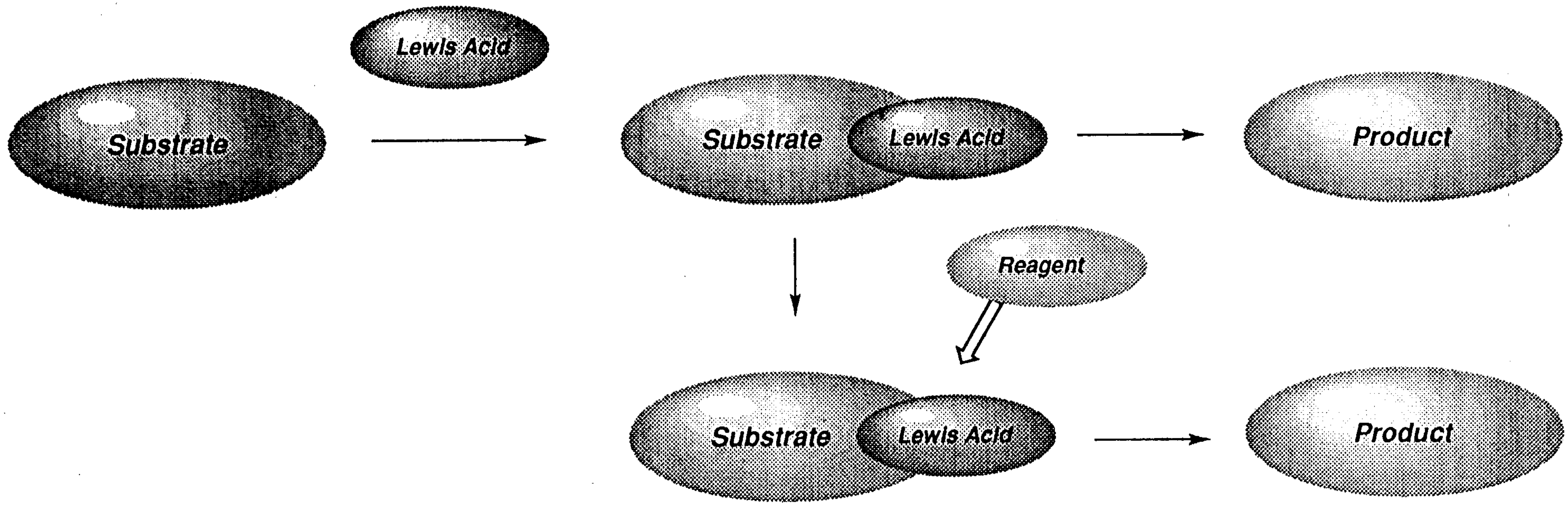
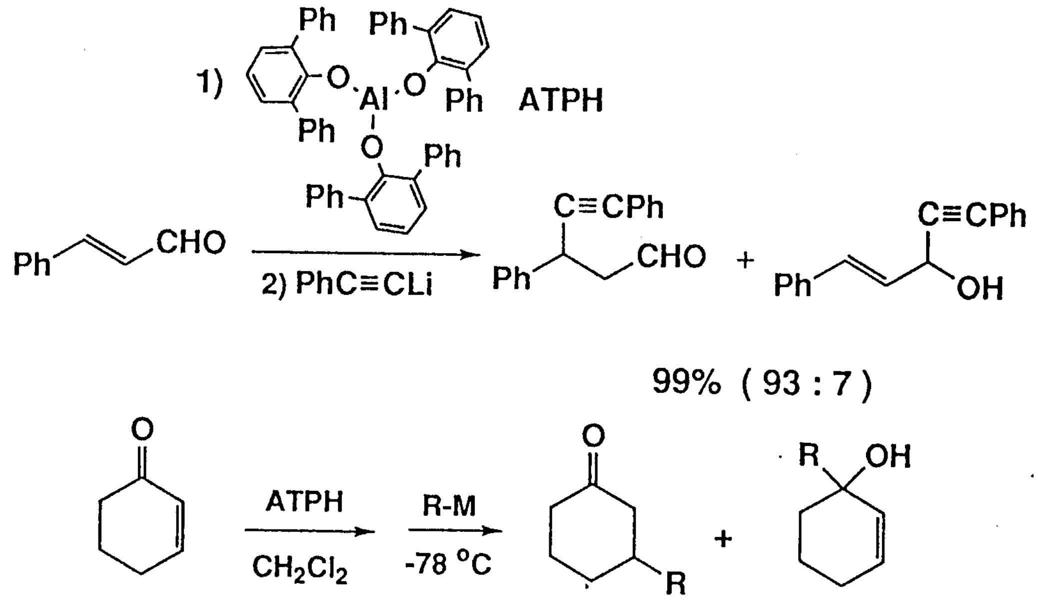


