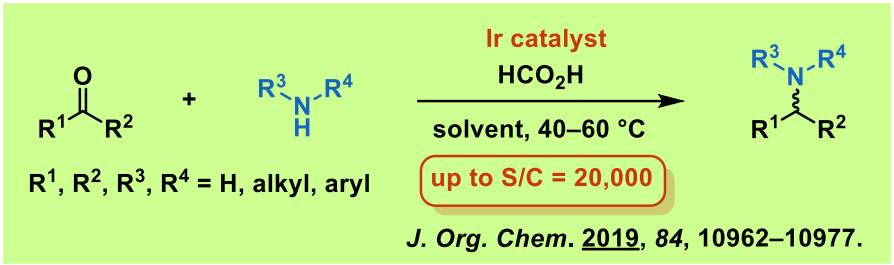
Reductive Amination

Part 1: Reductive Amination Catalysts

Part 2: Asymmetric Reductive Amination Catalysts

Reductive Amination Catalysts

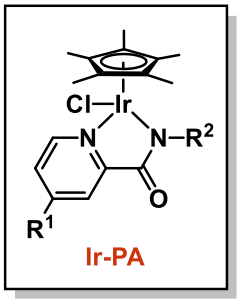


J. Org. Chem. 2019, *84*, 10962–10977.

- Preparation of primary, secondary or tertiary amines from carbonyl compounds
- High catalytic activity
- Using formic acid as a hydrogen source
- High functional group tolerance (e.g., -NO_2, -CN, -Br…)

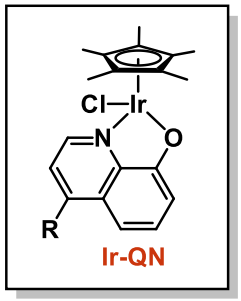
Iridium Complexes for Reductive Amination

For primary amine synthesis



Ir-PA	R^1	R^2	Application
Ir-PA1	H	4-$Me_2NC_6H_4$	For general ketones
Ir-PA2	Me_2N	4-$Me_2NC_6H_4$	High reactivity
Ir-PA3	Me_2N	H	For steric hyndered ketones
Ir-PA4	H	4-$CF_3C_6H_4$	For electron deficient ketones
Ir-PA5	H	4-$NO_2C_6H_4$	For electron deficient ketones

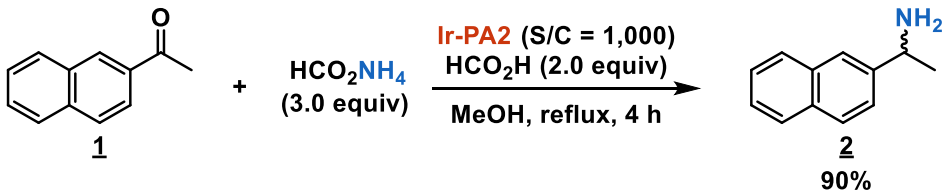
For secondary or tetiary amine synthesis



Ir-QN	R	Application
Ir-QN1	H	For general ketones
Ir-QN2	Me_2N	High reactivity

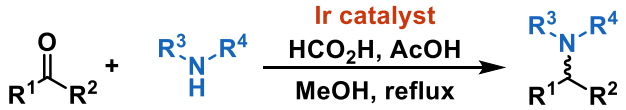
Please see this brochure for details https://www.kanto.co.jp/dcms_media/other/OFC-05-EN.pdf

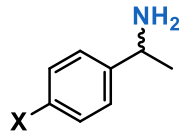
Typical Procedure



To a solution of ketone **1** (20 mmol) in methanol (10 mL) was added ammonium formate (3.78 g, 60 mmol), formic acid (1.51 mL, 40 mmol) and **Ir-PA2** (1.29 mg, 0.02 mmol) under Ar atmosphere. After stirring for 4 h under reflux, the solvent was evaporated under a vacuum. An aqueous solution of NaOH was added to the resulting residue and extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography to afford amine **2** (90% yield).

