ASYMMETRIC HYDROGENATION OF KETONES

chiral Ru cat:

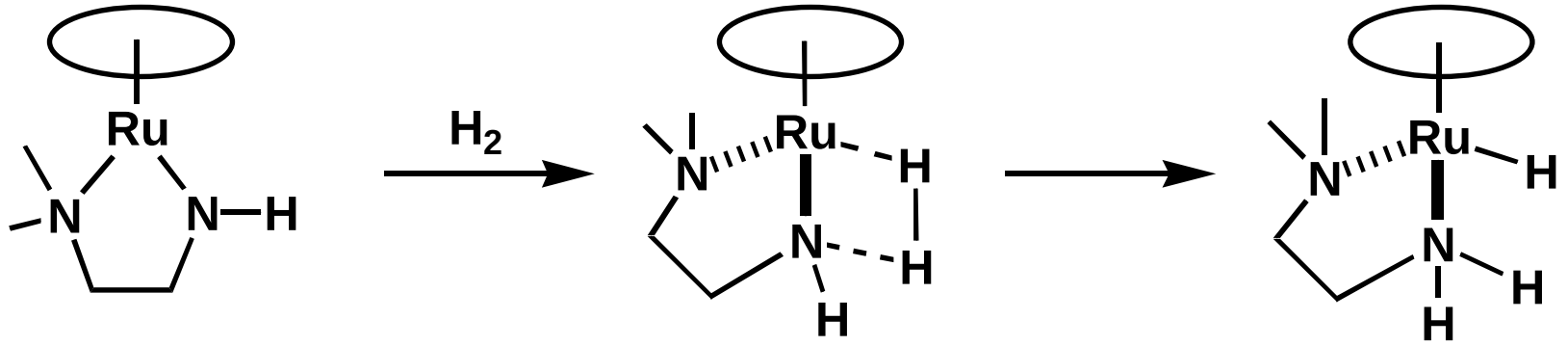
- **$RuCl_2$(binap)(chiral diamine) + base**

  Ohkuma, Noyori, **1995, 1998**

- **Cp*RuCl(cod) + chiral diamine + base**

  Ito, Hirakawa, Ikariya, **1998**

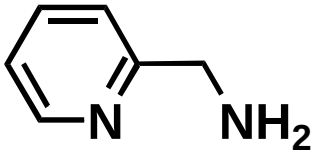
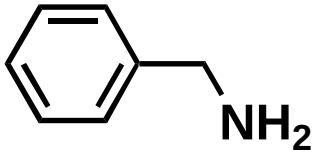
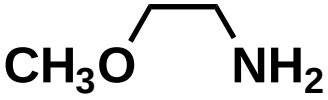
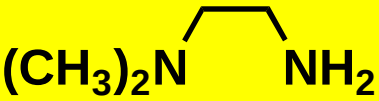
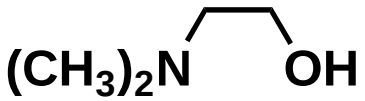
A key step of H_2 activation