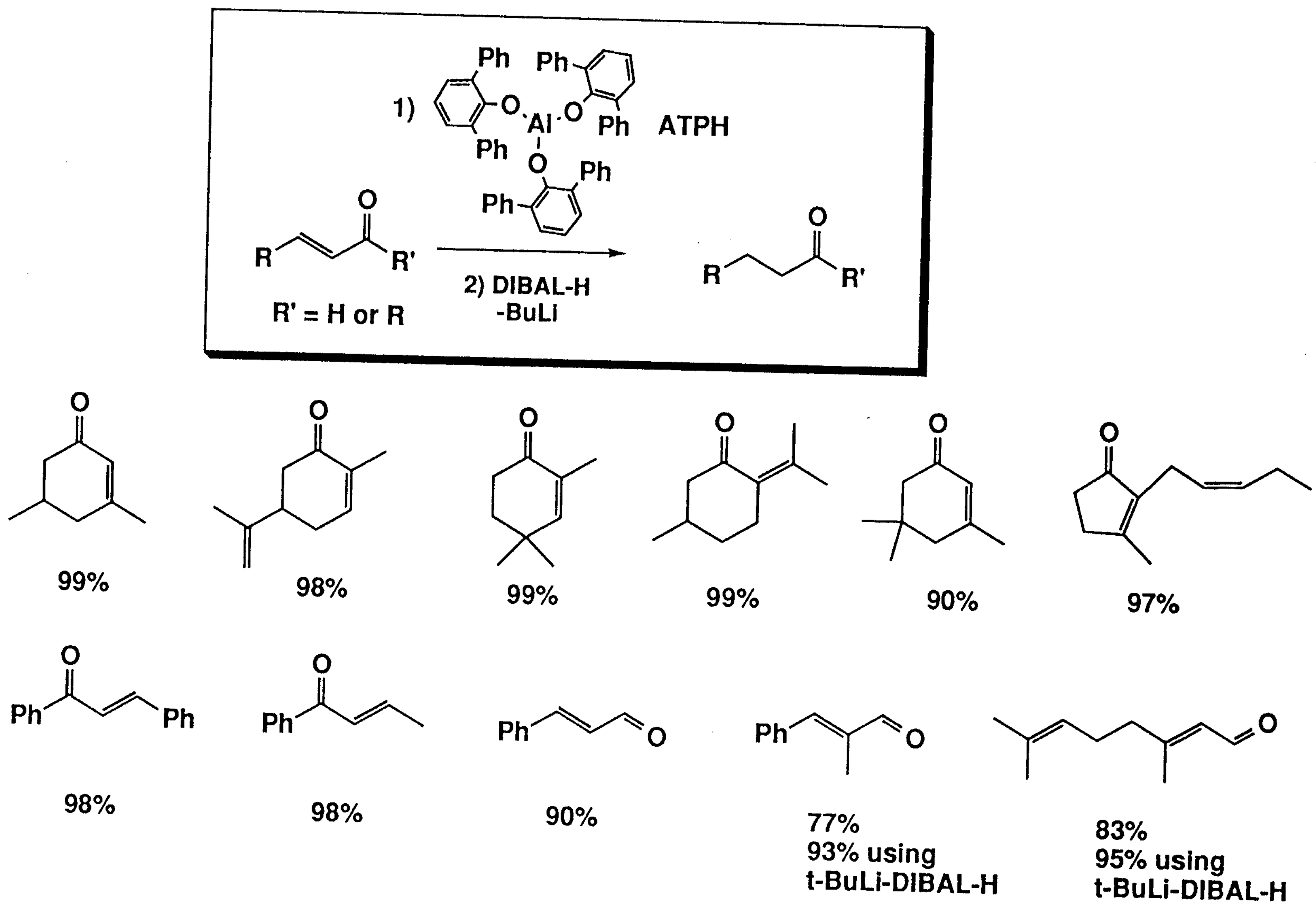

*Classical Lewis Acids: $AlCl_3$, $BF_3$, $SnCl_4$, $TiCl_4$*
*Designer Lewis Acids: Ligand Design, Chiral Lewis Acids*

