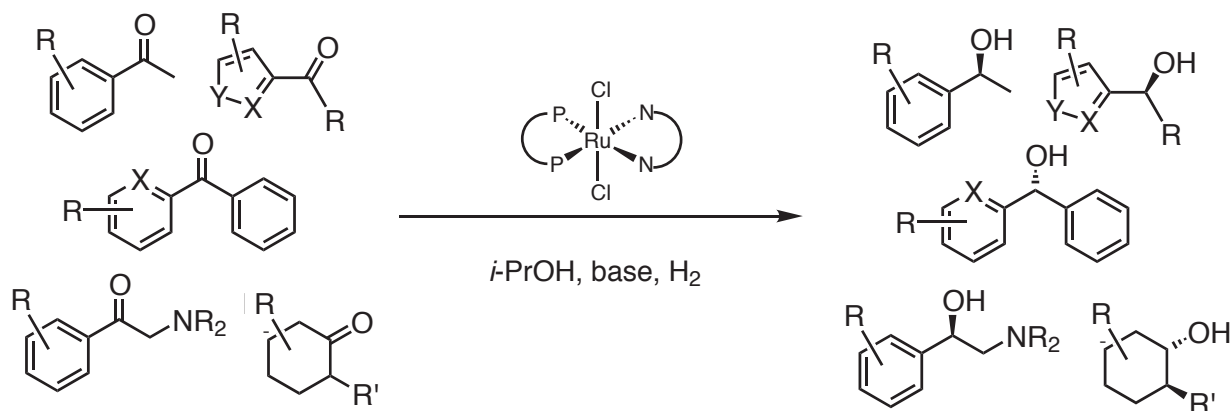
More than 50 preformed catalysts for Noyori-type asymmetric hydrogenations are available.

In addition to our standard product range of catalysts we can also manufacture Noyori catalysts, at multi-kilo scale, using customer specified bisphosphine and diamine combinations.

1 R. Noyori et al. *Angew.Chem.Int.Ed.* **1997**, 37, 1703

2 Reviews: R. Noyori et al. *Angew.Chem.Int.Ed.* **2002**, 41, 2008 (Nobel Lecture); *Angew.Chem.Int.Ed.* **2001**, 40, 40

Reaction Scope



Typical conditions

i-PrOH / *t*-BuOK, 0.5% to 5% molar base to substrate

Offers

- very high selectivity (up to > 99% ee, > 99% chemical purity)
- high productivity (up to 40 % wgt/wgt substrate)
- low catalyst loadings (typical molar S/C 1,000/1 to 50,000/1)

Mixtures of solvents (e.g. *t*-BuOH/MeOH, *i*-PrOH/water, *i*-PrOH/toluene) can be used as well as different bases (e.g. KOH, K₂CO₃). Base-sensitive substrates can be hydrogenated under carefully optimized conditions.

Standard Noyori Hydrogenation Kit

[Xyl-P-Phos RuCl₂ DPEN]

[Xyl-P-Phos RuCl₂ DAIPEN]

[BINAP RuCl₂ DPEN]

[BINAP RuCl₂ DAIPEN]

[P-Phos RuCl₂ DPEN]

[P-Phos RuCl₂ DAIPEN]

[Tol-BINAP RuCl₂ DAIPEN]

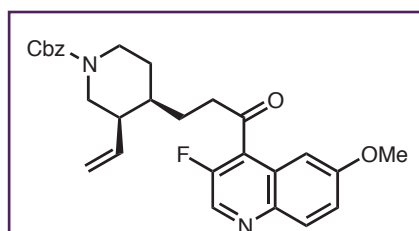
Recommended initial screening conditions

Catalyst (0.02 mmol) and substrate (0.2 mmol, S/C 100/1) are hydrogenated in *i*-PrOH in the presence of *t*-BuOK 1M in *t*-BuOH (10% base to substrate) at 30 to 50°C under 5 to 30 bar hydrogen.