Ru–amide complex

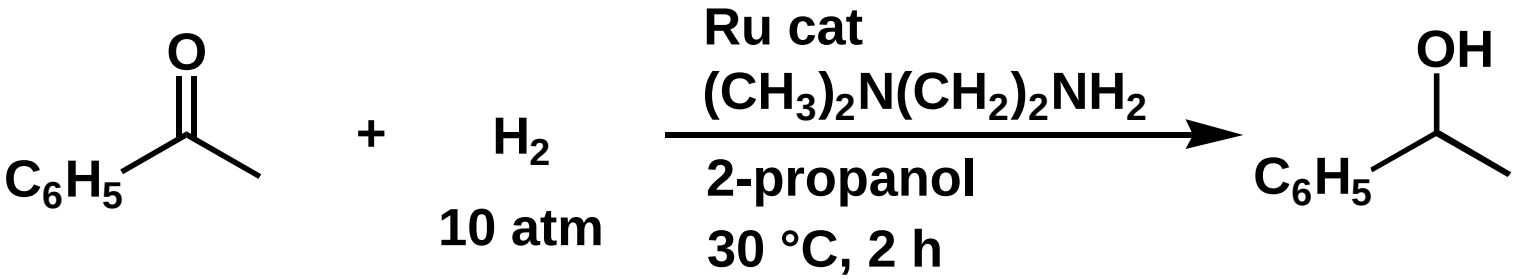
Ru–amine complex

EFFECT OF LIGAND STRUCTURES ON ACTIVITY

amine	conv, %[a]	amine	conv, %[a]	amine	conv, %[a]
none	<1		37		57
	3		41		0
	2		98		0
	6		100		0

Conditions: acetophenone:Ru:diamine:KOH = 100:1:1:1 P_{H2} = 1 atm, 30 °C,1 h, 2-propanol [a] Determined by ^{1}H NMR.

CATALYST PRECURSOR FOR THE HYDROGENATION

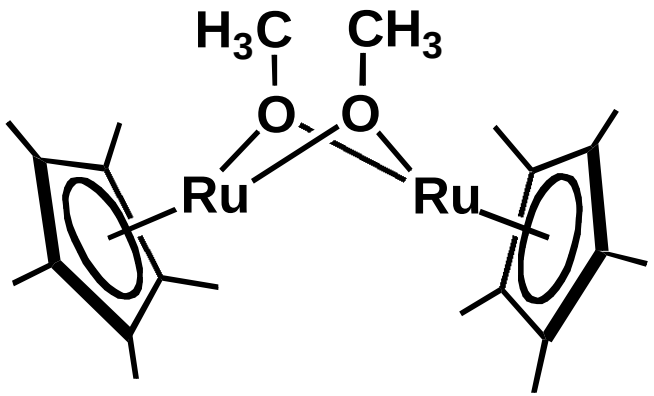


ketone:Ru:diamine = 1000:1:1

TOF = 100

TOF = product mol/cat mol·h

Ru cat:



SOLVENT EFFECT ON THE TURNOVER NUMBERS

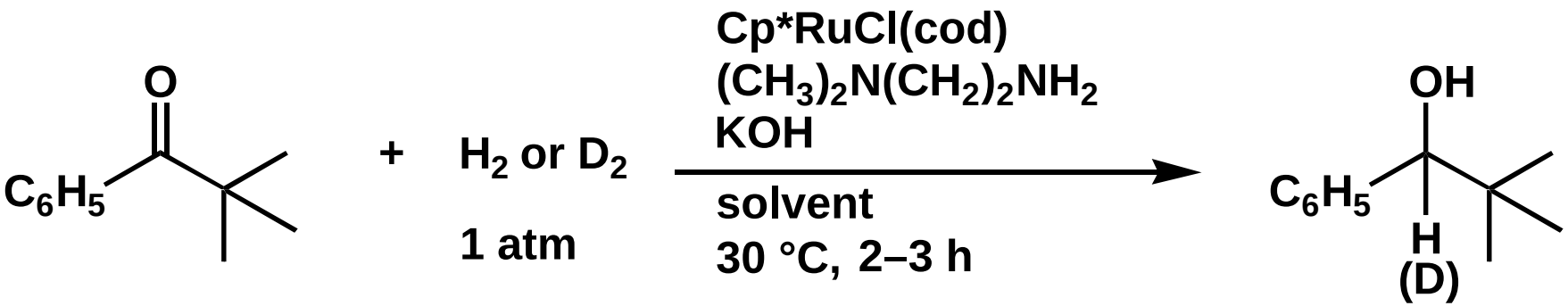
solvent	TON[a]
methanol	70
ethanol	300
2-propanol	200
tert-butyl alcohol	20
THF	65
CH_3CN	30
DMF	70
CH_2Cl_2	0
hexane	0