*Diels-Alder Reaction, Aldol Synthesis, Ene Reaction, Friedel-Crafts Reaction, Esterification, Amidation, Michael Reaction, Claisen Rearrangement, Carbonyl Addition, etc. etc.*

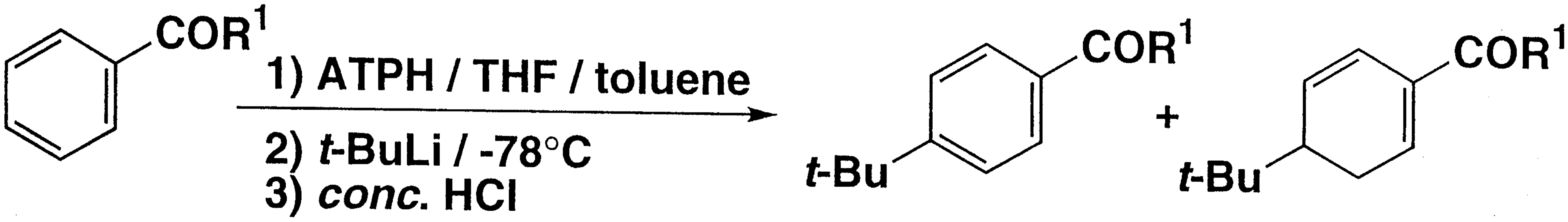



( R-M = BuLi ) : 75% ( >99 : 1 )
( R-M = BuMgBr ) : 77% ( >99 : 1 )
( R-M = PhLi ) : 86% ( >99 : 1 )