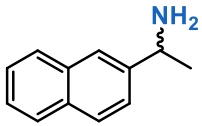
Substrate Scope



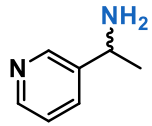


Ir-PA1 (S/C = 1,000)

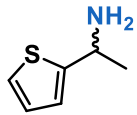
X	yield (%)
NO_2	94
CN	96
Br	99
OMe	97



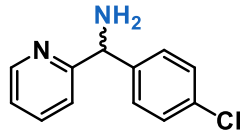
Ir-PA2 (S/C = 20,000)
90% yield



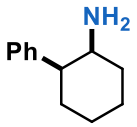
Ir-PA1 (S/C = 1,000)
92% yield



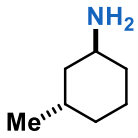
Ir-PA1 (S/C = 1,000)
89% yield



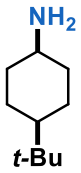
Ir-PA5 (S/C = 500)
82% yield



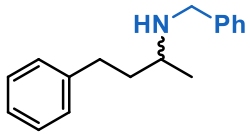
Ir-PA1 (S/C = 500)
81% yield
cis/*trans* = 98:2



Ir-PA1 (S/C = 500)
75% yield
cis/*trans* = 4:96

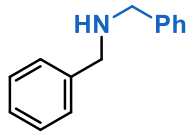


Ir-PA1 (S/C = 500)
97% yield
>99% *cis*

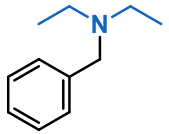


Ir-QN2 (S/C = 10,000) [a]
88% yield

[a]Solvent was *i*-PrOH.



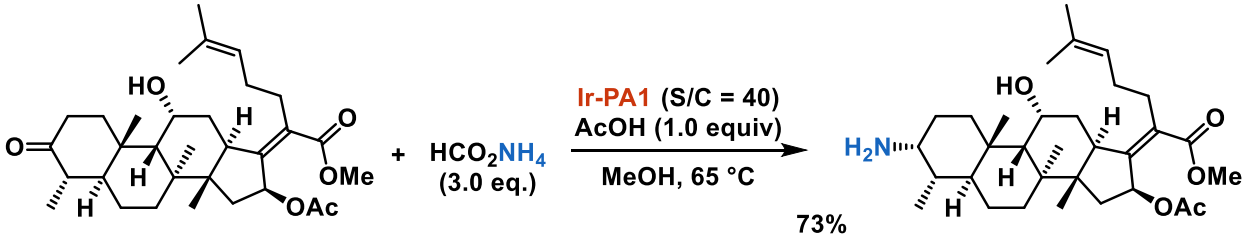
Ir-PA2 (S/C = 10,000)
99% yield



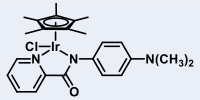
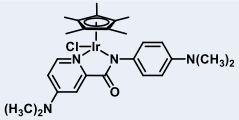
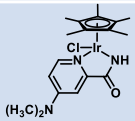
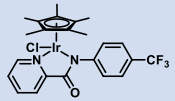
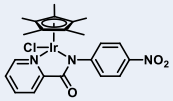
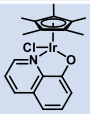
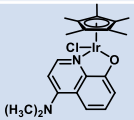
Ir-QN2 (S/C = 10,000) [b]
95% yield

[b]Solvent was THF.

