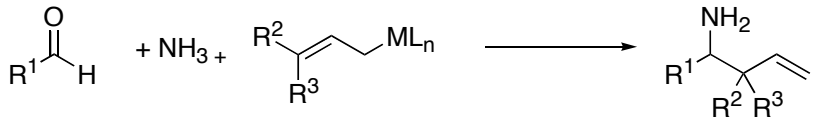
□-Aminoallylation of Aldehydes with Ammonia: Stereoselective Synthesis of Homoallylic Primary Amines



Masaharu Sugiura, Keiichi Hirano and Shu Kobayashi

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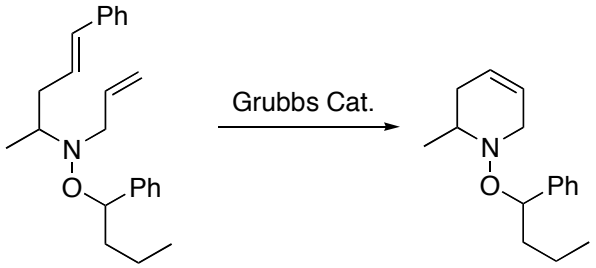
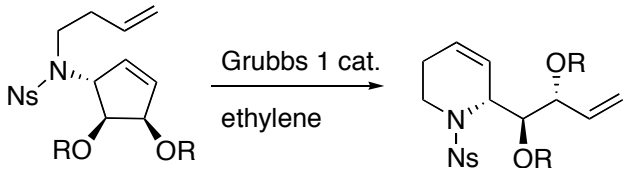
Uses of Homoallylic Amines

