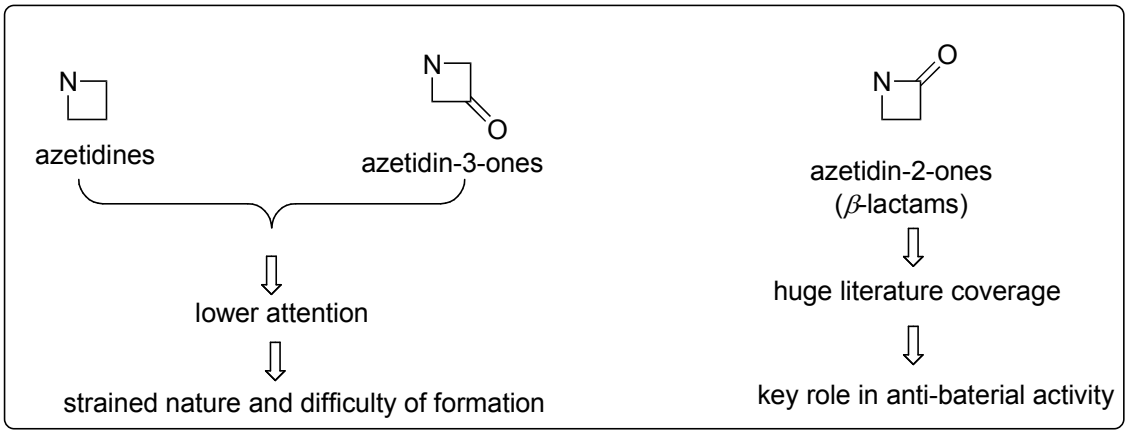
Syntheses of Azetidines and Azetidin-2-ones

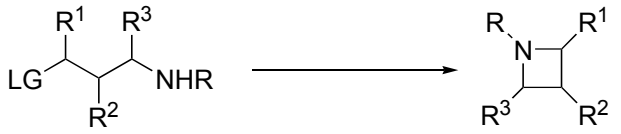


Contents (based on a recent review: Brandi A. et al. *Chem. Rev*. **2008**, *108*, 3988.)

1. Azetidines synthesis

1) Cyclization by nucleophilic substitution of amine nucleophiles

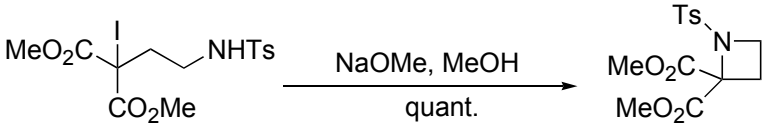
i) To Use Halides, Sulfonic esters, triflates, etc. as Leaving groups



LG= X, OMs, OTf, OTs

R= alkyl, Ar, OBn

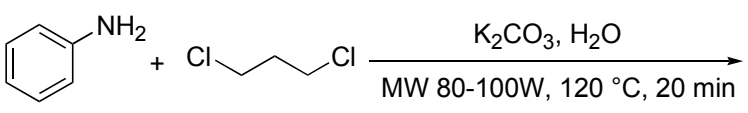
eg 1.



1 **2**

CL **1988**, 1065.

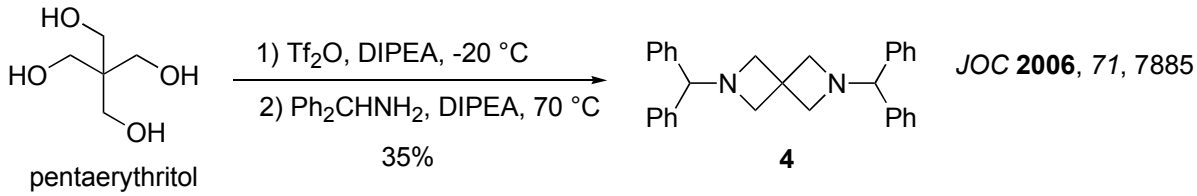
eg 2.



3

JOC **2006**, *71*, 135.

eg 3.



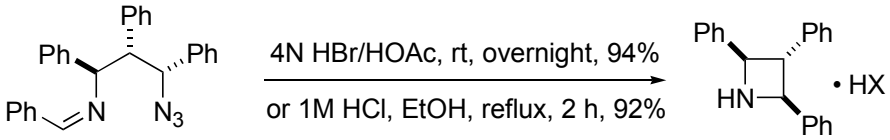
JOC **2006**, *71*, 7885

eg 4.

OBC **2007**, *5*, 3510

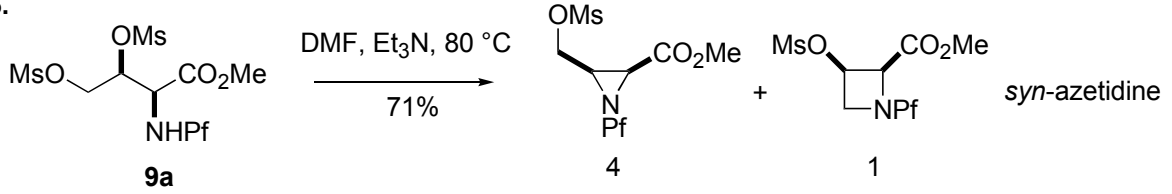
5 **6**

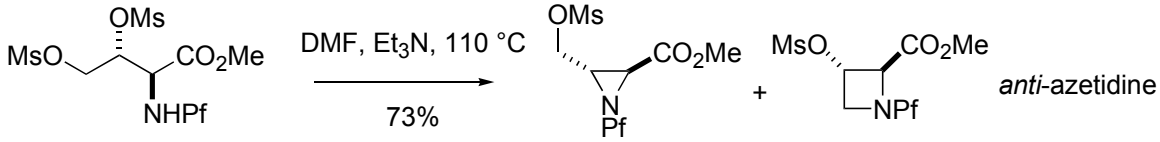
eg 5.

