

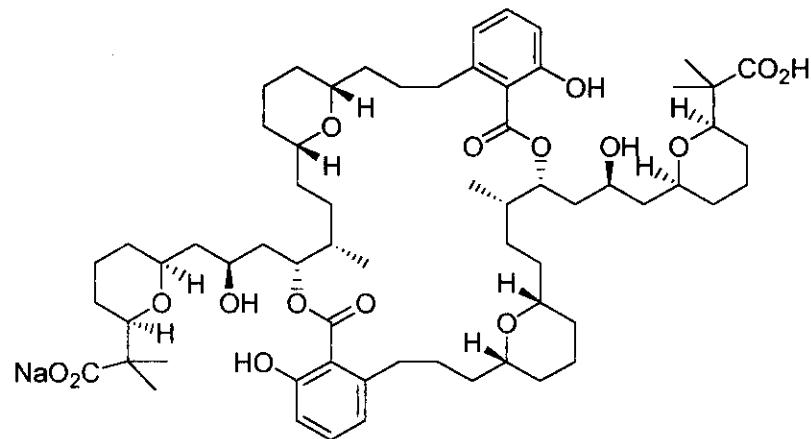
**Current Literature**

(Beomjun Joo 03/27/04)

# Total Synthesis of (+)-SCH 351448

Eun Lee *et al.* JACS 2004, 126, 2680-2681

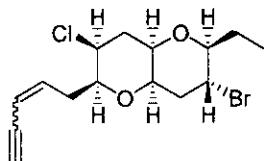
School of Chemistry and Molecular Engineering, Seoul National University, Seoul 151-747, Korea



**SCH-351448**  
activator of low-density lipoprotein receptor (LDL-R)

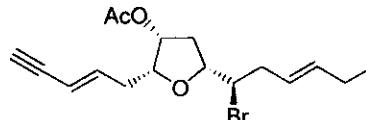
Key Reaction:  $\beta$ -Alkoxyacrylate Radical Cyclization

# Total Synthesis Using $\beta$ -Alkoxyacrylate Radical Cyclization by Eun Lee Group



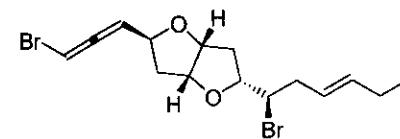
(E and Z)-Dactomelynes

JACS 1995, 117, 8017-



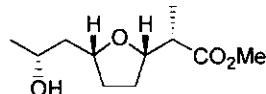
(-)-*trans*-Kumausyne

Tet. Lett. 1997, 38, 7757-



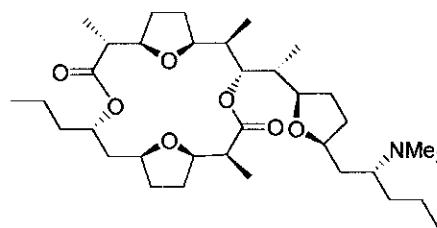
(-)-Kumausallene (Formal)