Ring Closing Metathesis

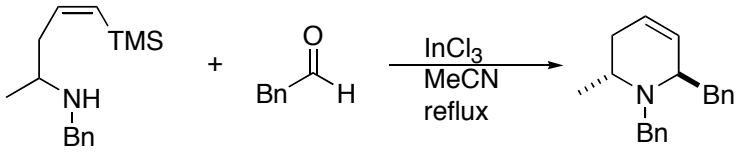


Chem Comm., 2000, 1771-1772

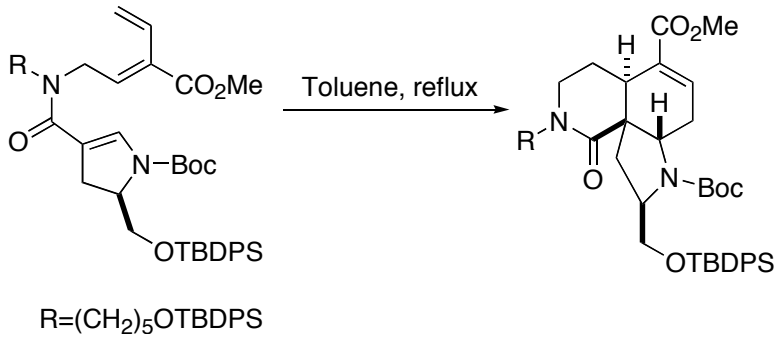


Chem Comm., 2000, 1501-1502

In Other Types of Reactions



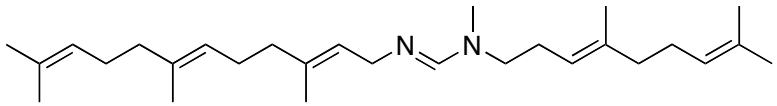
JOC, 2003, 7880-7883



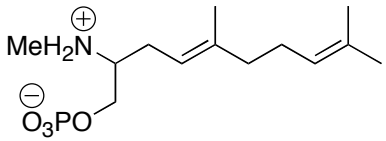
R=$(CH_2)_5$OTBDPS

JACS 1999, 866-867

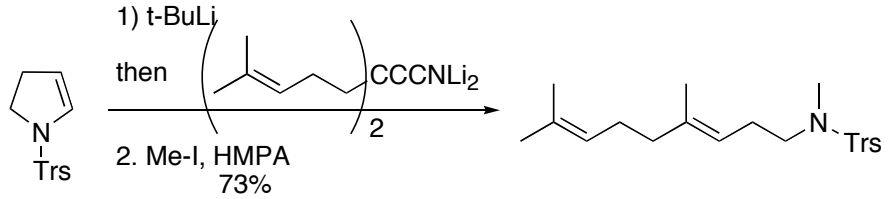
Squalene Synthetase Inhibitors



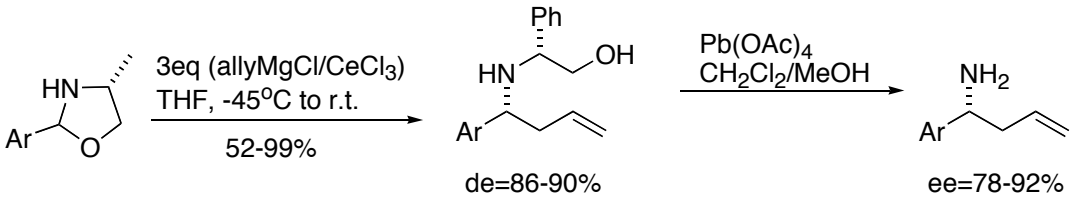
JOC **2001**, 531-537



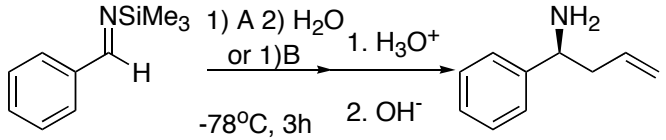
Synthesis of Homoallylic Amines



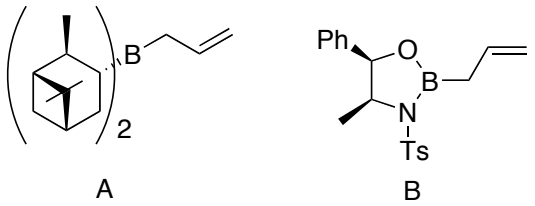
JOC **2001**, 531-537



Tetrahedron Asym. **1997**, 1895-1946

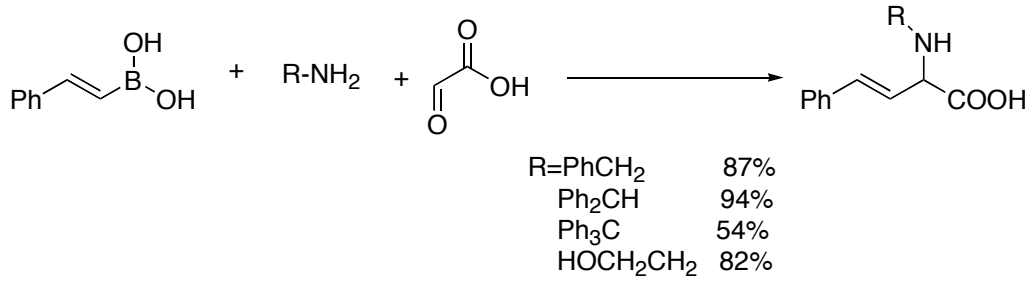


A: 70%, 73% ee No H_2O
90%, 92% ee w/ H_2O
B: 89%, 92% ee No H_2O



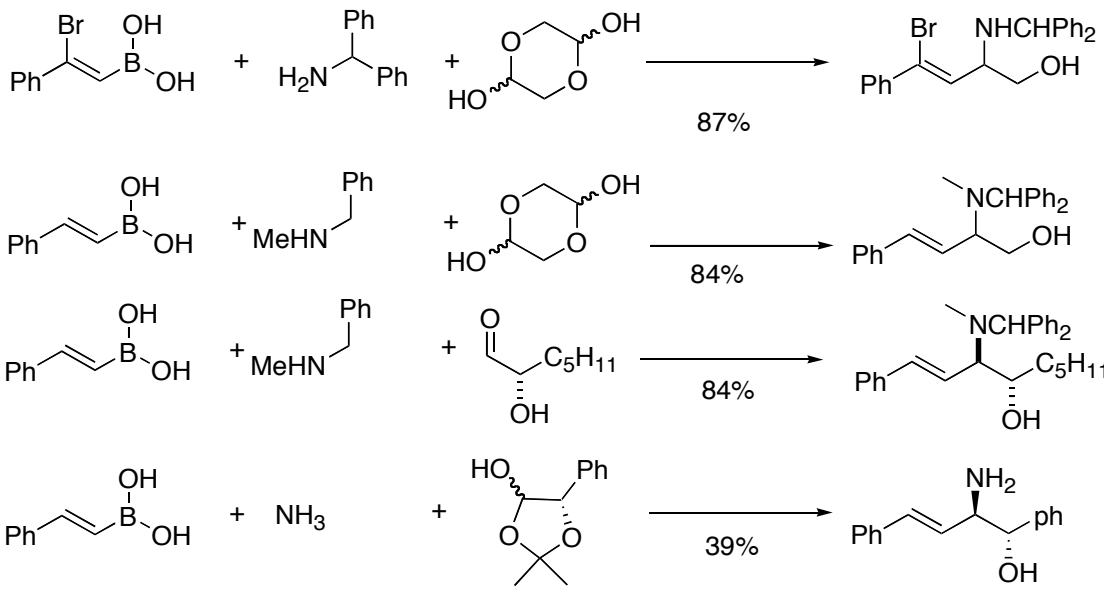
Angew. Chem. Int. Ed. **1999**, 825-826

Important Work on Allylic Amines



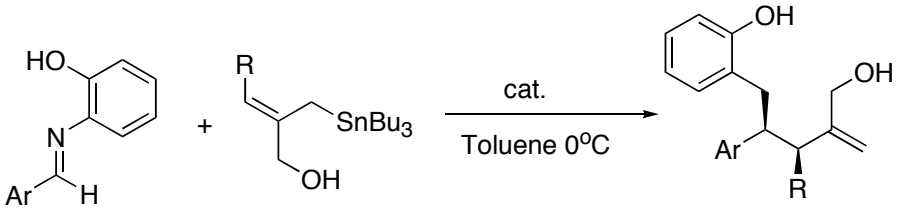
R=$PhCH_2$ 87%
Ph_2CH 94%
Ph_3C 54%
$HOCH_2CH_2$ 82%

JACS **1997,** 445-446



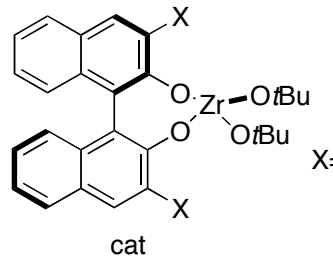
JACS **1998,** 11798-11799