*J. Am. Chem. Soc., 116, 4131 (1994): Synlett, 519 (1994).*

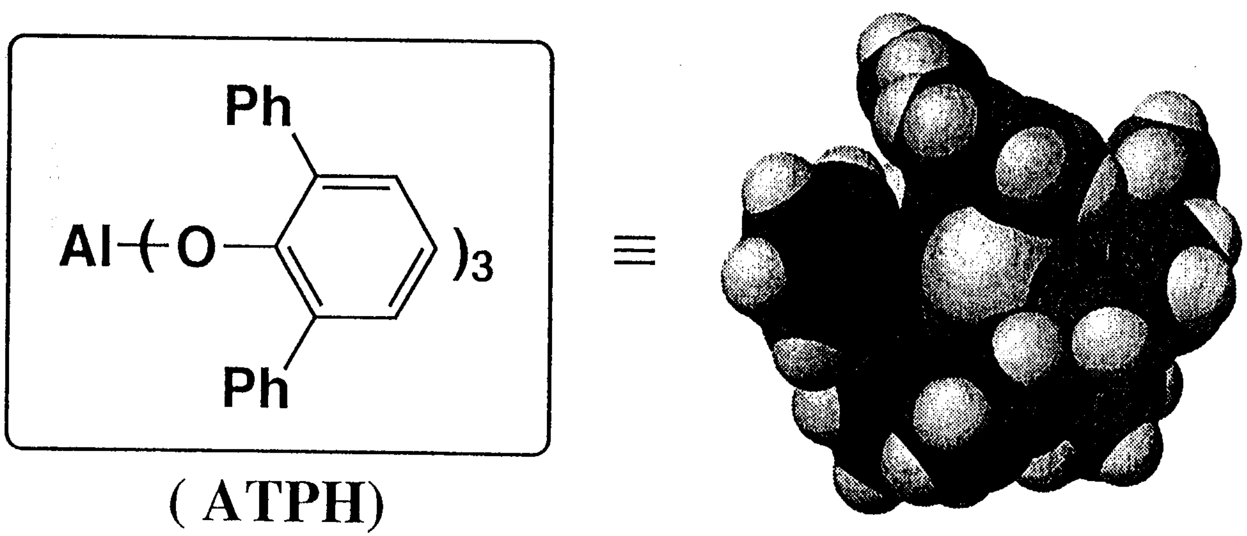

1)
Ph
Ph
O
Al
O
Ph
Ph
O
Ph
Ph
ATPH
R
O
R'
R' = H or R
2) DIBAL-H
-BuLi
R
O
R'
O
99%
O
98%
O
99%
O
99%
O
90%
O
97%
Ph
O
Ph
98%
Ph
O
98%
Ph
O
90%
Ph
O
77%
93% using
t-BuLi-DIBAL-H
O
83%
95% using
t-BuLi-DIBAL-H

# Conjugate Addition to Aromatic Carbonyl Compounds Complexed with ATPH



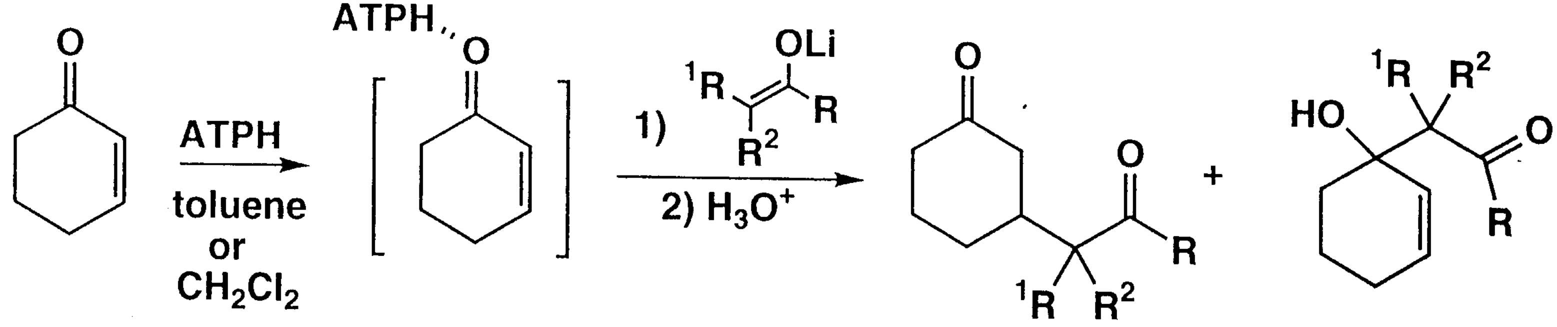

$R^1$ = H, 81% ( <1 : >99 )
$R^1$ = Me, 93% ( <1 : >99 )

K. Maruoka, M. Ito and H. Yamamoto, *J. Am. Chem. Soc.*, *117*, 9091 ( 1995 ).

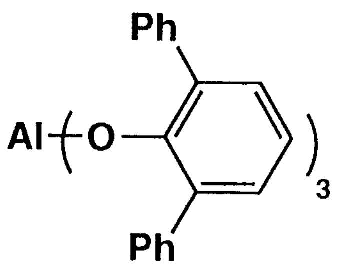



( ATPH)

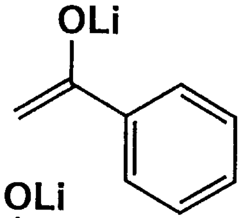
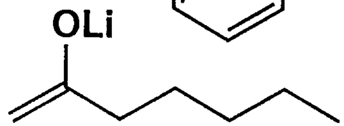
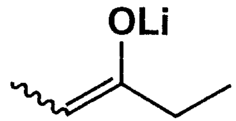
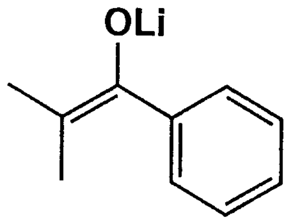
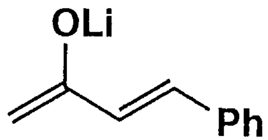
# Addition of Various Kinds of Lithium Enolates to Cyclohexenone Complexed with ATPH