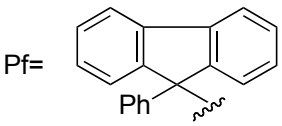


ARKIVOC **2005**, *xiii*, 8

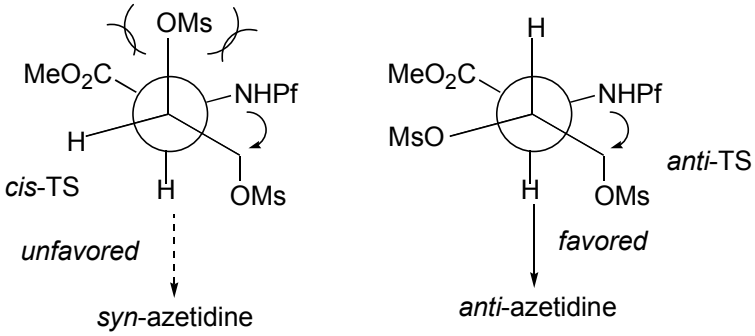
eg 6.



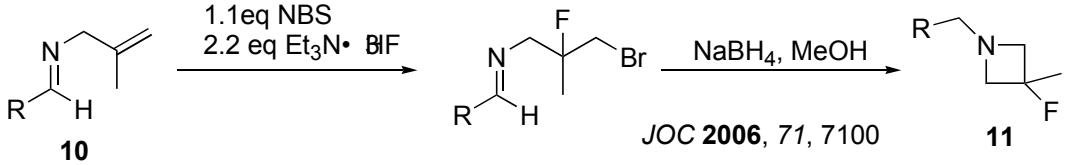




JOC **2002**, *67*, 3637



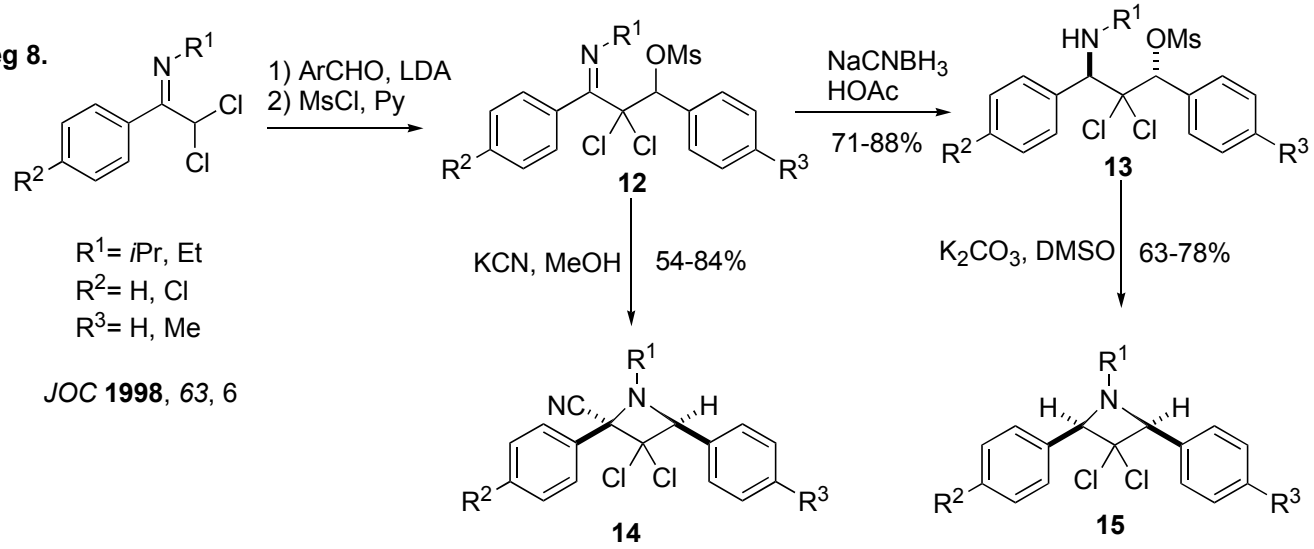
eg 7.



JOC **2006**, *71*, 7100

61-70%

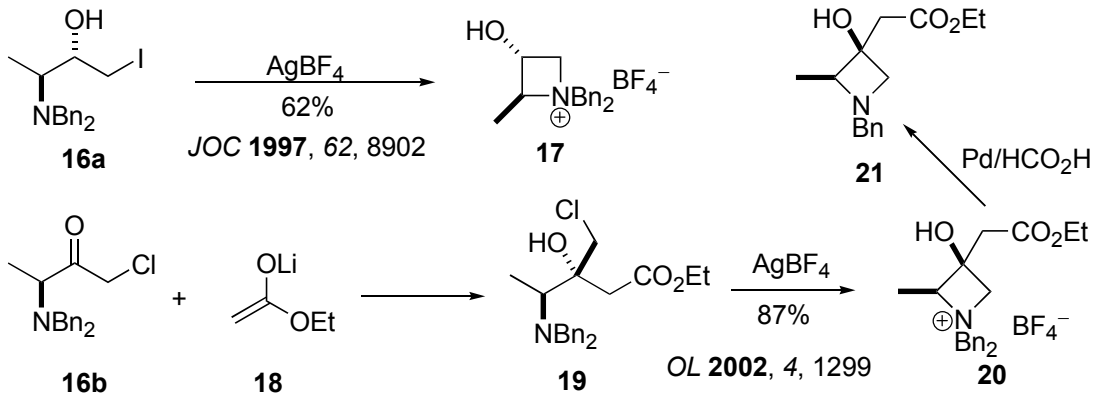
eg 8.



R^1= *i*Pr, Et
R^2= H, Cl
R^3= H, Me

JOC **1998**, *63*, 6

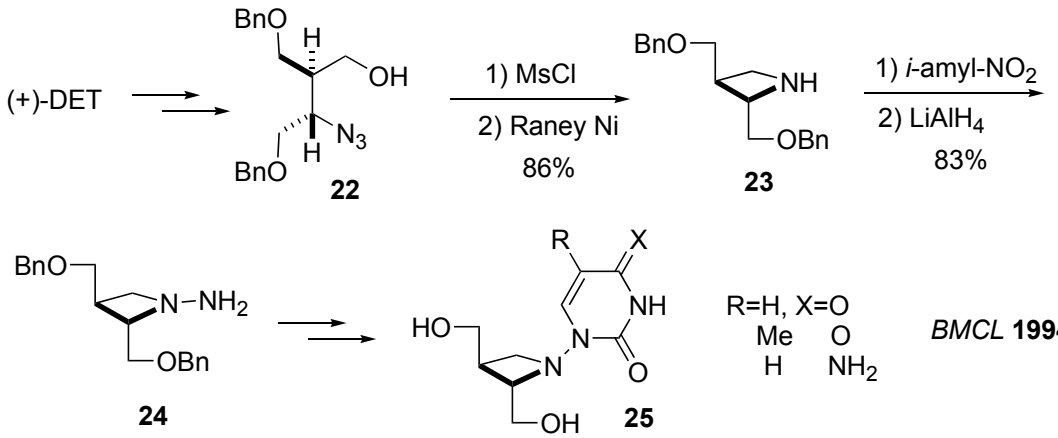
eg 9.