Kobayashi's Work Toward Homoallylic Amine Synthesis



R=Me 71-84% yield
87-95% ee

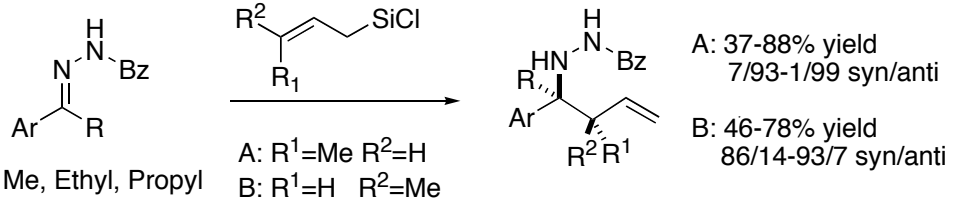
R=H 68-85% yield
96-99% ee



X=Cl or Br

cat

Angew. Chem. Int. Ed. **2001**, 1896-1898

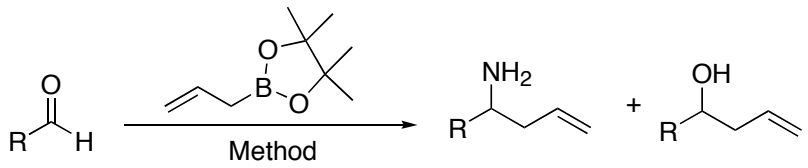


A: 37-88% yield
7/93-1/99 syn/anti

B: 46-78% yield
86/14-93/7 syn/anti

JOC **2002,** 67, 5359-5364

-Aminoallylation of Aldehydes with Ammonia



R	Method	Yield	
Ph	A	84	3
Ph	B	80	8
p-NO_2Ph	A	96	<1
p-BrPh	A	92	5
p-MeOPh	A	91	4
o-HOPh	A	76	<1
(pyridin-2-2yl)	A	85	nd
(thiophen-2-yl)	A	77	12
(*E*)-PhCH=CH	A	75	3
$Ph(CH_2)_2$	C	78	3
c-C_6H_{11}	C	80	4
(+/–)PhCHMe	C	69	4
HO_2C	B	Quant	nd

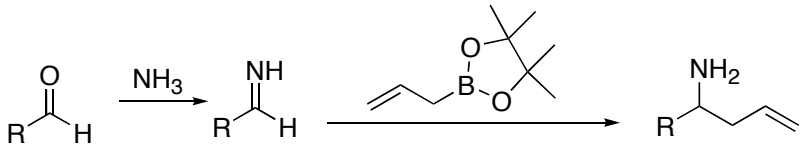
Method A- Pre-mixing of Aldehyde and liquid ammonia in ethanol for 2hr at -10 °C.
Then allylboronate was addedand the reaction was stirred at -10 °C for 3hrs, then at rt for 1hr before work-up.

Method B- Pre-mixing of Aldehyde and 28-20 wt% aqueous ammonia in ethanol for 30 min at rt.
Then allylboronate was added and the reaction was stirred at rt for 2hr before work-up.