Tet. Lett. 1998, 317-



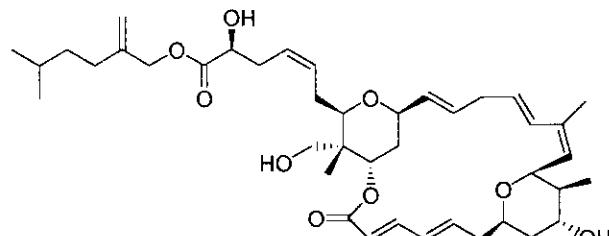
(+)-Methyl Nonactate

Org. Lett. 1999, 1, 1127-



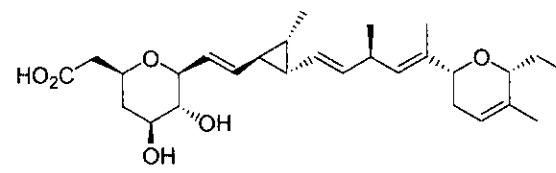
Pamamycin-607

JACS 2002, 124, 49, 14655-



Lasonolide A

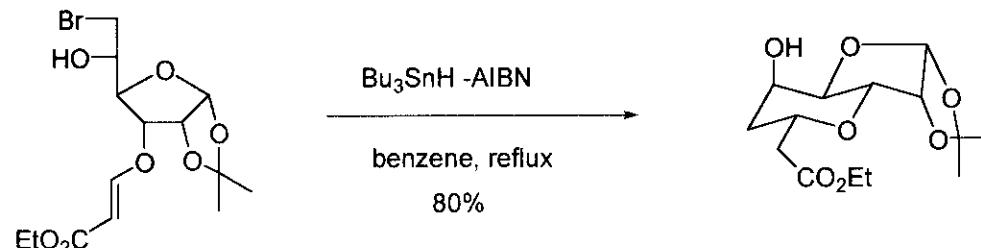
JOC 2003, 68, 8080-



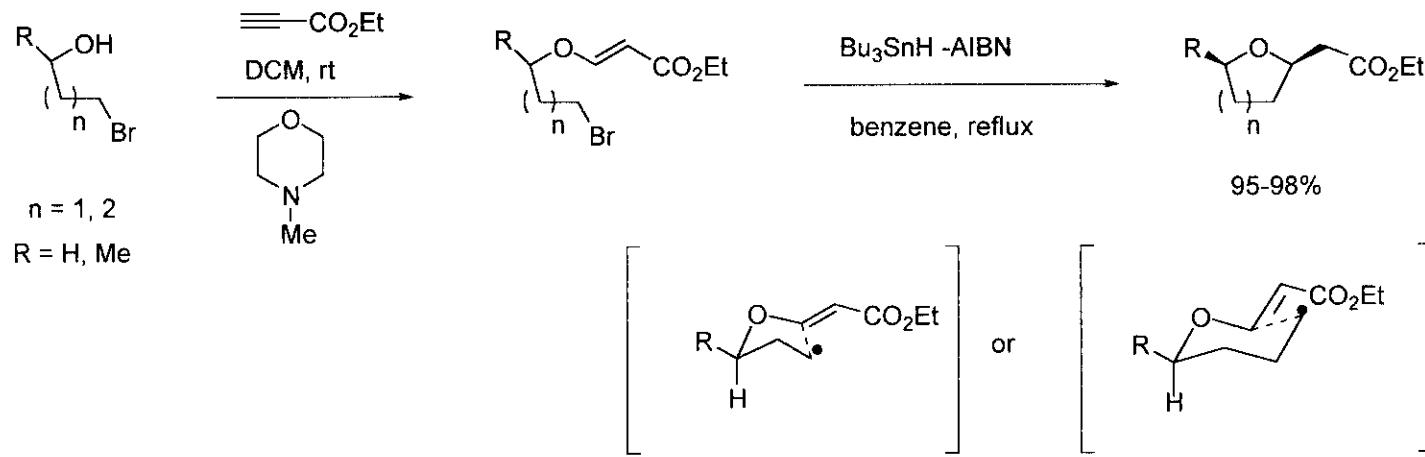
(+)-Ambruticin

ACIEE 2002, 41, 176-

## $\beta$ -Alkoxyacrylate Radical