JOC **1997**, *62*, 8902

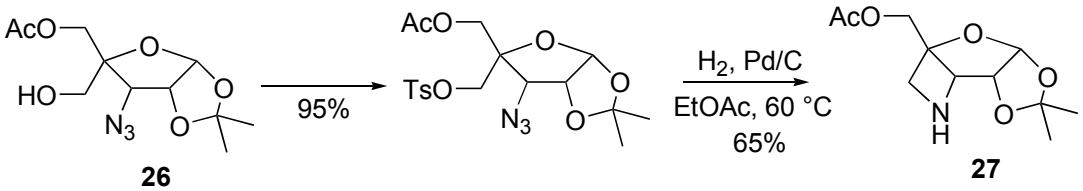
OL **2002**, *4*, 1299

eg 10.



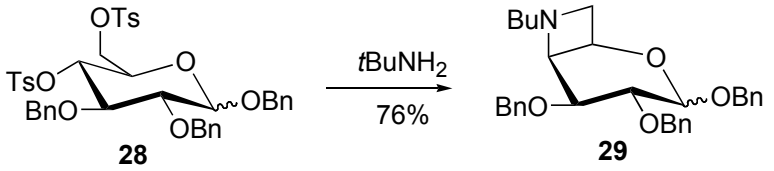
BMCL **1994**, *4*, 2083

eg 11.



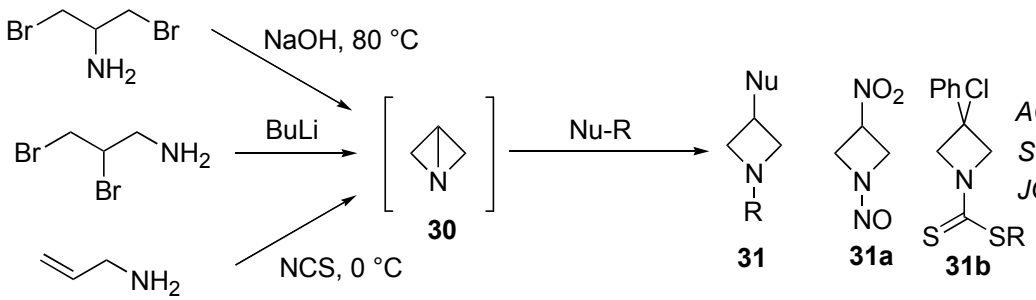
T **2003**, *59*, 1333

eg 12.



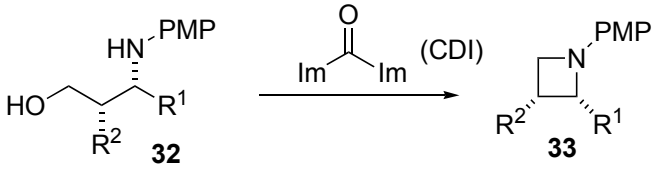
Carb. Res. **1997**, *299*, 253

eg 13.



ACIE. **1969**, *80*, 70
SC. **1998**, *28*, 3949
JOC. **1995**, *60*, 4943

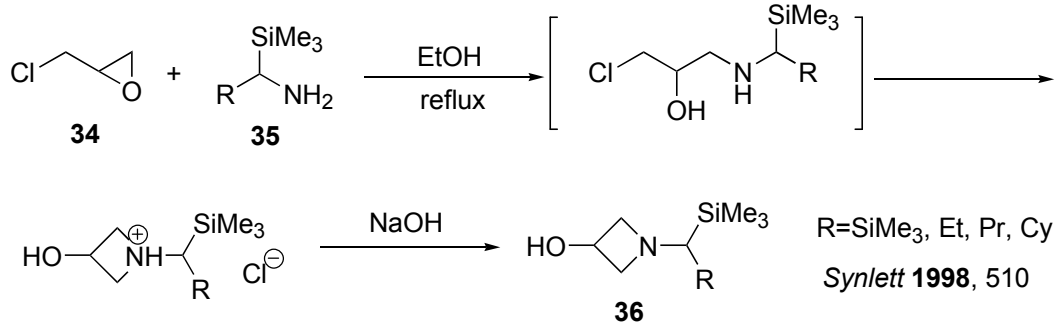
eg 14.



JOC. **2006**, *71*, 4147

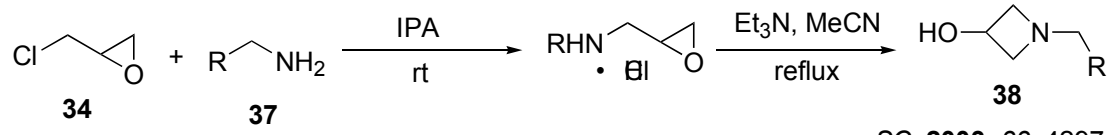
ii) Opening of Epoxides

eg 15.



R=$SiMe_3$, Et, Pr, Cy
Synlett **1998**, 510

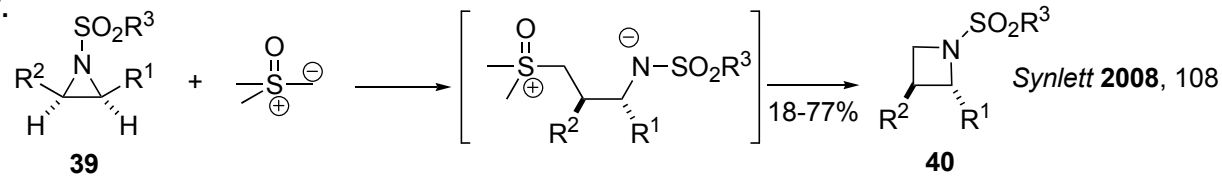
eg 16.