Application



C. K. Hill, J. F. Hartwig, *Nat. Chem.* 2017, *9*, 1213–1221.

Structure	Product No.	Package	Structure	Product No.	Package
Reductive Amination Catalysts					
 Ir-PA1	07127-68	100 mg	 Ir-PA2	07429-68	100 mg
	07127-95	500 mg		07429-95	500 mg
 Ir-PA3	07430-68	100 mg	 Ir-PA4	07964-68	100 mg
	07430-95	500 mg		07964-95	500 mg
 Ir-PA5	07965-68	100 mg			
	07965-95	500 mg			
 Ir-QN1	07128-68	100 mg	 Ir-QN2	07966-68	100 mg
	07128-95	500 mg		07966-95	500 mg

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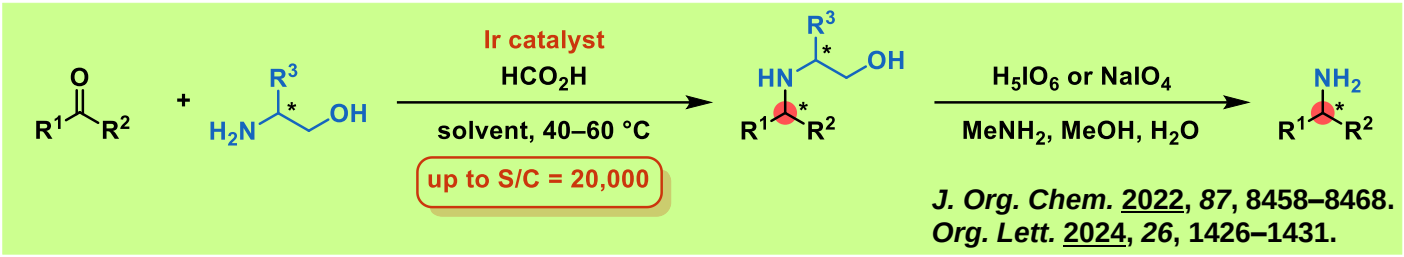
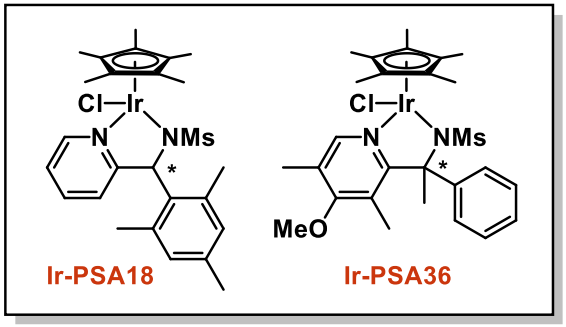
Asymmetric Reductive Amination Catalysts



J. Org. Chem. 2022, *87*, 8458–8468.
Org. Lett. 2024, *26*, 1426–1431.

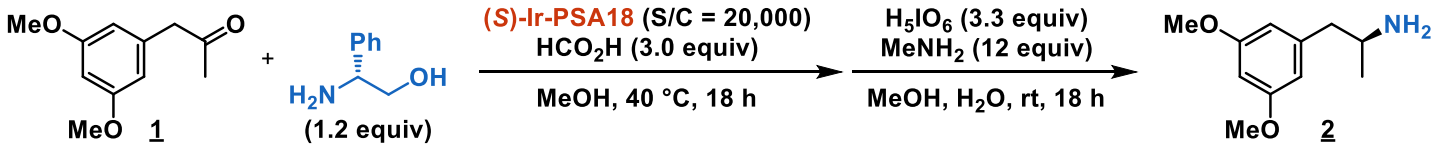
Chiral Iridium Complexes for Asymmetric Reductive Amination



- Preparation of chiral primary amines (β-aminotetralins, α-amino acids …)
- Using chiral amino alcohol as a chiral auxiliary
- Easy removal of chiral auxiliaries under mild oxidative conditions
- High catalytic activity and diastereoselectivity
- Using formic acid as a hydrogen source

Please see the brochure for details https://www.kanto.co.jp/dcms_media/other/OFC-12_EN.pdf