Cyclization

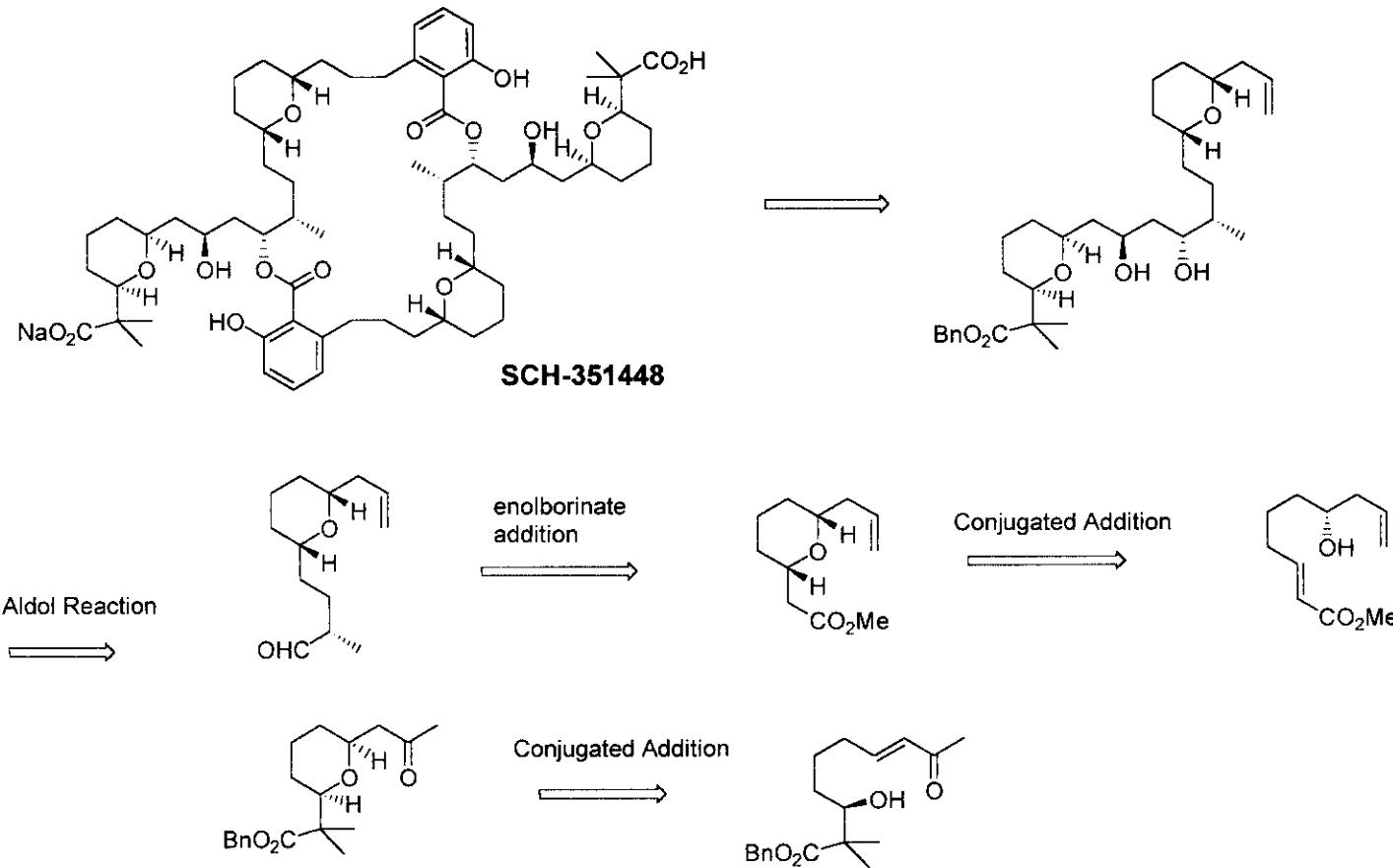


Y. Araki et al, Tet. Lett. 1989, 30, 2829-



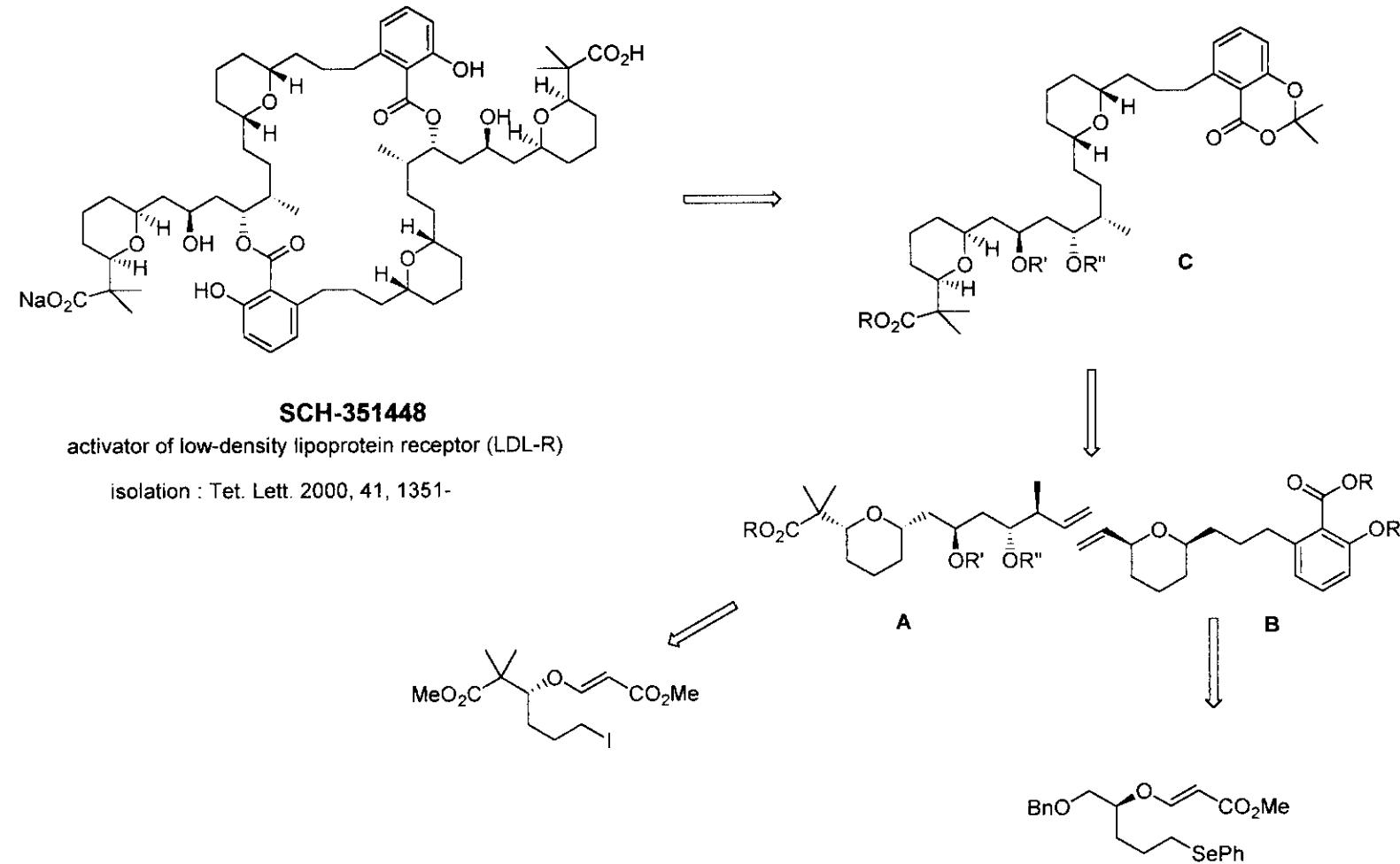
Eun Lee, Jin Sung Tae et al Tet. Lett. 1993, 34, 4831-