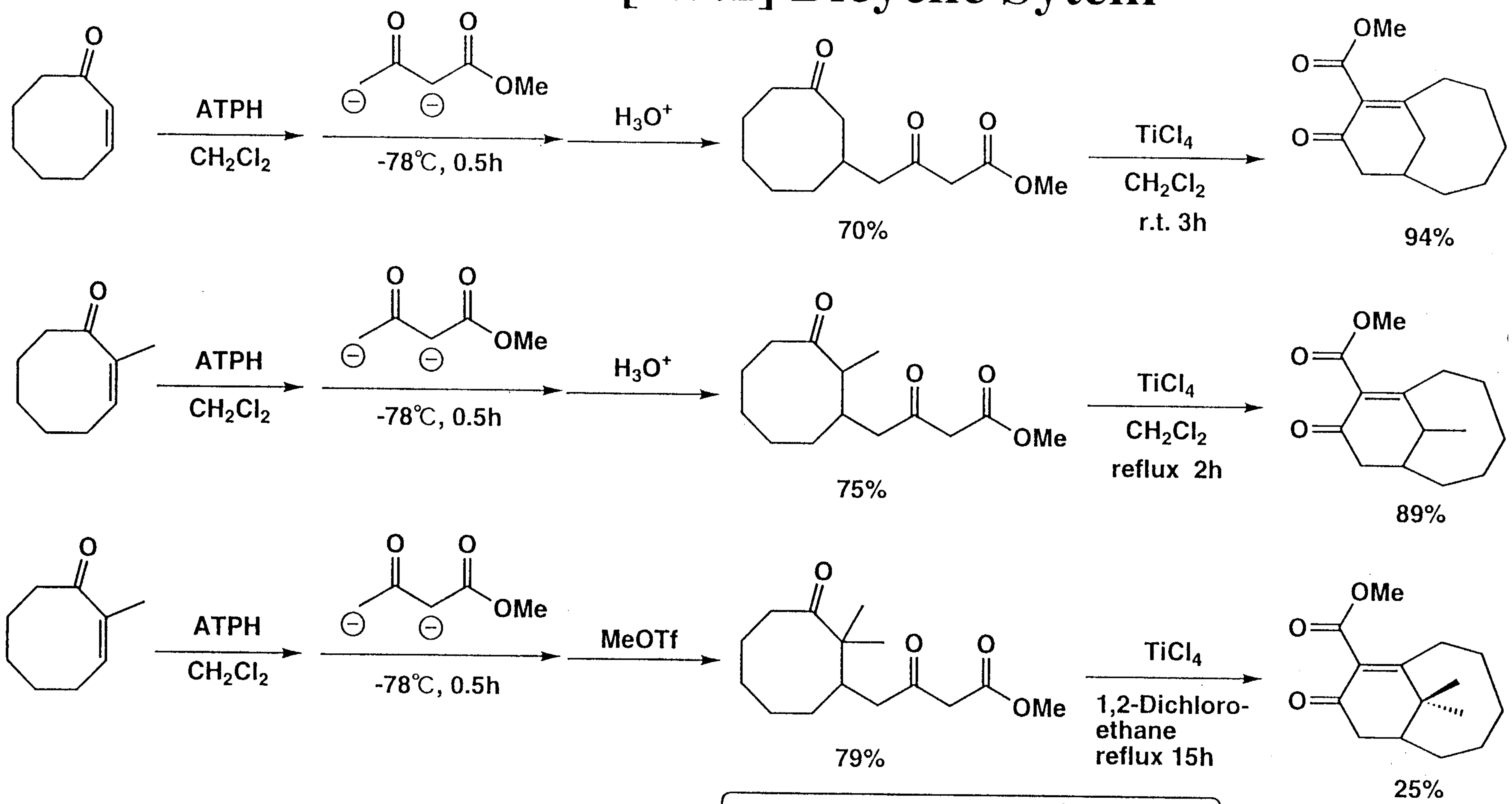

1.4-adduct + 1,2-adduct

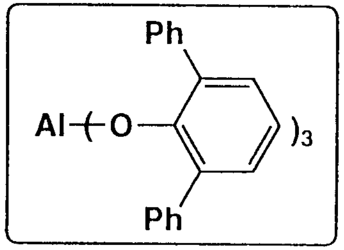



ATPH

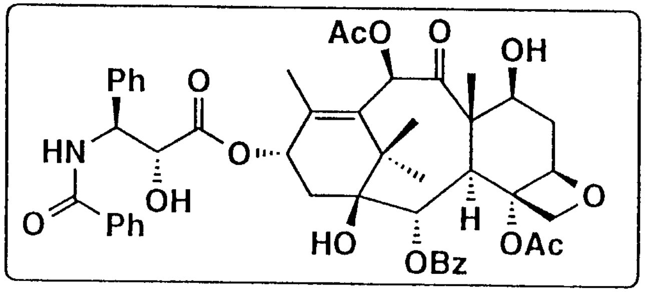
| | | |
| --- | --- | --- |
|  | -78°C, 0.3h | 98%( >99 : 1 ) |
|  | -78°C, 1h | 96%( >99 : 1 ) |
