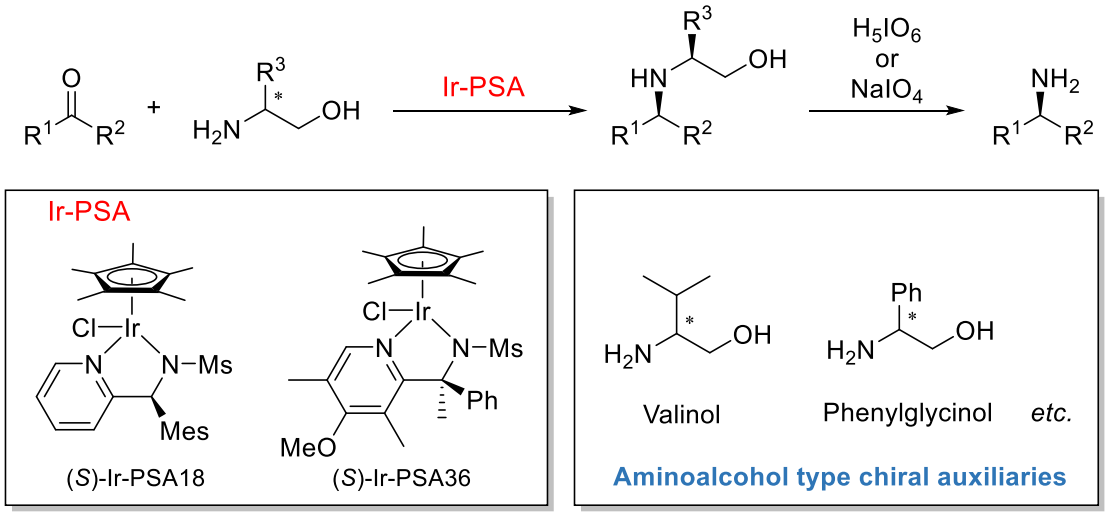
KANTO CHEMICAL CO., INC.

2022/10/06

Catalysts for Asymmetric Reductive Amination –Ir-PSA series–

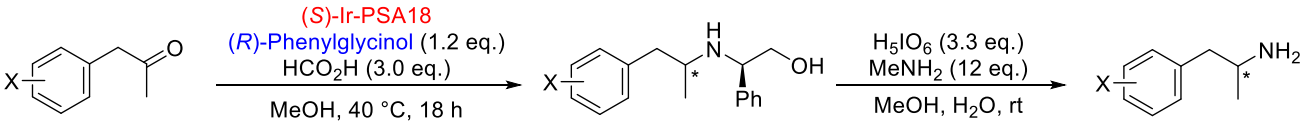


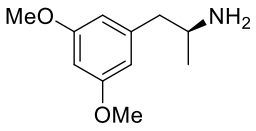
Ir-PSA

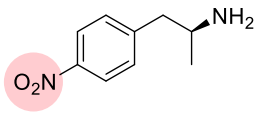
Kanto Chemical has developed novel asymmetric reductive amination catalysts, Ir-PSA for preparation of optically active amines.

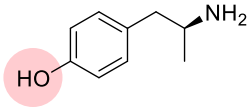
Optically active amines are important compounds such as intermediates of pharmaceuticals. Conventional methods for synthesis of optically active amines include optical resolution of racemic amines and enantioselective or diastereoselective reduction of pre-prepared imines. These were not efficient methods due to low yield, long steps and poor functional group tolerance. Therefore, we improved our original reductive amination catalysts (Ir-PA, Ir-QN) into asymmetric catalysts (Ir-PSA) and developed an efficient method for preparation of optically active amines. In this method, combination of chiral Ir-PSA and an inexpensive aminoalcohol-based chiral auxiliary enables efficient asymmetric reductive amination of ketones to afford corresponding optically active amines in high yield and high stereoselectivity. It is especially effective for amines that are difficult to obtain by conventional asymmetric synthesis. And the aminoalcohol moiety can be easily and quantitatively removed under mild oxidative conditions. This method is a practical reaction with excellent functional group tolerance. Ir-PSA are available in both *S* and *R* enantiomers. Ir-PSA18 is especially effective for the asymmetric reductive amination of phenylacetones, and Ir-PSA36 is effective for the 2-tetralones.