Typical procedure



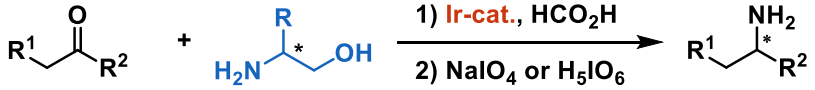
1

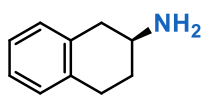
2

91%, 95% ee

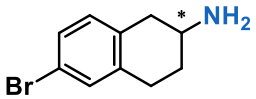
To a mixture of ketone **1** (966 mg, 4.97 mmol), (*R*)-phenylglycinol (828 mg, 6.04 mmol) and HCO_2H (566 µL, 15.0 mmol) in MeOH (5 mL) was added **(*S*)-Ir-PSA18** (0.168 mg, 0.252 µmol) under Ar atmosphere. The reaction vessel was connected to inert gas line of balloon because of CO_2 gas evolution during the reaction. After stirring for 18 h at 40 °C, the reaction was quenched by adding a sat. $NaHCO_3$ aq., and the mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. To a mixture of this crude material, 40% $MeNH_2$ aq. (5.0 mL, 60 mmol) in MeOH/H_2O (1/1, 30 mL) was added H_5IO_6 (3.77 g, 16.5 mmol). After stirring for 18 h, the reaction was quenched by adding a sat. $NaHCO_3$ aq. and 10% (w/w) $Na_2S_2O_3$ aq., and the mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography to afford optically active amine (*S*)-**2** (889 mg, 91%, 95% ee).

Substrate Scope

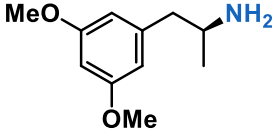




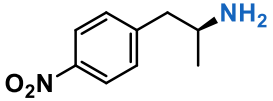
S/C = 5,000
80% isolated yield
82% ee



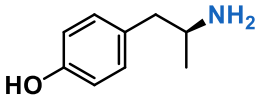
S/C = 1,000
86% isolated yield
82% ee



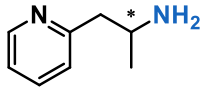
S/C = 20,000
91% isolated yield
95% ee



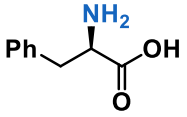
S/C = 5,000
93% isolated yield
96% ee



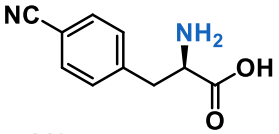
S/C = 5,000
68% isolated yield
97% ee



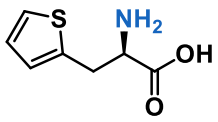
S/C = 5,000
81% isolated yield
90% ee



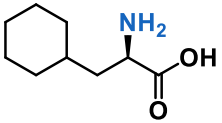
S/C = 20,000
74% isolated yield
96% ee



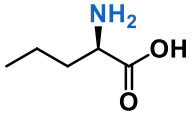
S/C = 2,000
75% isolated yield
96% ee



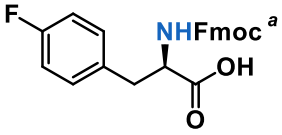
S/C = 2,000
73% isolated yield
98% ee



S/C = 2,000
84% isolated yield
99% ee



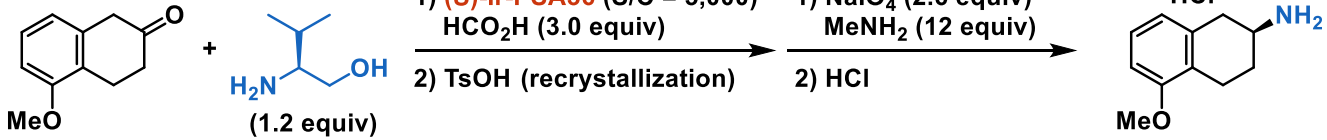
S/C = 2,000
88% isolated yield
98% ee



S/C = 2,000
78% isolated yield
98% ee

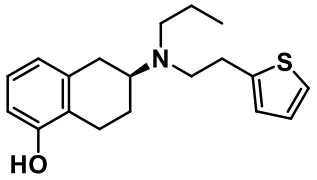
[a] *N*-Fmoc amide could be obtained by sequential Fmoc-amidation.