|  ( E : Z ) = 91 : 9 | -90°C, 0.3h | 85%( >99 : 1 ) |
|  | -90°C, 0.3h | 75%( >99 : 1 ) |
|  | -78°C, 0.3h | 90%( >99 : 1 ) |

# Construction of [5.3.1] Bicyclic Sytem



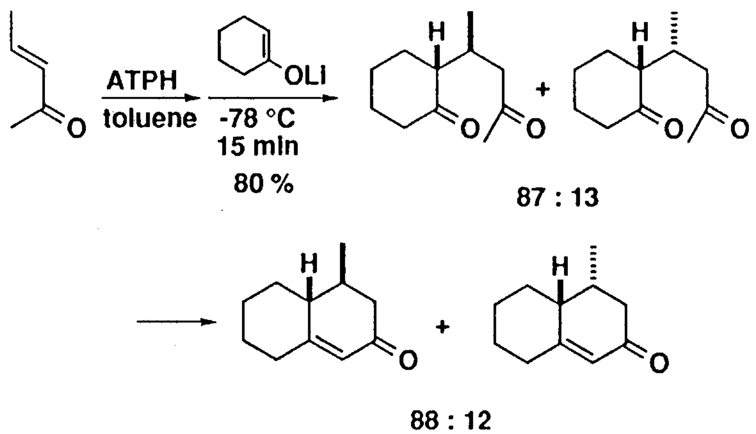




(ATPH)