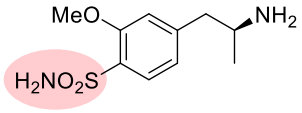
- **Reaction examples by Ir-PSA18**

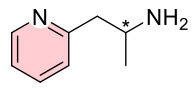


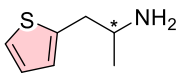

S/C = 20,000
91% Isolated yield
95% ee

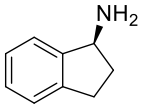

S/C = 5,000
93% Isolated yield
97% ee

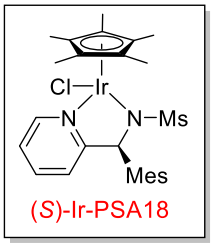

S/C = 5,000
68% Isolated yield
97% ee

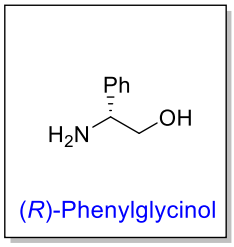

S/C = 1,000
95% Isolated yield
95% ee


S/C = 5,000
81% Isolated yield
90% ee

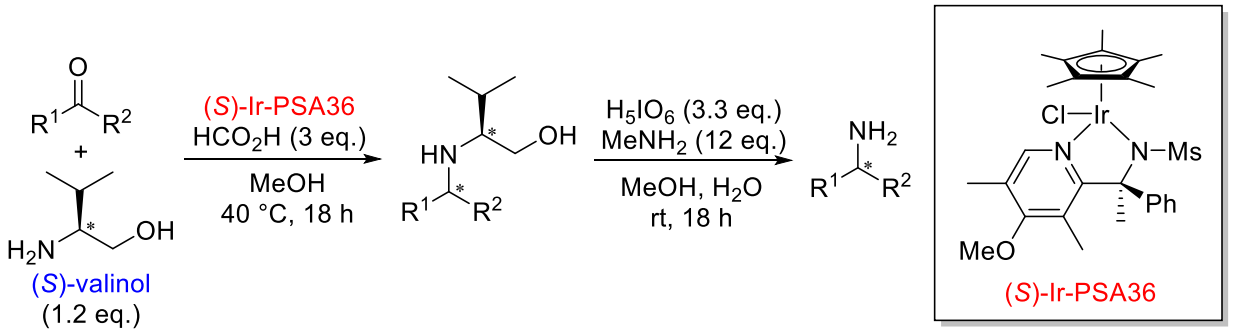

S/C = 3,000
85% Isolated yield
91% ee

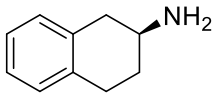

S/C = 500
87% isolated yield
98% ee

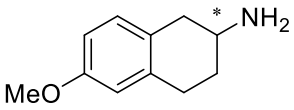


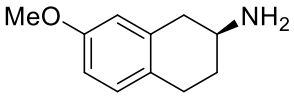


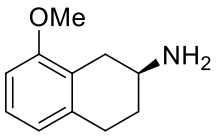
- **Reaction examples by Ir-PSA36**

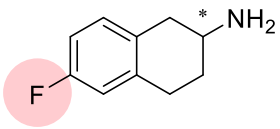


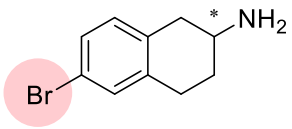

S/C = 5,000
80% isolated yield
82% ee

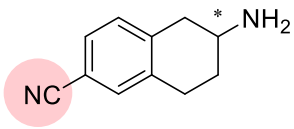

S/C = 5,000
94% isolated yield
86% ee

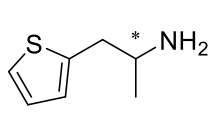

S/C = 5,000
91% isolated yield
84% ee


S/C = 5,000
87% isolated yield
87% ee

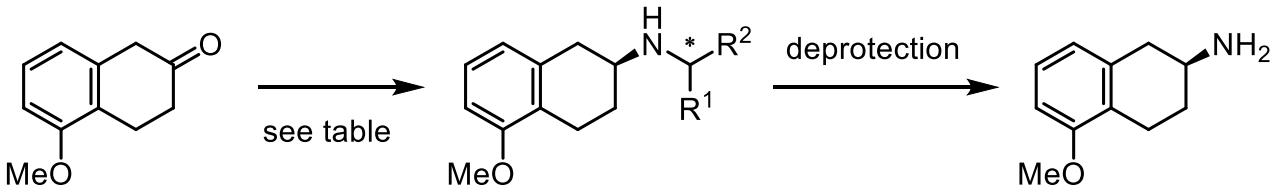

S/C = 5,000
77% isolated yield
82% ee


S/C = 1,000
86% isolated yield
84% ee

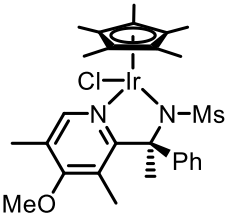

S/C = 1,000
93% isolated yield
81% ee


S/C = 5,000
81% isolated yield
92% ee

- **Comparison with other asymmetric reductive aminations**



entry	conditions	yield (%)	ee (%)[a]
1	1) (*R*)-1-phenylethanol (1.2 eq.) TsOH·H_2O (0.04 eq.), toluene, reflux 2) $NaBH_4$ (1.5 eq.), IPA, –20 °C	90	53
2	1) (*S*)-valinol (1.2 eq.), $MgSO_4$ MeCN, 60 °C 2) $NaBH_4$ (1.54 eq.), MeOH, –10 °C	99	9
4	1) (*S*)-valinol (1.2 eq.), $MgSO_4$ MeCN, 60 °C 2) H_2 (0.3 MPa), Pd/C (10 wt%), MeOH, 40 °C	63	15
3	(*S*)-valinol (1.2 eq.), (*S*)-Ir-PSA36 (S/C = 10,000) HCO_2H (3.0 eq.), MeOH, 40 °C, 18 h	96	82