SC. **2003**, *33*, 4297

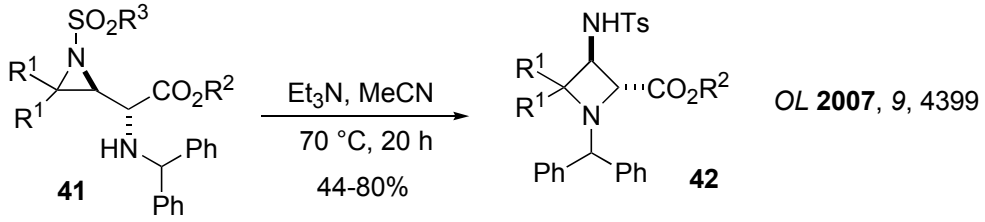
iii) Opening of Aziridines

eg 17.



Synlett **2008**, 108

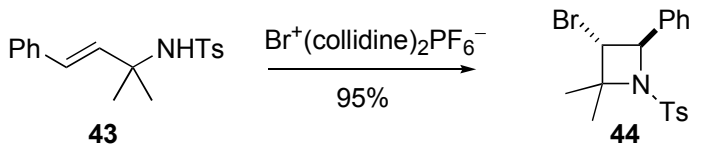
eg 18.



OL **2007**, *9*, 4399

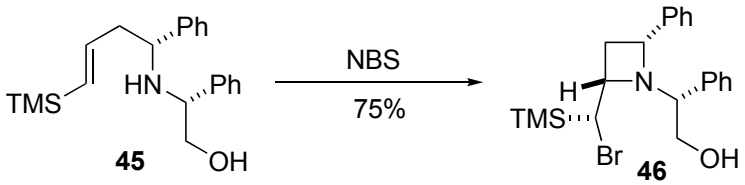
iv) Opening of Bromonium, Iodonium or Seleniranium Intermediates

eg 19.



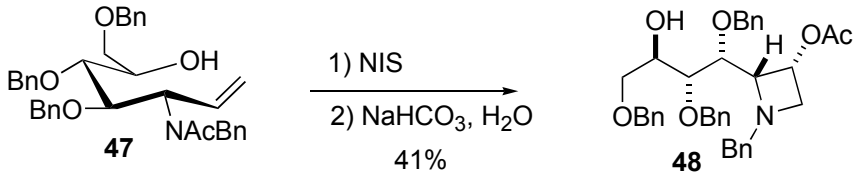
EJOC **2000**, 3007

eg 20.



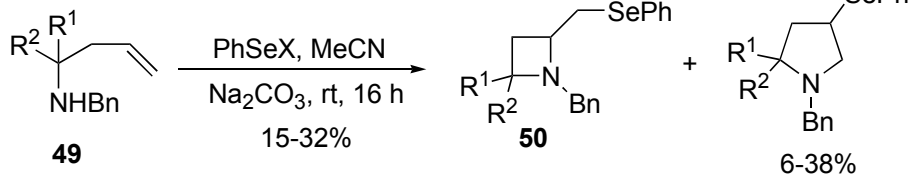
EJOC **2007**, 4517

eg 21.



Carb. Res. **2002**, *337*, 273

eg 22.

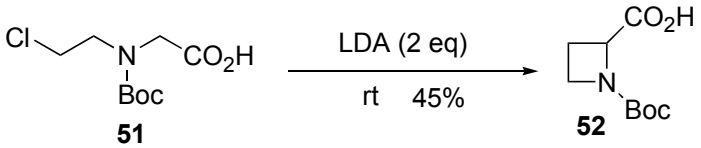


EJOC **2002**, 995

2) Cyclization by C-C bond formation

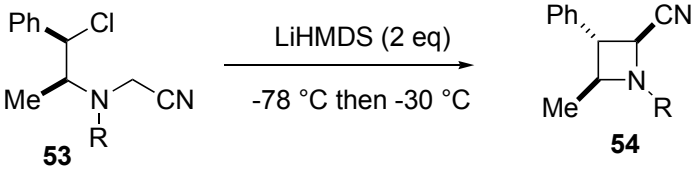
i) Carbanion-mediated cyclization

eg 23.



CC. **1994**, 879

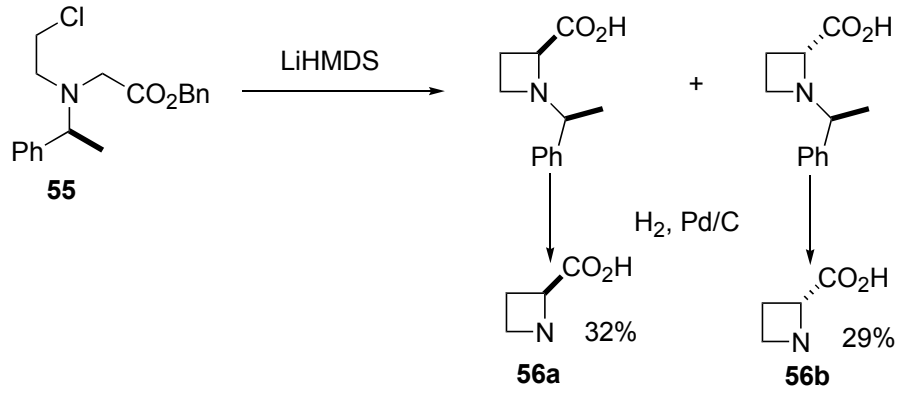
eg 24.



R= Me (78%)
Bn (84%)

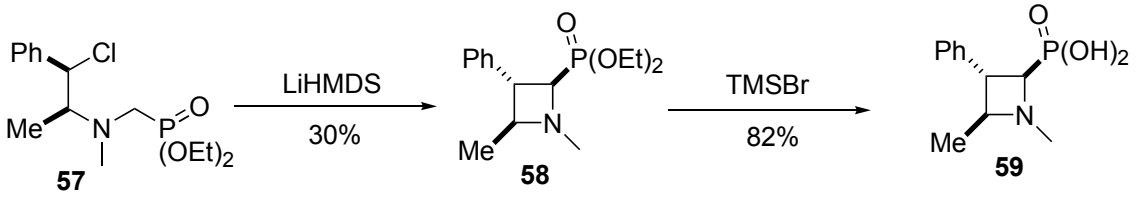
TA **2003**, *14*, 2407

eg 25.