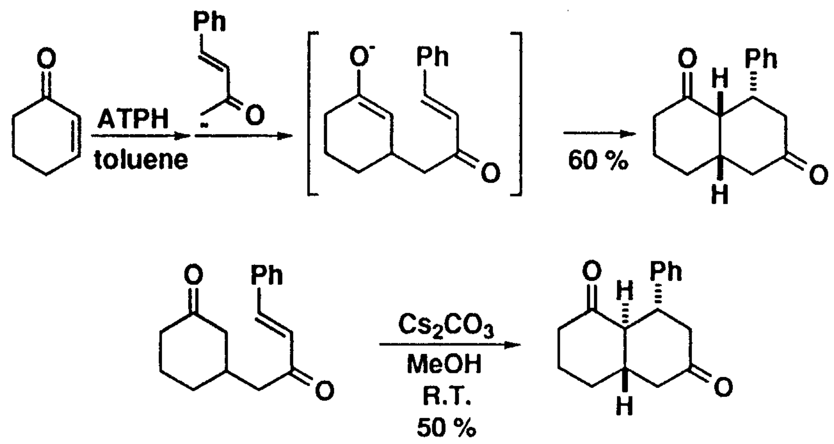



TAXOL

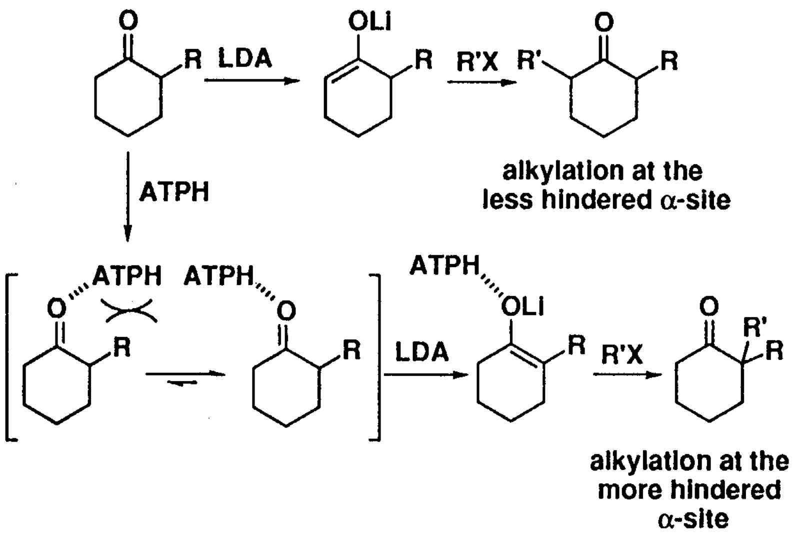
## *REGIOSELECTIVE ROBINSON ANNULATION*



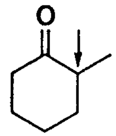
*INTRAMOLECULAR MICHAEL ADDITON*



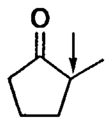
***Regioselective Alkylation of Unsymmetrical Ketones***



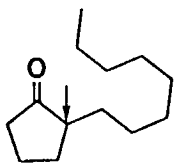
## *Regioselective alkylation of unsymmetrical ketones*



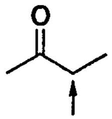
MeOTf 53% (32 : 1)
OctOTf 88% (>99 : 1)
Allyl-Br 53% (>99 : 1)
Allyl-I 69% (>99 : 1)
$CH{\equiv}CCH_2Br$ 61% (>20 : 1)



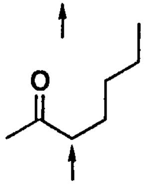
OctOTf 99% (>20 : 1)
Allyl-I 55% (>99 : 1)



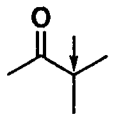
MeOTf 75% (5.1 : 1)



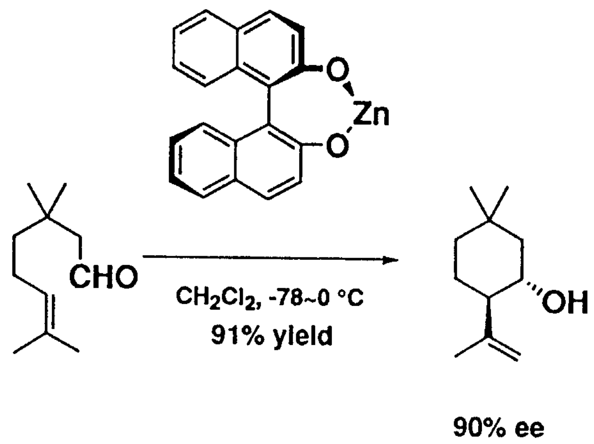
OctOTf 69% (24 : 1)