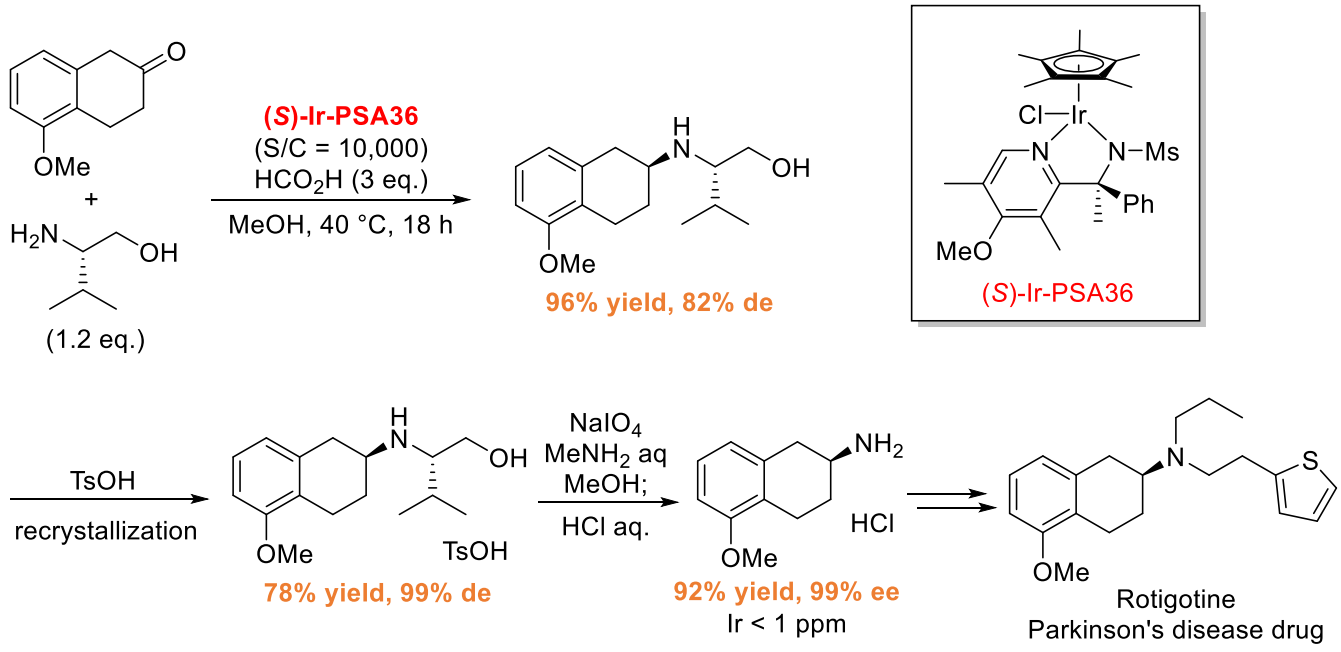


(*S*)-Ir-PSA36

[a] Determined after deprotection.

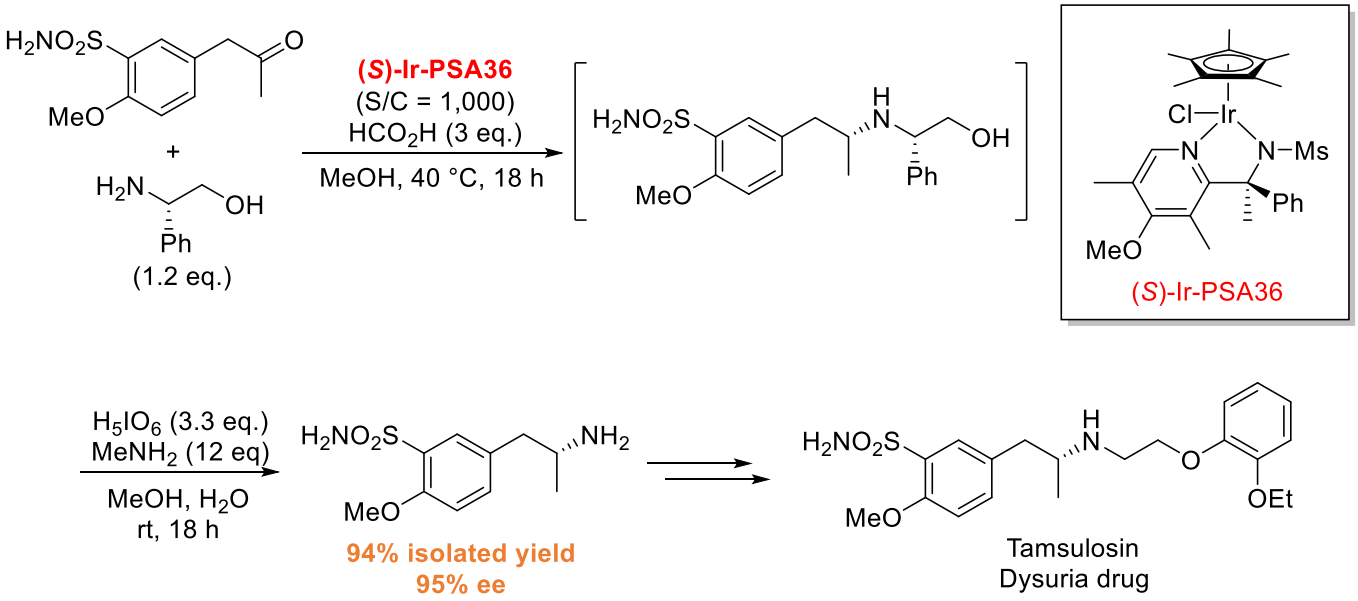
This method exhibits superior stereoselectivity compared to sodium borohydride reduction and Pd catalytic hydrogenation.

- **Application to Rotigotine intermediate synthesis**



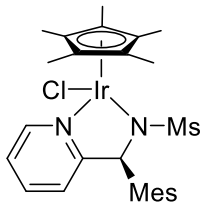
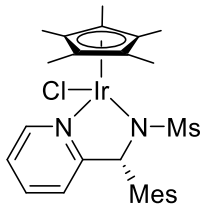
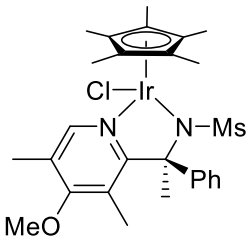
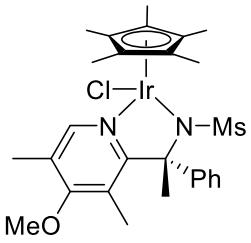
The optical purity can be easily increased by recrystallization of the diastereomeric intermediate.

