JM

Kit guide: Asymmetric transfer hydrogenation catalysts

JM Johnson Matthey

Catalyst overview

Product number	CAS number	Product description	Formula	Mol. weight
C1-000	192139-92-7	[(R,R)-TsDPEN Ru(p-cymene)Cl]	$C_{31}H_{35}ClN_2O_2RuS$	636.20
C1-001	1097730-63-6	[(R,R)-MsDPEN Ru(p-cymene)Cl]	$C_{25}H_{31}ClN_2O_2RuS$	560.11
C1-007	3067212-22-7	[(1S,4R)(1S,2S)-CsDPEN Ru (p-cymene)Cl]	$C_{34}H_{43}ClN_2O_3RuS$	696.31
C1-008	1026995-71-0	[(R,R)-FsDPEN Ru(p-cymene)Cl]	$C_{30}H_{28}ClF_5N_2O_2RuS$	712.13
C1-010	192139-90-5	[(S,S)-TsDPEN Ru(p-cymene)Cl]	$C_{31}H_{35}ClN_2O_2RuS$	636.20
C1-011	329371-25-7	[(S,S)-MsDPEN Ru(p-cymene)Cl]	$C_{25}H_{31}ClN_2O_2RuS$	560.11
C1-017	n/a	[(1R,4S)(1R,2R)-CsDPEN Ru (p-cymene)Cl]	$C_{34}H_{43}ClN_2O_3RuS$	696.31
C1-018	1026995-72-1	[(S,S)-FsDPEN Ru(p-cymene)Cl]	$C_{30}H_{28}ClF_5N_2O_2RuS$	712.13
C1-020	174813-82-2	[(R,R)-TsDPEN Ru(mesitylene)Cl]	$C_{30}H_{33}ClN_2O_2RuS$	622.18
C1-030	174813-81-1	[(S,S)-TsDPEN Ru(mesitylene)Cl]	$C_{30}H_{33}ClN_2O_2RuS$	622.18
C1-100	213603-12-4	[(R,R)-TsDACH Ru(p-cymene)Cl]	$C_{23}H_{33}ClN_2O_2RuS$	538.11
C1-110	192057-12-8	[(S,S)-TsDACH Ru(p-cymene)Cl]	$C_{23}H_{33}ClN_2O_2RuS$	538.11
C1-300	1192620-83-9	C3-[(R,R)-teth-TsDPEN RuCl]	$C_{30}H_{31}ClN_2O_2RuS$	620.17
C1-304	162123-45-0	C3-[(R,R)-teth-MtsDPEN RuCl]	$C_{32}H_{35}ClN_2O_2RuS$	648.22
C1-308	1629123-54-1	C3-[(R,R)-teth-TrisDPEN RuCl]	$C_{38}H_{47}ClN_2O_2RuS$	732.38
C1-309	851051-42-8	C3-[(S,S)-teth-TsDPEN RuCl] dimer	$C_{60}H_{66}Cl_6N_4O_4Ru_2S_2$	1386.18
C1-310	851051-43-9	C3-[(S,S)-teth-TsDPEN RuCl]	$C_{30}H_{31}ClN_2O_2RuS$	620.17
C1-314	1630734-19-8	C3-[(S,S)-teth-MtsDPEN RuCl]	$C_{32}H_{35}ClN_2O_2RuS$	648.22
C1-318	1630734-20-1	C3-[(S,S)-teth-TrisDPEN RuCl]	$C_{38}H_{47}ClN_2O_2RuS$	732.38
C1-319	851136-36-2	C3-[(R,R)-teth-TsDPEN RuCl] dimer	$C_{60}H_{66}Cl_6N_4O_4Ru_2S_2$	1386.18
C1-358	1629123-68-7	C4-[(R,R)-teth-TrisDPEN RuCl]	$C_{39}H_{49}ClN_2O_2RuS$	746.40
C1-368	1630736-02-5	C4-[(S,S)-teth-TrisDPEN RuCl]	$C_{39}H_{49}ClN_2O_2RuS$	746.40
C3-020	1244963-99-2	[(R,R)-TsDPEN IrCp*Cl]	$C_{31}H_{36}ClIrN_2O_2S$	728.37
C3-021	2598217-78-6	[(R,R)-MsDPEN IrCp*Cl]	$C_{25}H_{32}ClIrN_2O_2S$	652.27
C3-022	895579-52-9	[(1R,4S)(1R,2R)-CsDPEN IrCp*Cl]	$C_{34}H_{44}ClIrN_2O_3S$	788.46
C3-030	1099830-90-6	[(S,S)-TsDPEN IrCp*Cl]	$C_{31}H_{36}ClIrN_2O_2S$	728.37
C3-031	1085182-50-8	[(S,S)-MsDPEN IrCp*Cl]	$C_{25}H_{32}ClIrN_2O_2S$	652.27
C3-032	895579-53-0	[(1S,4R)(1S,2S)-CsDPEN IrCp*Cl]	$C_{34}H_{44}ClIrN_2O_3S$	788.46

Substrate scope and key reaction features

Asymmetric transfer hydrogenation is a technology of choice for the reduction of C=O and C=C double bonds to manufacture chiral alcohols and chiral amines. The catalysts demonstrate excellent tolerance to a wide variety of functional groups including NO_2, CN, COOR, $CONR_2$, OH, and NH_2. They are effective across both acidic and basic conditions.