JOC. **2005**, *70*, 9028

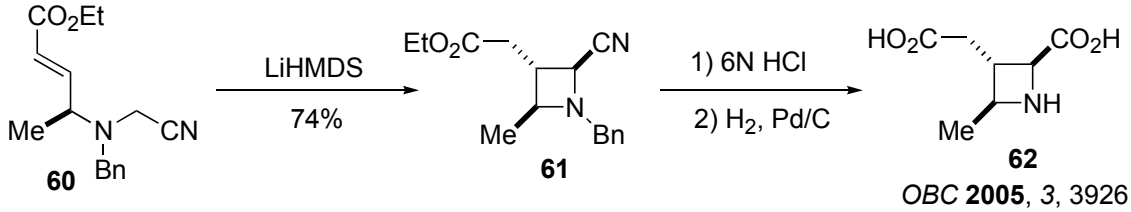
eg 26.



57 **58** **59**

TL **2002**, *43*, 4633

eg 27.

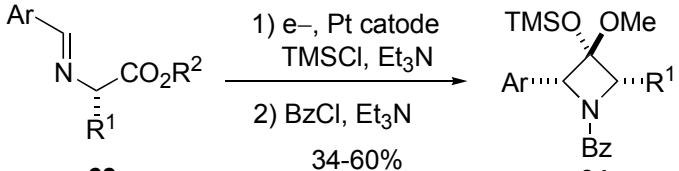


60 **61** **62**

OBC **2005**, *3*, 3926

ii) Radical cyclization involving C=O group

eg 28.

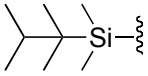


63 **64**

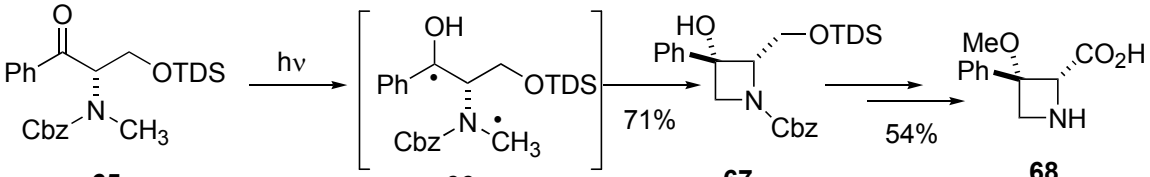
JACS **2003**, *125*, 11591

OL **2006**, *8*, 1323

TDS:



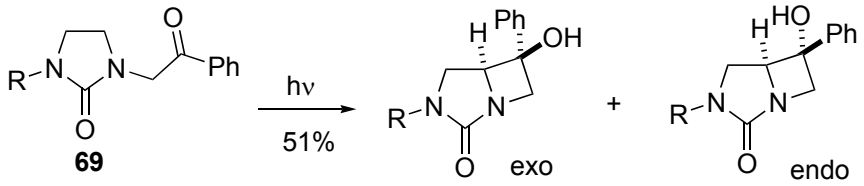
eg 29.



65 **66** **67** **68**

Helv. Chim. Acta **1998**, 81, 1803

eg 30.

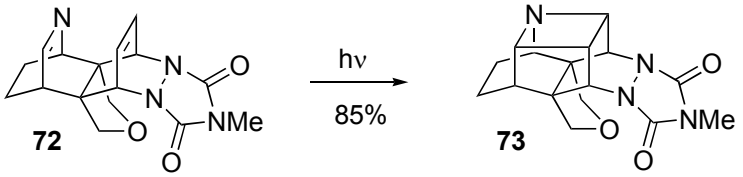


69 **70** **71**

CEJ **2002**, *8*, 2464

3) Cycloaddition

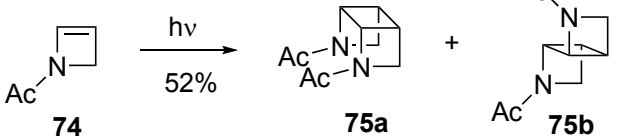
eg 31.



72 **73**

EJOC **2000**, 743

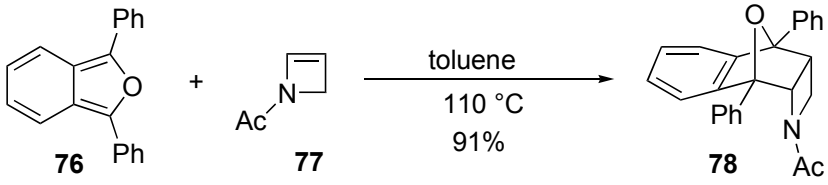
eg 32.



74 **75a** **75b**

TL **1998**, *39*, 5481

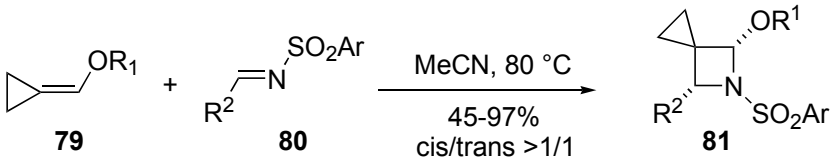
eg 33.



76 **77** **78**

TL **1999**, *40*, 443

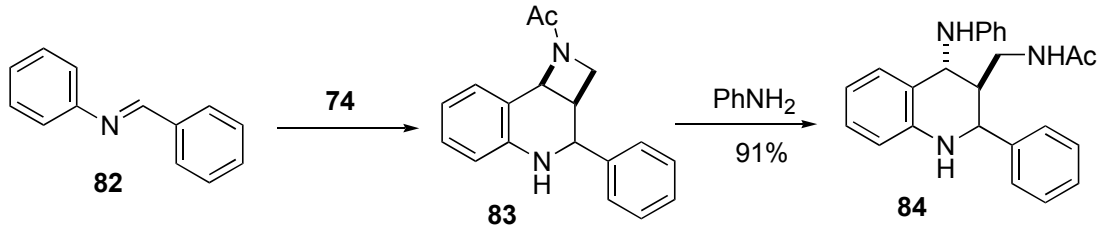
eg 34.



79 80 81

ACIE **2006**, *45,* 5176

eg 35.