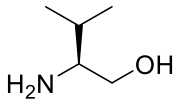
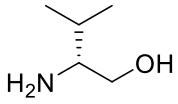
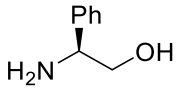
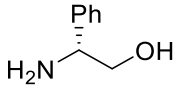
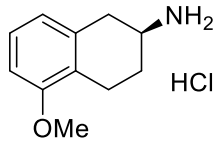
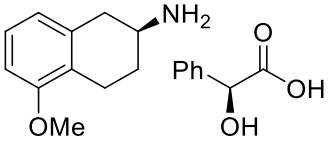
- **Application to Tamsulosin intermediate synthesis**



Process shortening and cost reduction can be expected in optically active amine synthesis.

Product list

Product		Grade	Product No.	Package
	(*S*)-Ir-PSA18 Chloro[(*S*)-N-{1-(4-pyridin-2-yl(2,4,6-trimethylphenyl)methyl}methanesulfonamidato](pentamethylcyclopentadienyl)iridium(III)	for asymmetric synthesis	07060-68	100 mg
	(*R*)-Ir-PSA18 Chloro[(*R*)-N-{1-(4-pyridin-2-yl(2,4,6-trimethylphenyl)methyl}methanesulfonamidato](pentamethylcyclopentadienyl)iridium(III)	for asymmetric synthesis	07071-68	100 mg
	(*S*)-Ir-PSA36 Chloro[(*S*)-N-(1-(4-methoxy-3,5-dimethylpyridin-2-yl)-1-phenylethyl)methanesulfonamidato](pentamethylcyclopentadienyl)iridium(III)	for asymmetric synthesis	07658-68	100 mg
	(*R*)-Ir-PSA36 Chloro[(*R*)-N-(1-(4-methoxy-3,5-dimethylpyridin-2-yl)-1-phenylethyl)methanesulfonamidato](pentamethylcyclopentadienyl)iridium(III)	for asymmetric synthesis	07035-68	100 mg

Product		Grade	Product No.	Package
	L-Valinol		44078-32	25 g
			44078-52	5 g
	(*R*)-(-)-2-Amino-3-methyl-1-butanol		42247-2A	5 g
	(*S*)-(+)-Phenylglycinol		30757-1A	1 g
	D(-)-α- Phenylglycinol		18382-2A	25 g
			18382-1A	5 g
$NaIO_4$	Sodium periodate	Guaranteed reagent for JIS	37233-00	500 g
			37233-20	100 g
			37233-30	25 g
H_5IO_6	Orthoperiodic acid	Guaranteed reagent	32061-30	25 g
	(*S*)-2-Amino-5-methoxytetralin hydrochloride	for asymmetric synthesis	01770-55	5 g
	(*S*)-2-Amino-5-methoxytetralin(*S*)-mandelate	for asymmetric synthesis	01769-55	5 g

Patent application by Kanto Chemical Co.

Application number

- WO2014175267
- JP2022-075375
- JP2022-075379

Related Information

Brochure:

Iridium Catalyst for Chiral Amine Synthesis

Related Page:

"Catalysts" Product Page

Publications

- **Asymmetric Transfer Hydrogenative Amination of Benzylic Ketones Catalyzed by Cp*Ir(III) Complexes Bearing a Chiral *N*-(2-Picolyl)sulfonamidato Ligand**
  T.Kawada, K.Yabushita, T.Yasuda, T.Ohta, T.Yajima, K.Tanaka, N.Utsumi, M.Watanabe, K.Murata, Y.Kayaki, S.Kuwata, and T.Katayama
  The Journal of Organic Chemistry, 87(13), 8458-8468(2022)

- **Development of an Efficient Method for the Synthesis of Chiral Amines by Using New Chiral Iridium Catalyst.**
  T.Kawada, T.Katayama
  THE CHEMICAL TIMES, 264, 26-31 (2022).

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