Large Scale Reaction



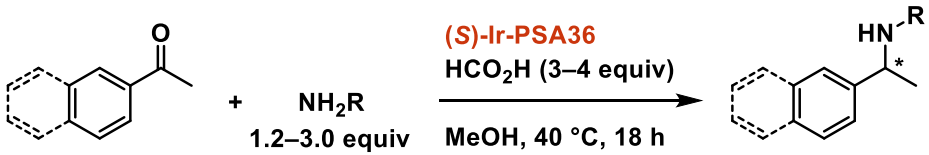
150 g scale

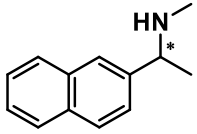
72% (from ketone)
>99% ee
Ir < 1 ppm



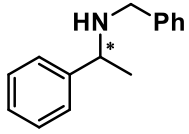
Rotigotine
For Parkinson's disease

Direct Asymmetric Reductive Amination to *N*-Alkylamines

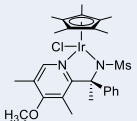
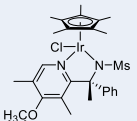
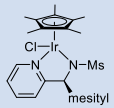
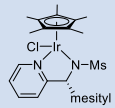
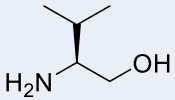
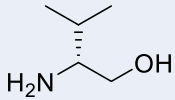
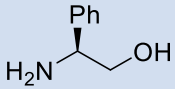
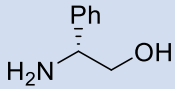




S/C = 1,000
>99% yield
69% ee



S/C = 500
94% yield
73% ee

Structure	Product No.	Package	Structure	Product No.	Package
Asymmetric Reductive Amination Catalyst, Reagents					
 (*S*)-Irr-PSA36	07658-68	100 mg	 (*R*)-Ir-PSA36	07035-68	100 mg
 (*S*)-Ir-PSA18	07060-68	100 mg	 (*R*)-Ir-PSA18	07071-68	100 mg
 L-Valinol	44078-52	5 g	 (*R*)-(-)-2-Amino-3-methyl-1-butanol	42247-2A	5 g
	44078-32	25 g		42247-3A	25 g
 (*S*)-(+)-Phenylglycinol	30757-1A	1 g	 D(-)-α-Phenylglycinol	18382-1A	5 g
	30757-2A	5 g		18382-2A	25 g
$NaIO_4$ Sodium periodate	37233-30	25 g	H_5IO_6 Orthoperiodic acid	32061-30	25 g
	37233-20	100 g			
	37233-00	500 g			

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Our Products (Catalysts and Ligands)
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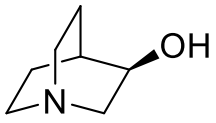
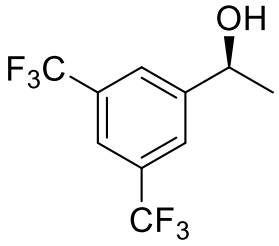
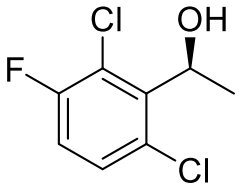
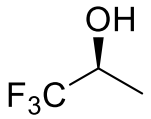
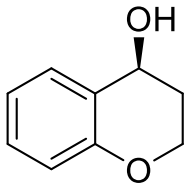
Product Examples We can Offer