Conditions: Ru cat 0.2 mol%, H_2 10 atm, 30 °C, 2 h

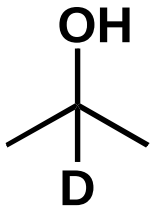
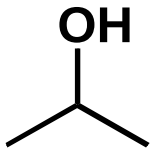
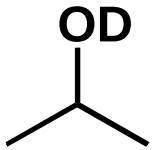
Ru cat = $(Cp^*RuOCH_3)_2$ + $(CH_3)_2N(CH_2)_2NH_2$

[a]TON = product mol/cat mol

ISOTOPE LABELING EXPERIMENTS

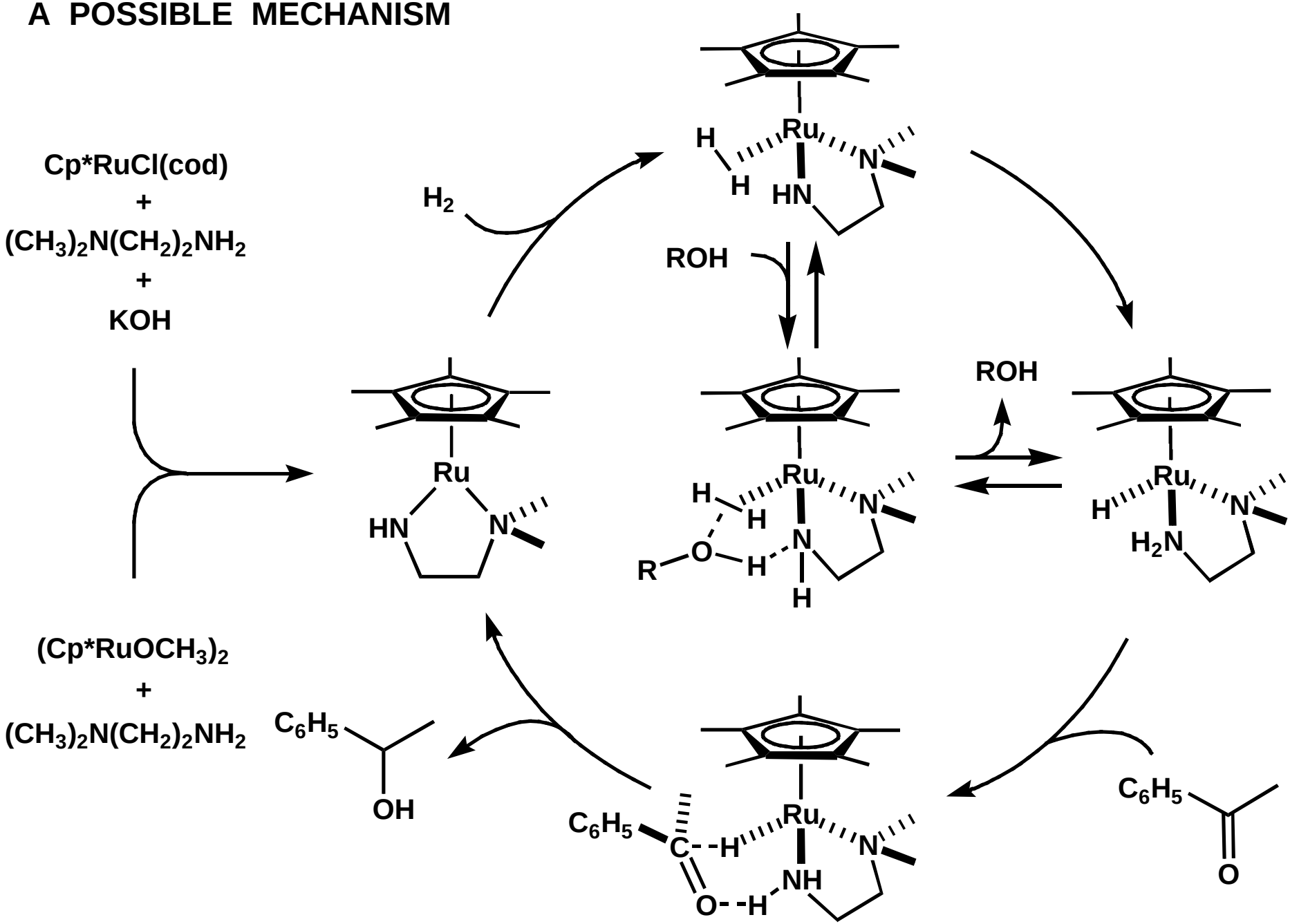


ketone:Ru:diamine:KOH = 100:1:1:1 ~100% yield

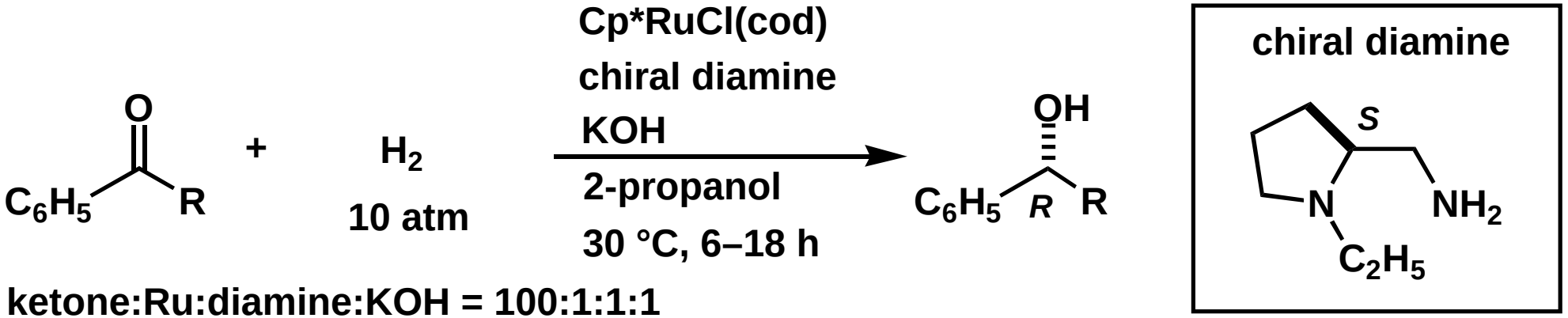