## Previous Synthetic Effort toward (+)-SCH 351448

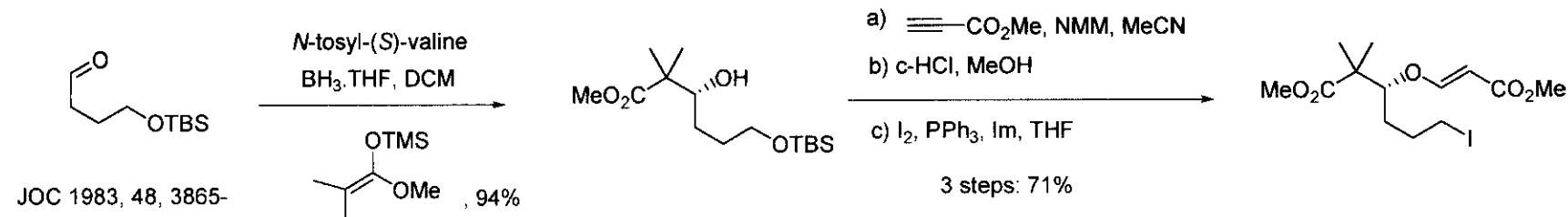


J. K. De Brabander et al. Org. Lett. 2002, 4, 4, 481-484

## (+)-SCH 351448 and Its Retrosynthetic Analysis

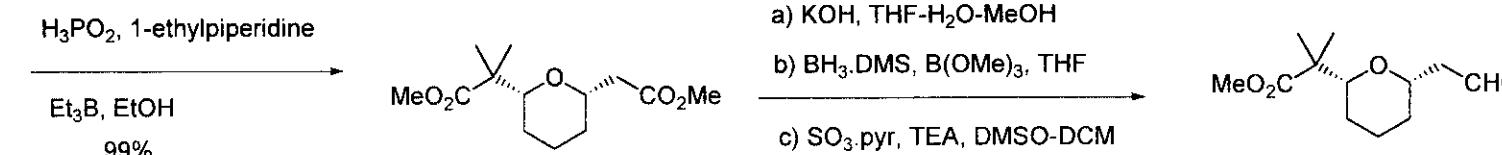


## Synthesis of the Fragment A



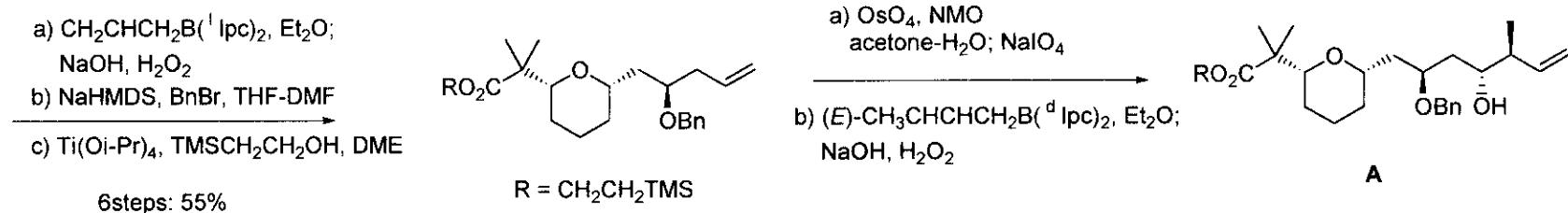