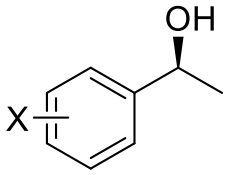


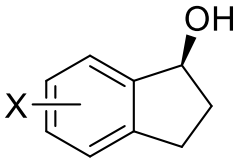


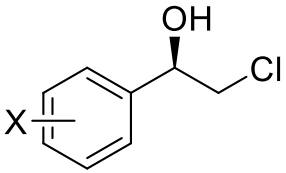


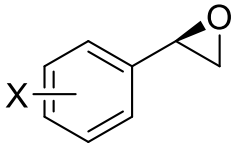


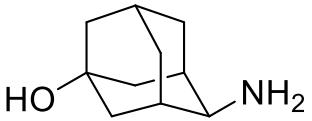


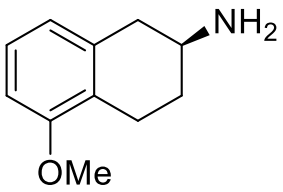


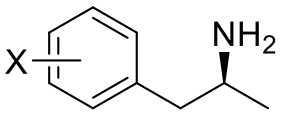


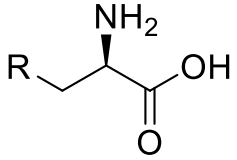


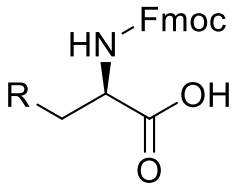


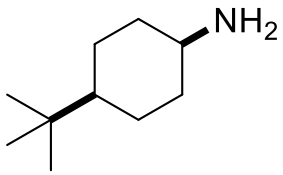






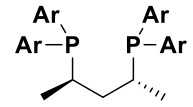




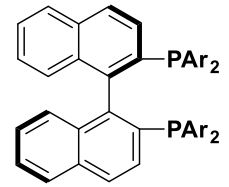


- We can also supply these compounds in bulk scale.
- Both enantiomers are available.
- Only a part of products is listed here.
- If you need other compounds, please feel free to contact us.

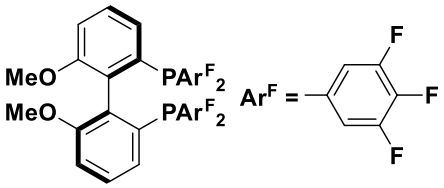
Ligand Examples We can Offer

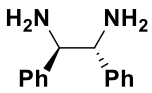


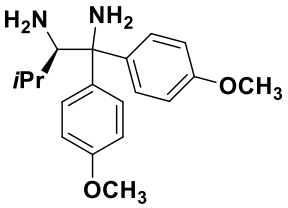
Ar = 3,5-*i*Pr$_2$C$_6$H$_3$
3,5-(CH$_3$)$_2$C$_6$H$_3$
Ph

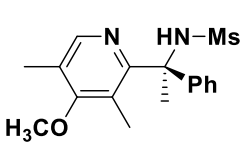


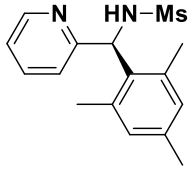
Ar = 3,5-(CH$_3$)$_2$C$_6$H$_3$
4-CH$_3$C$_6$H$_4$
Ph

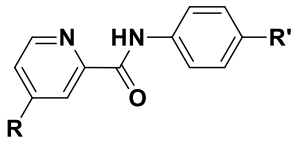


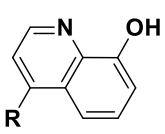


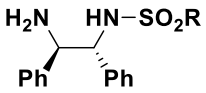




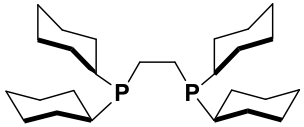


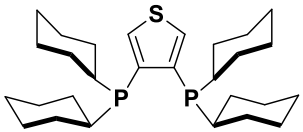


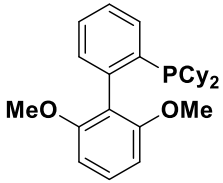


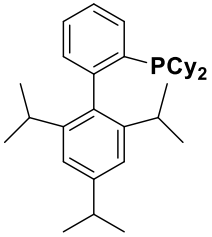


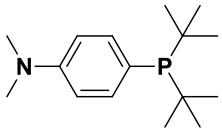
R = 4-(CH$_3$)C$_6$H$_4$
CH$_3$
Bn
2,6-(CH$_3$)$_2$Bn
*i*Bu
10-Camphor











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