H_2 or D_2	solvent	D content, %[a]
H_2		0
D_2		7
D_2		90

[a] Determined by ^{1}H NMR and D NMR.

A POSSIBLE MECHANISM

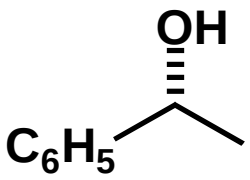


ASYMMETRIC HYDROGENATION WITH CHIRAL Ru CATALYSTS

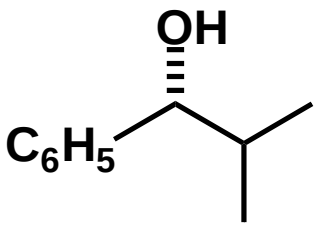


ketone:Ru:diamine:KOH = 100:1:1:1

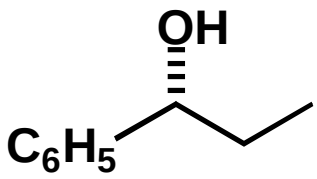
examples:



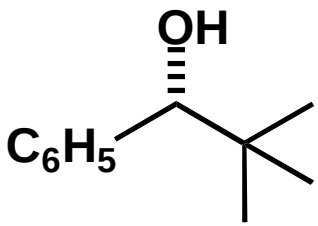
72% *ee* (*R*)