### Chiral BoraneMukaiyama-Aldol Rxn

JOC 1991, 56, 2276-



### hypophosphite radical rxn

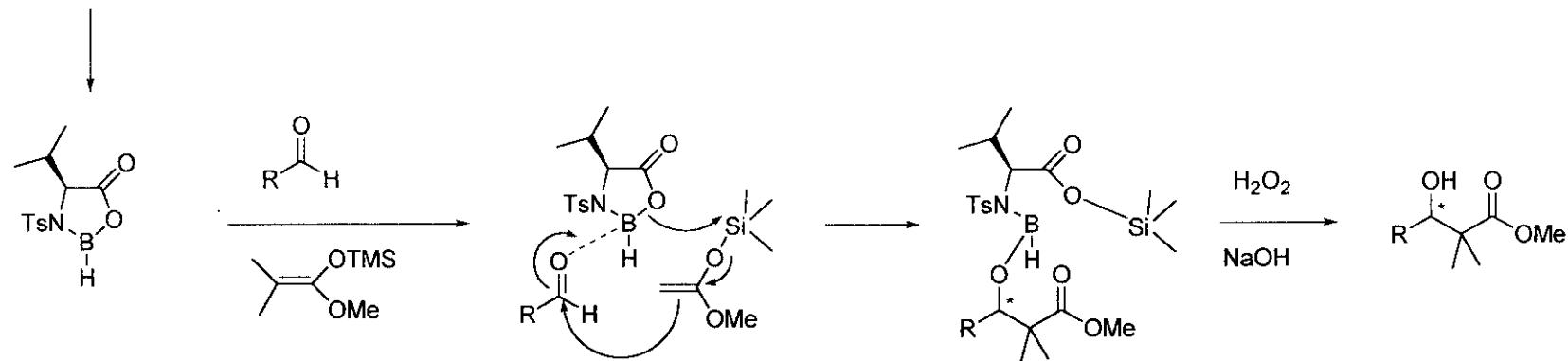
Tet. Lett. 2002, 43, 7295-



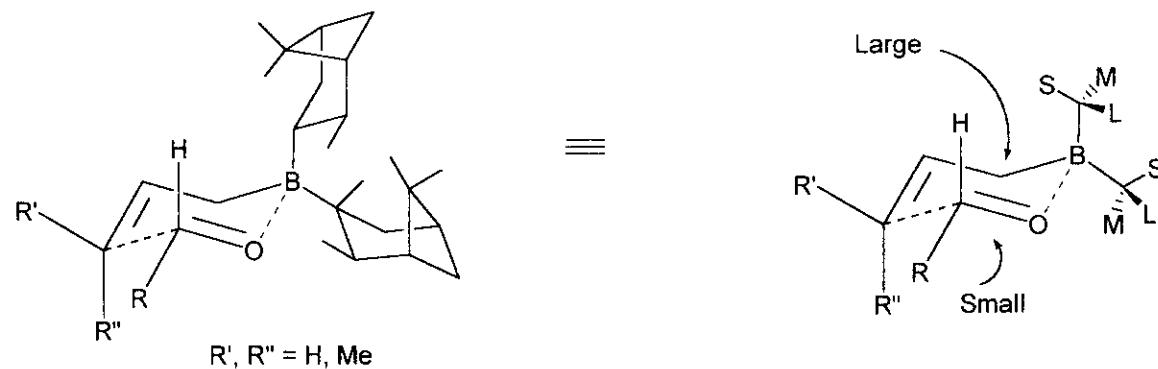
- Chiral BoraneMukaiyama-Aldol Rxn

S. kiyooka *et al.* JOC 1991, 56, 2276-

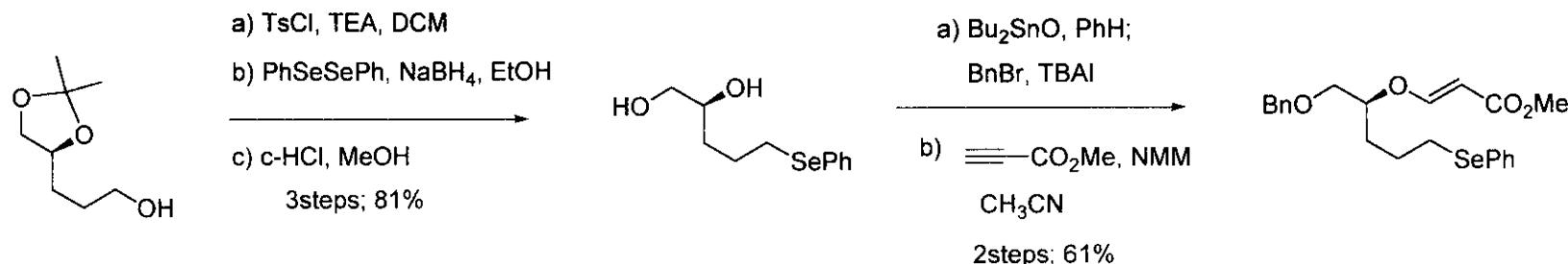
*N*-tosyl-(*S*)-valine,  $\text{BH}_3\cdot\text{THF}$