Research Collaboration

Johnson Matthey Catalysts has established a distinguished reputation for providing resources and catalysis expertise in the areas of catalyst screening, selection and reaction optimization in collaboration with pharmaceutical and fine chemicals customers¹.

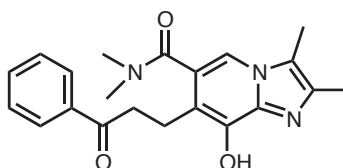
Our history of research collaborations employing Noyori technology includes joint projects with a variety of both pharmaceutical and fine chemical companies. Of notable interest, the [Xylyl-P-Phos RuCl₂ DAIPEN] catalyst has been proven to be the superior catalyst in several commercial applications.



Viquidacin, NXL101 (topoisomerase inhibitor)²

S/C 1,000/1, 50°C, 0.33 M
10 bar, 1% t-BuOK, *i*-PrOH

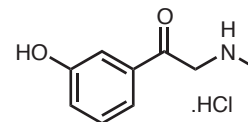
70% isolated yield,
>97% purity, > 99% ee



Potassium-competitive acid blockers³

S/C 3,000/1, 80°C,
30 bar H₂, > 1eq. t-BuOK,
i-PrOH/*t*-BuOH/H₂O

full conversion, >95% ee



α₁-Adrenergic receptor agonist⁴

S/C 20,000/1, 1 hour
30 bar H₂, 67°C - 80°C,
> 3 eq. KOH 10M, *i*-PrOH

full conversion, 97% ee
> 97% NMR purity

With strategically located production facilities in US, EU, India and China, we can efficiently and cost effectively deliver to our customers and their global partners.

1 Details of Johnson Matthey's Research Collaborations are available for viewing via an archived twenty minute webinar at www.jm Catalysts.com/pharma.

2 Collaboration with Novexel. New Horizons in Catalysis, Cologne December 2009, B. Ledoussal, Talk 13.

3 Collaboration with Nycomed. Asymmetric Catalysis on Industrial Scale, second edition, Wiley-VCH, 2010, Chapter 5.

4 Collaboration with Lonza AG. Tetrahedron: Asymmetry 21 (2010), pp. 2479-248.



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Selected Noyori Catalyst Products

Compound	Catalog #	Mol Wt
(R)-PPhos RuCl ₂ (R,R)-Dpen	C1-400	1028.9
(S)-PPhos RuCl ₂ (S,S)-Dpen	C1-410	1028.9
(R)-Xyl-P-Phos RuCl ₂ (R,R)-Dpen	C1-402	1141.11
(S)-Xyl-P-Phos RuCl ₂ (S,S)-Dpen	C1-412	1141.11
(R)-PPhos RuCl ₂ (R)-Daipen	C1-600	1031.1
(S)-PPhos RuCl ₂ (S)-Daipen	C1-610	1031.1
(R)-Xyl-PPhos RuCl ₂ (R)-Daipen	C1-602	1243.3
(S)-Xyl-PPhos RuCl ₂ (S)-Daipen	C1-612	1243.3
(R)-BINAP RuCl ₂ (R)-Dpen	C1-420	1006.94
(S)-BINAP RuCl ₂ (S)-Dpen	C1-430	1006.94
(R)-BINAP RuCl ₂ (R)-Daipen	C1-620	1167.15
(S)-BINAP RuCl ₂ (S)-Daipen	C1-630	1167.15
(R)-Tol-BINAP RuCl ₂ (R)-Daipen	C1-621	1167.15
(S)-Tol-BINAP RuCl ₂ (S)-Daipen	C1-631	1167.15
(R)-BINAP RuCl ₂ (S)-Daipen	C1-670	1167.15
(S)-BINAP RuCl ₂ (R)-Daipen	C1-680	1167.15
(R)-Xyl-P-Phos RuCl ₂ (S,S)-Dpen	C1-452	1141.11
(S)-Xyl-P-Phos RuCl ₂ (R,R)-Dpen	C1-462	1141.11

For additional information on our technologies, please contact us at inquiries@jmus.com.