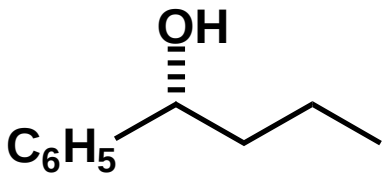
73% *ee* (*R*)



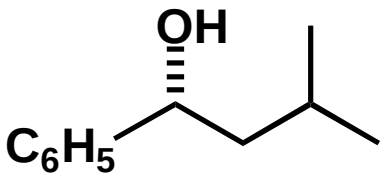
79% *ee* (*R*)



81% *ee* (*R*)

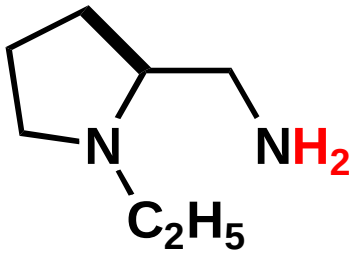


79% *ee* (*R*)

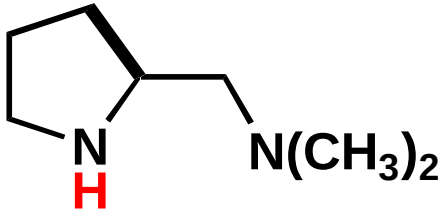


88% *ee* (*R*)

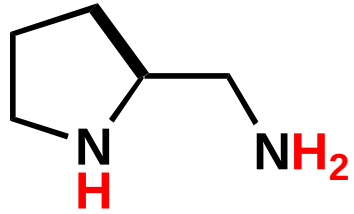
EFFECT OF STRUCTURES OF DIAMINES ON THE *ee* VALUES



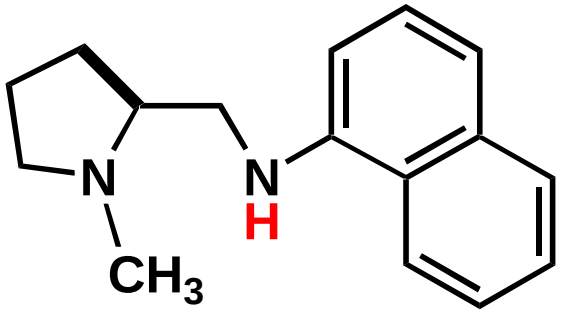
72% *ee* (*R*)



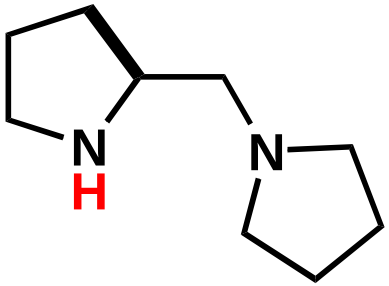
13% *ee* (*S*)



3% *ee* (*R*)