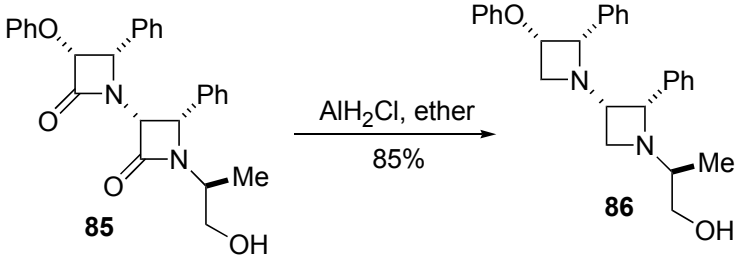
82 83 84

CC **2002**, 444

4) Reduction of Azetidin-2-ones

$LiAlH_4$ diborane alane/ether DIBAL-H AlH_2Cl

eg 36.

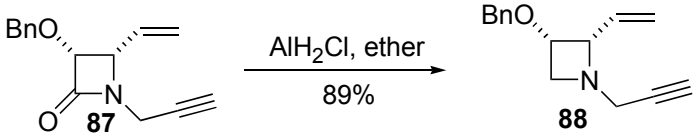


85 86

*JACS.***1983**, *105*, 6339

*JOC.***1991**, *56*, 5263

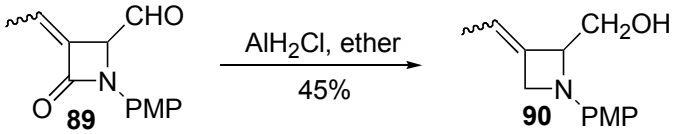
eg 37.



87 88

*JOC.***1998**, *63*, 6786

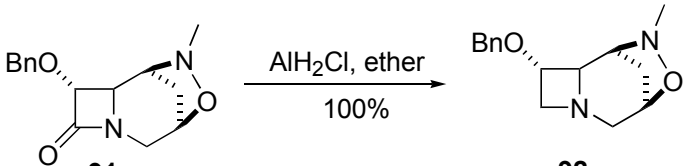
eg 38.



89 90

*JOC.***1994**, *59*, 7994

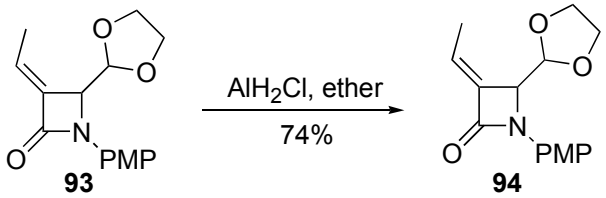
eg 39.



91 92

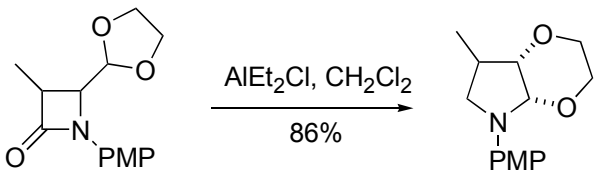
*EJOC.***2005**, 1680

eg 40.



93 94

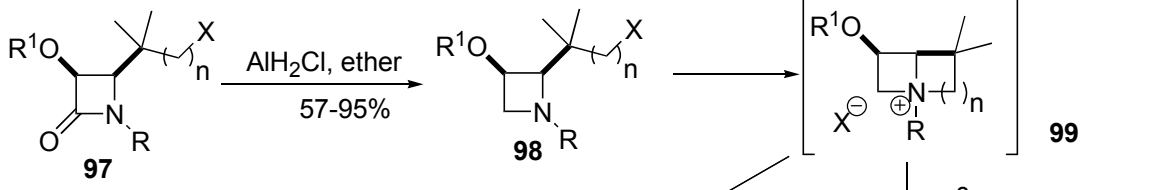
*JOC.***1994**, *59*, 7994



95 96

*JOC.***1999**, *64*, 9596

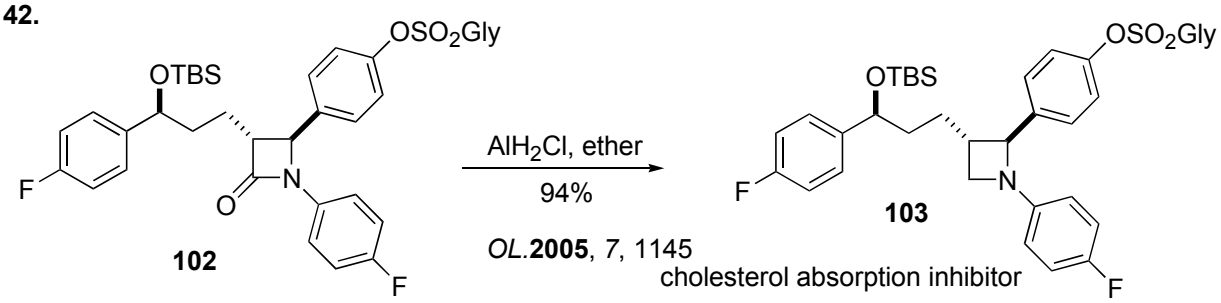
eg 41.



R= Bn, allyl, tBu, Cy
R^1= Me, Bn
X= Cl, Br
n= 0, 1
OL.**2006**, *8*, 1105

Nu= Cl, Br
OH, CN, N_3

eg 42.

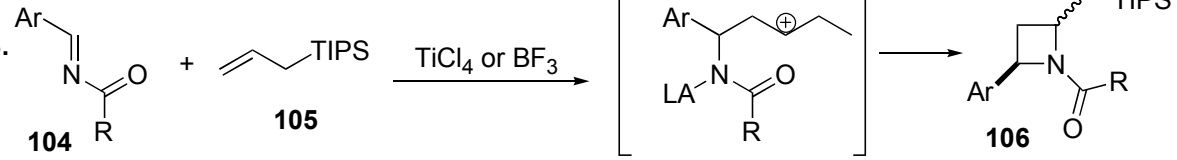


OL.**2005**, *7*, 1145
cholesterol absorption inhibitor

5) Other methods

i) Eletrophilic Attack on C=C

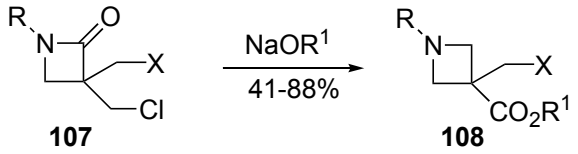
eg 43.