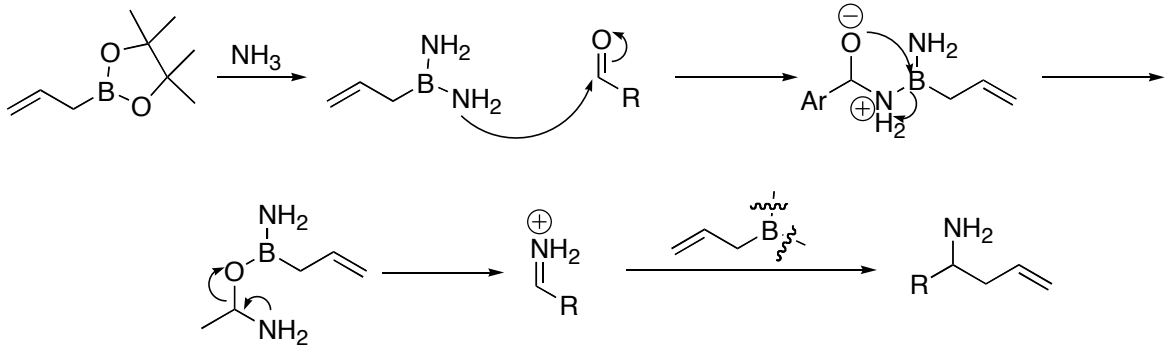
Method C- Pre-mixing of allylboronate and liquid ammonia in ethanol for 30 min at rt.
Then the aldehyde in ethanol was added and the reaction was stirred at rt for 2hr before work-up

Possible Reaction Pathways

Methods A and B



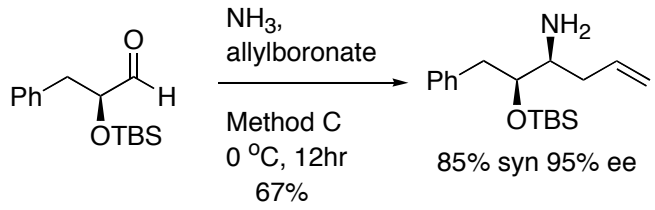
Method C

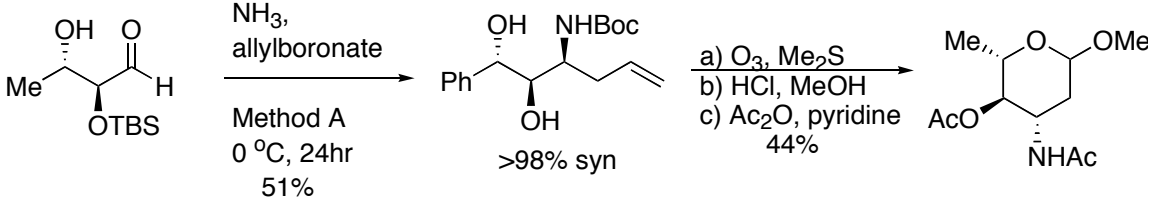


*Org. Let.***2004**, 1167-1169

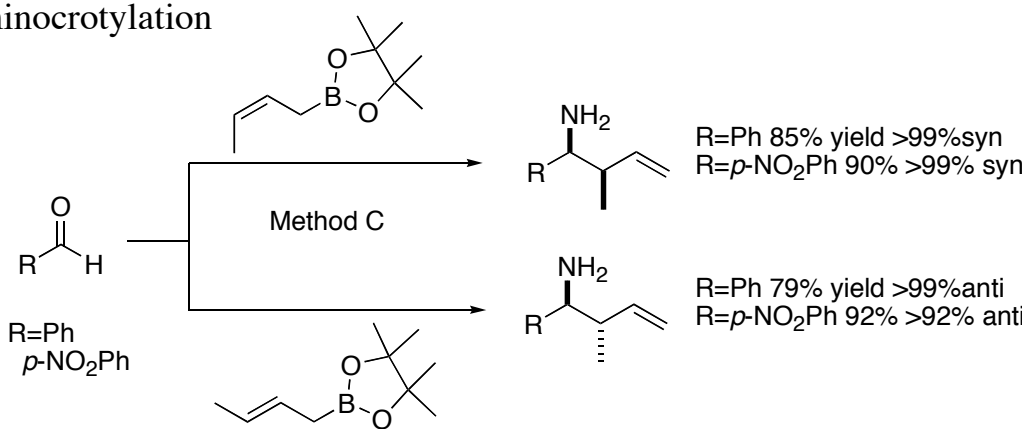
Selective □-Aminoallylation of Aldehydes with Ammonia

Diastereoselective Reactions of □□Oxyaldehydes





Stereospecific □□Aminocrotylation



Conclusions

Kobayashi has reported a direct route to unsubstituted homoallylic amines through the use of ammonia as the Nitrogen source.

The works well with a variety of aromatic aldehydes, though currently the methodology has not been expanded beyond these substrates.

The reaction has been shown to be highly selective both in %ee and syn/anti ratio when using □-Oxyaldehydes.Stereospecific □-Aminocrotylations have been shown to giive excellent selectives.

Currently the reaction has not been shown to be highly stereoselective in the presence of chiral boronate reagentsthough work in this area is on going