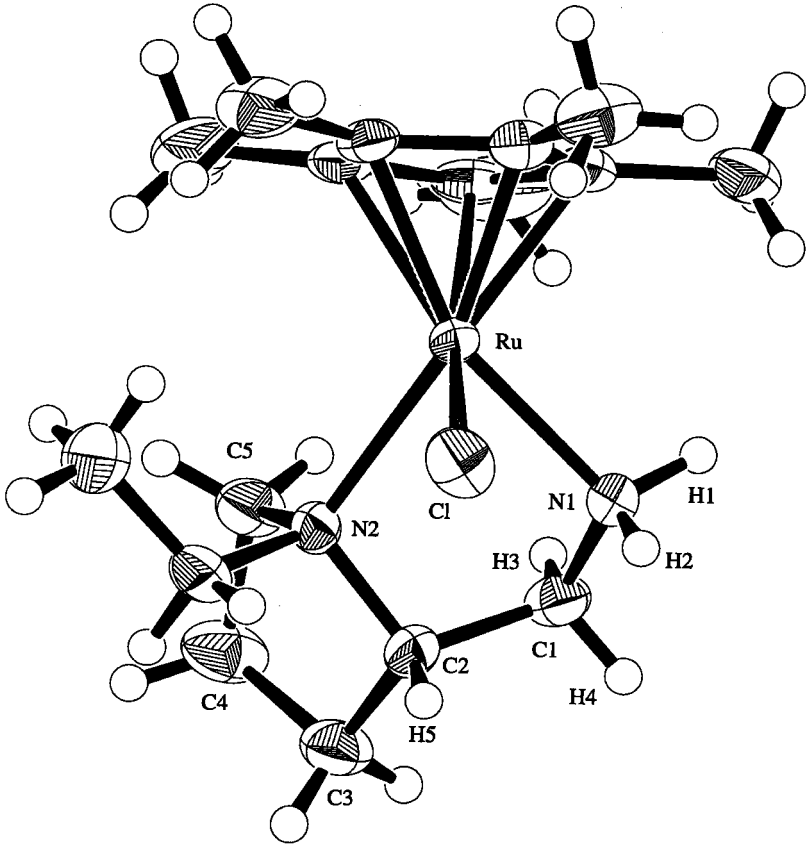


13% *ee* (*R*)

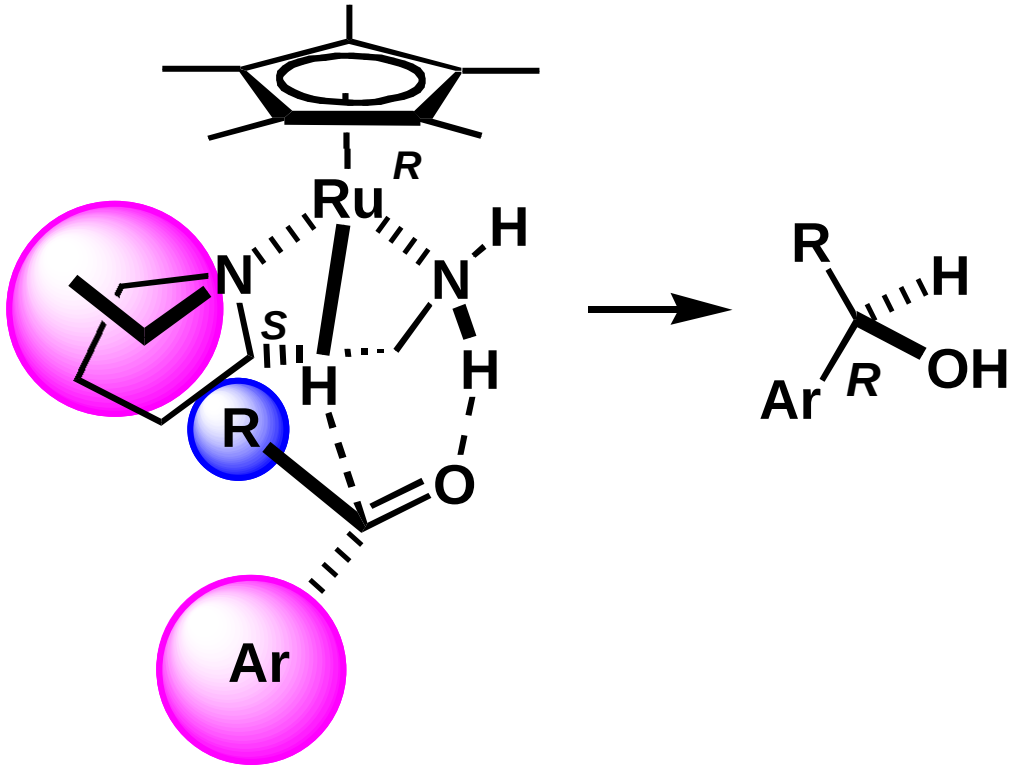


40% *ee* (*S*)

ENANTIO–FACE SELECTION OF KETONE



catalyst precursor



possible transition state