CL **1995**, 789

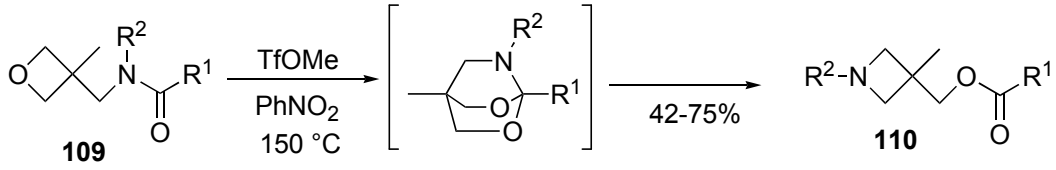
ii) Ring Rearrangement

eg 44.



TL **1991**, *32*, 4795

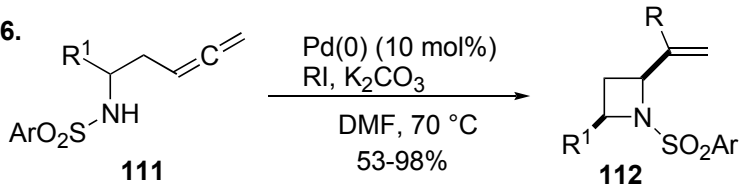
eg 45.



T **2002**, *58*, 7049

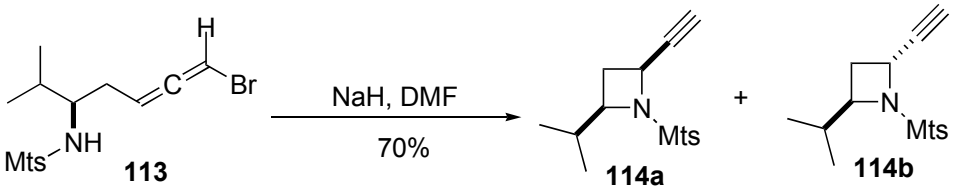
iii) Cyclization of β-amino allene

eg 46.



JOC. **2001**, *66*, 4904

eg 47.

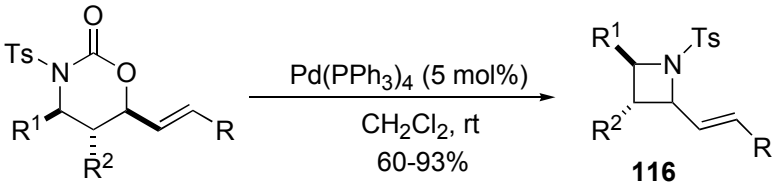


84 : 16

JACS. **2002**, *124*, 1525

iv) Pd-Catalyzed Decarboxylation

eg 48.

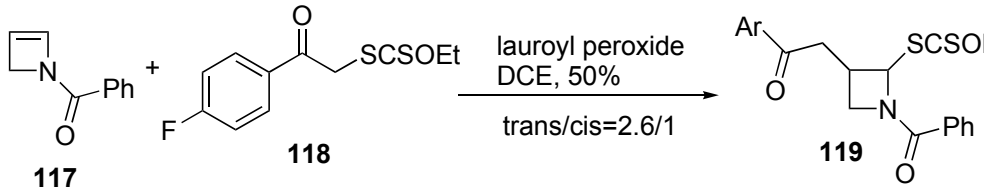


115 **116**

*JOC.***1994**, *59*, 1465

v) Others

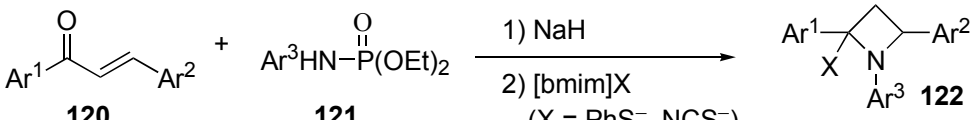
eg 49.



117 **118** **119**

*TL.***2000**, *41*, 9815

eg 50.



120 **121** **122**

76-89%

Synlett **2008**, 583

2. Important azetidine compounds

1) Natural products

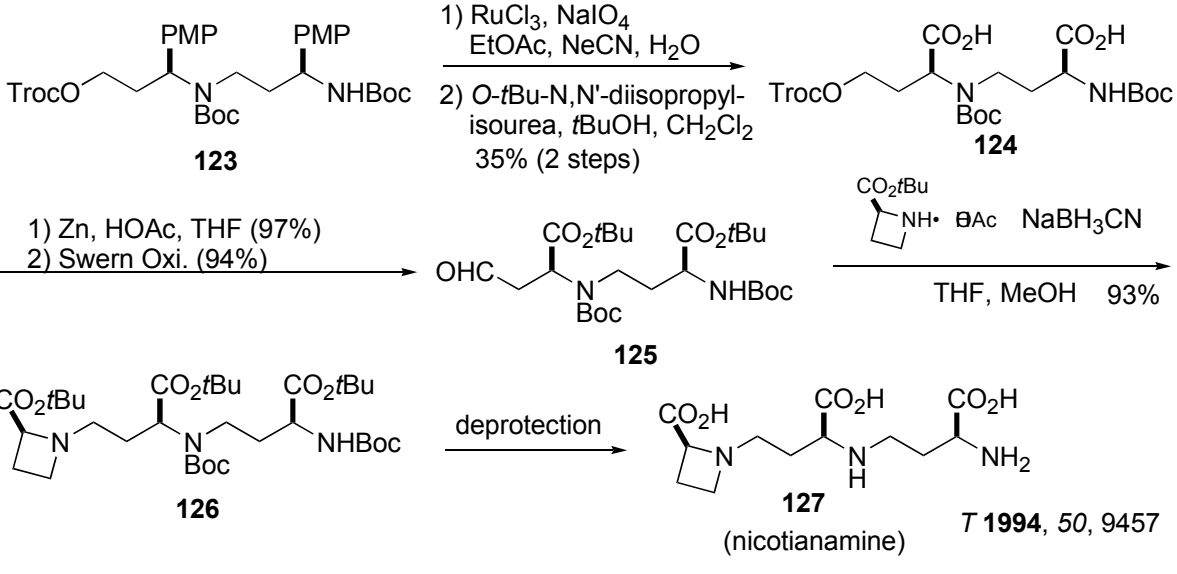
phytosiderophores
iron-chelating amino acids
promote uptake and transport of iron for chlorophyl biosynthesis