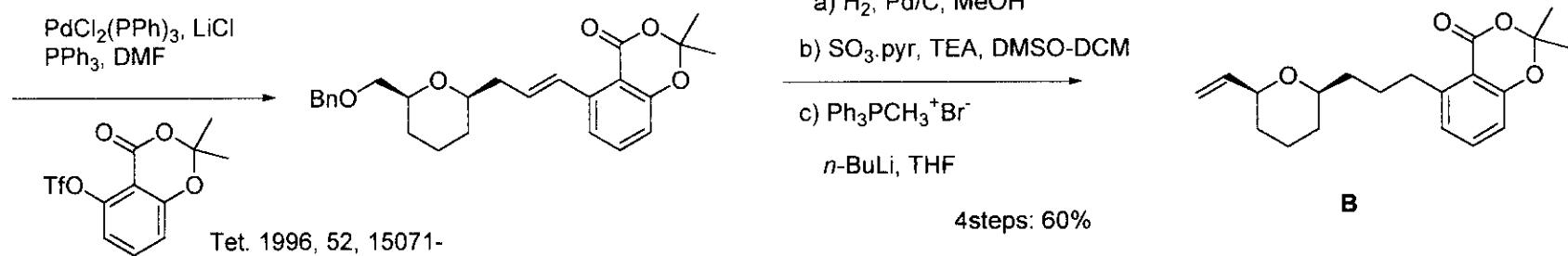
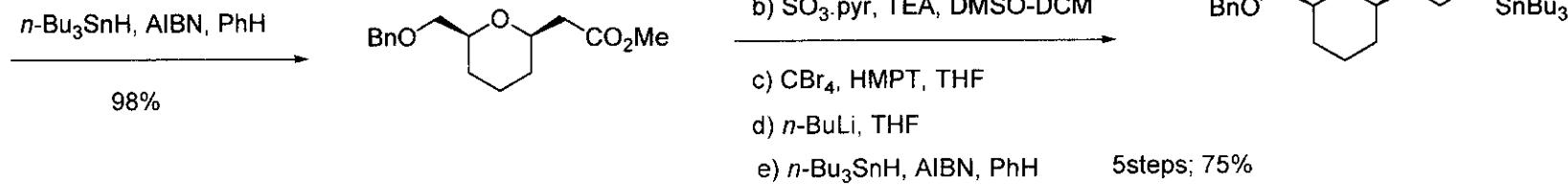
- Brown's Asymmetric Allylation and Crotylation



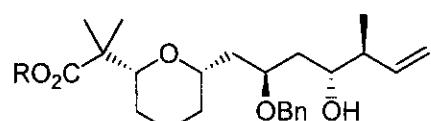
## Synthesis of the B Fragment



Aust. J. Chem. 1990, 43, 1391-

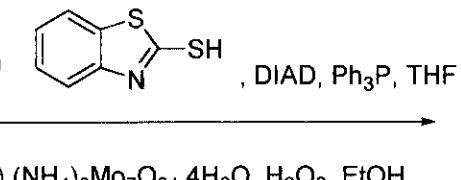
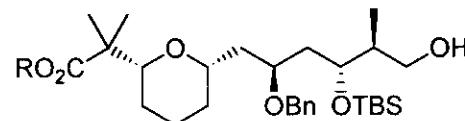


## Preparation of the C Fragment

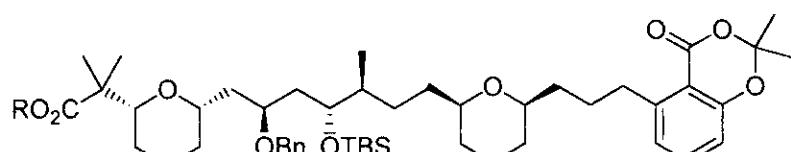
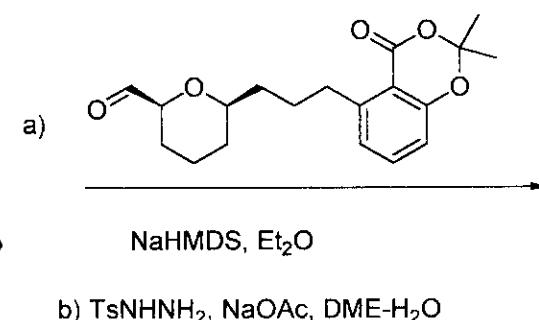
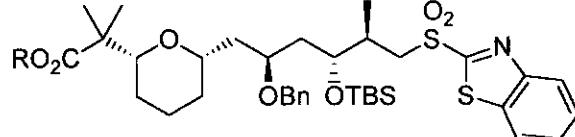


R = CH<sub>2</sub>CH<sub>2</sub>TMS

- a) TBSOTf, 2,6-lutidine, CH<sub>2</sub>Cl<sub>2</sub>  
 b) OsO<sub>4</sub>, NMO, acetone-H<sub>2</sub>O; NaIO<sub>4</sub>  
 c) NaBH<sub>4</sub>, EtOH



5 steps; 84%



C

## Completion of the Synthesis