For polyfunctionalised substrates, the highly active and robust Wills tethered ruthenium catalysts are often the best choice.

Dynamic kinetic resolution is possible when the substrates contain a stereogenic centre adjacent to the C=O bond. The highly chemoselective reduction of C=O groups is usually achieved without reduction of C=C bonds in the same molecule.

However, highly polarised double bonds (e.g. those with geminal CN groups) can be reduced using Ru-diamine complexes.

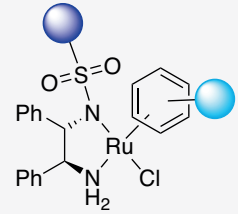
These systems are also effective for imine reductions and reductive aminations, provided that suitable reaction conditions are chosen.

	1st Gen Ru	1st Gen Ir	2nd Gen Ru
	Target molar substrate / catalyst		
Aromatic ketones	(500-5,000)	(500-5,000)	(1,000-10,000)
Cyclic imines	(100-1,000)	(500-5,000)	(1,000-10,000)
Alpha-halo ketones	(50-500)	(100-1,000)	(1,000-10,000)
Aliphatic ketones	(50-500)	(100-1,000)	(200-2,000)
Acyclic imines	(10-100)	(50-500)	(100-1,000)
Bulky ketones	(10-100)	(50-500)	(100-1,000)
Reductive amination	(10-100)	(50-500)	(100-1000)
Ketone/imines reduction with DKR	(10-100)	(50-500)	(200-2,000)
Ketones/imines hydrogenation	*	(50-500)**	(100-1000)
R enantiomers kit	C1-000; C1-020; C1-001; C1-100; C1-017; C1-008	C3-020; C3-021; C3-022	C1-309; C1-300; C1-304; C1-308; C1-358
S enantiomers kit	C1-010; C1-030; C1-011; C1-110; C1-007; C1-018	C3-030; C3-031; C3-032	C1-319; C1-310; C1-314; C1-318; C1-368

* Inactive unless the counterion is non coordinating
** Moderately active but improved with exchange to non-coordinating counter ion

Catalyst types

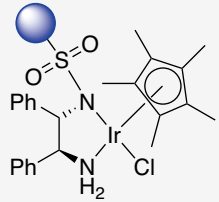
Ruthenium Noyori type catalysts



= p-Tol, Mes, camphoryl

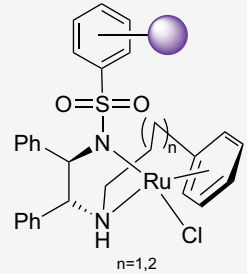
= 1-Me-4-^{i}Pr, 1,3,5-Me

Iridium Noyori type catalysts



p-Tol, Mes, camphoryl

Wills type catalysts



= 4-Me, 2,4,6-Me, 2,4,6-^{i}Pr

Recommended reaction conditions

Hydride source	Solvent
HCOOH/Et_3N 5/2 (azeotropic mixture)	Alcohols (EtOH, iPrOH), aprotic polar (THF, AcOEt, CH_3CN, DCM,etc)*
HCOOH/Et_3N 1/1 (or preformed mixture in variable ratios)	Alcohols (EtOH, iPrOH), aprotic polar (THF, AcOEt, CH_3CN, DCM,etc)*
NaOOCH (or preformed aq. solutions pH 5-8 NaOOCH/HCOOH)	Water, alcohols (MeOH, EtOH) or biphasic mixtures water /organic solvent (toluene, AcOEt)
NH_4OOCH (for reductive amination to primary amine)	Aprotic polar (THF, AcOEt, CH_3CN, DCM,etc), alcohols (EtOH, iPrOH, trifluoroethanol)
HCOOH/Et_3N 5/2 (azeotropic mixture with amines to give secondary or tertiary amine)	Trifluoroethanol (with amines to give secondary or tertiary amine)
Hydrogen (5-30 bar)	Alcohols (MeOH, EtOH)

* Reactions 'on water' also possible with substrates not soluble in water.

- Initial reaction conditions: molar substrate/catalyst 50-100/1 with large excess of hydride source (10-20 equivalents), 40°C to 60°C.
- Optimised conditions: see max target S/C loadings overleaf, 1-2 equiv. hydride source, 0.5-2M substrate. Allow for CO_2 venting.
- Addition of HCOOH, possibly dropwise, to control reaction rate in the presence of stoichiometric or sub-stoichiometric base (organic bases or NaOH or NaOOCH).
- Optimal conditions (different pH or HCOOH/Et_3N ratios) may vary for different catalysts.

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