actomyosin ATPase-activating activity

protein Kinase C inhibitory activity

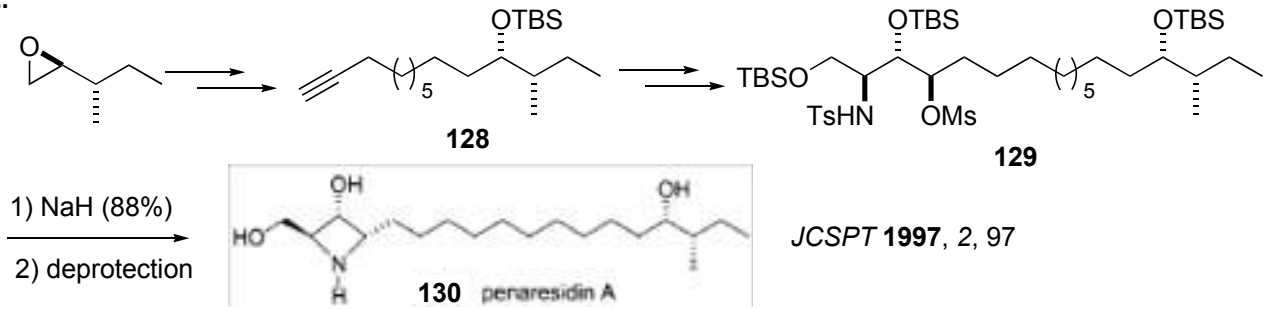
potent inhibitors of chitin synthetase

eg 51.



T **1994**, *50*, 9457

eg 52.

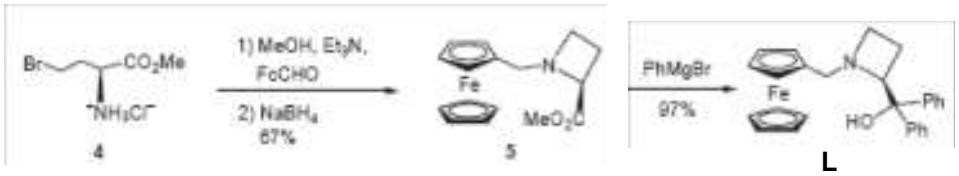


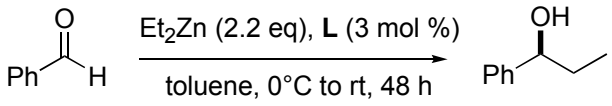
JCSPT **1997**, *2*, 97

actomyosin ATPase-activating activity

2) Ligands for Metal-Catalyzed Reactions

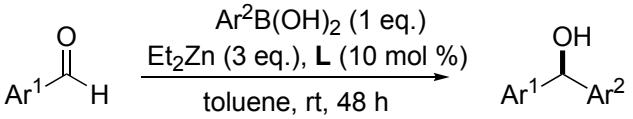
eg 53.





97% y., 98% ee

Synlett **2006**, 3443



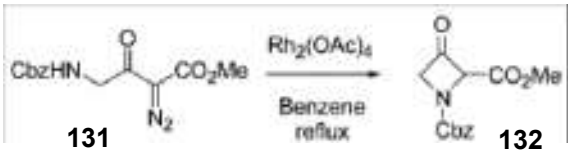
up to 99% y., 96% ee

eg 54.

for Suzuki reaction:
1–0.1 mol % cat., 77-87% y.
J Organomet Chem **2005**, *690*, 2306

3. Azetidine-3-ones synthesis mainly by NH insertion in diazo compounds

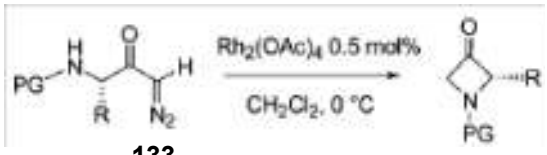
eg 55.



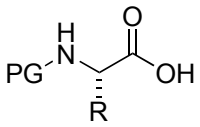
131 **132**

JOC **1985**, *50*, 5223

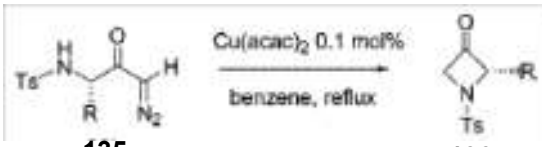
eg 56.



133 **134**



eg 57.

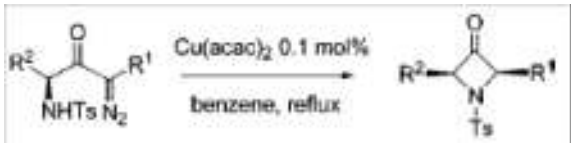


135 **136**

R = Me	34%
R = $PhCH_2$	45%
R = $MeS(CH_2)_2$	57%

JCSPT **1999**, *1*, 2277

eg 58.

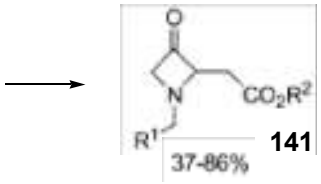


137 **138**

R^1 = Pr; R^2=t-$BuPh_2SiOCH_2$	61%
R^1 = $MeOCH_2CH_2$; R^2=t-$BuPh_2SiOCH_2$	65%
R^1 = Me; R^2=t-$BuPh_2SiOCH_2$	71%
R^1 = Me; R^2=Ph	47%

J Organomet Chem **2005**, *690*, 5636 *TL* **2004**, *45*, 3355

eg 59.

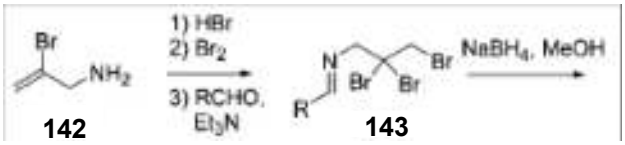


139 **140** **141**

R^1= n-Pr, c-hex, Bn, Ph
4-$MeOC_6H_4$, 4-$NO_2C_6H_4$, 4-BrC_6H_4
R^2= Et, Bn

EJOC **2006**, 2440

eg 60.



142 **143** **144** **145**

TL **2001**, *42*, 2373