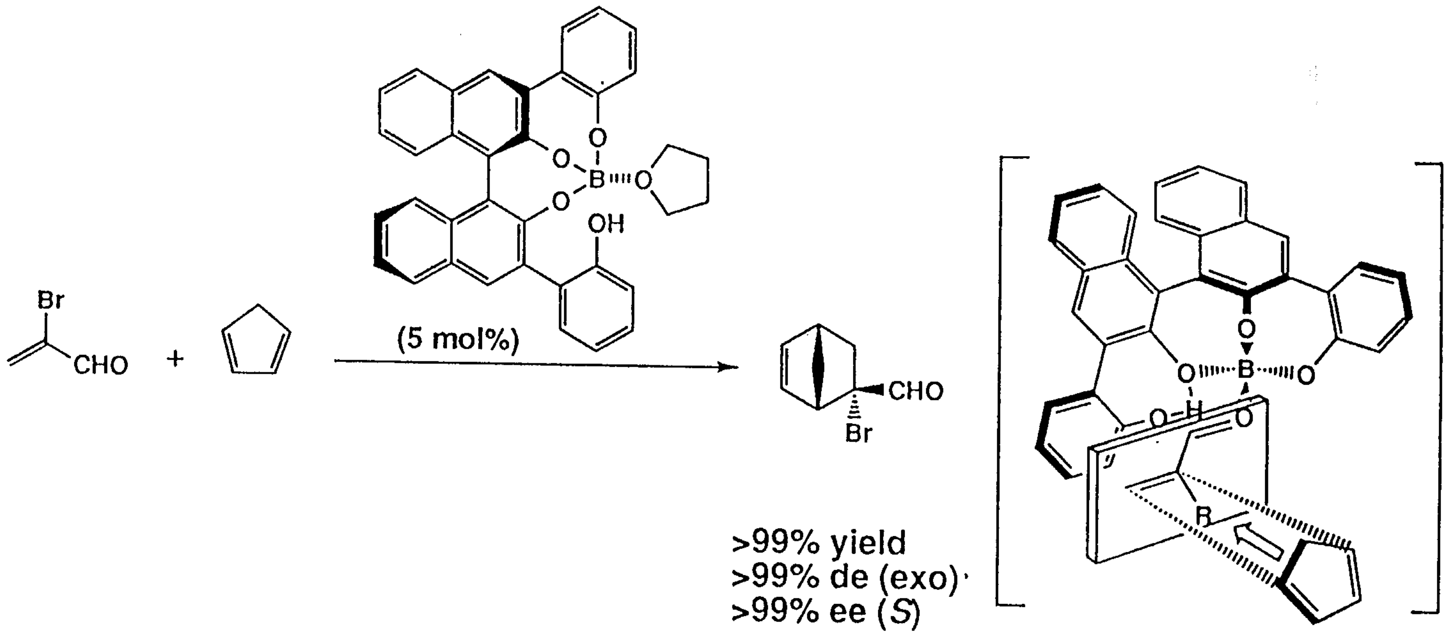
OctOTf 89% (>20 : 1)



OctOTf 71% (>99 : 1)

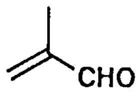
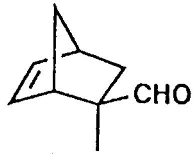
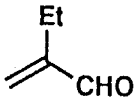
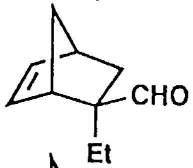
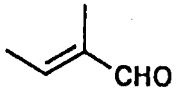
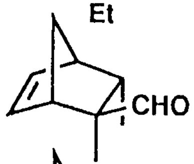
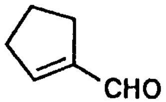
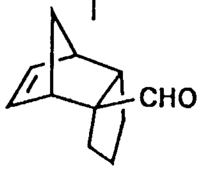
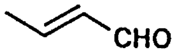
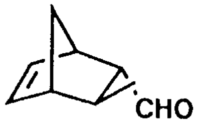


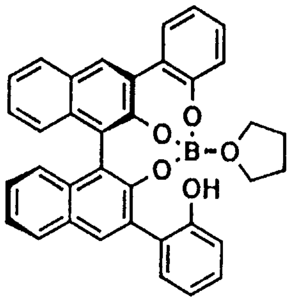

*Tetrahedron Lett., 26, 5535 (1985)*




J. Am. Chem. Soc., 116, 1561 (1994)

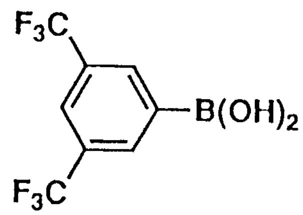
*Table.* ***Asymmetric Diels-Alder Reaction Catalyzed by (R)-BLA***

| Dienophile | Diene | Product | Yield | %ee (confign) | exo : endo |
|---|---|---|---|---|---|
|  |  |  | >99 | 98.6 (*R*) | >99 : 1 |
|  | |  | >99 | 92.2 | 97 : 3 |
|  | |  | >99 | 98.4 | >99 : 1 |
|  | |  | >99 | 93.1 | 98 : 2 |
|  | |  | 12 | 36.0 | 11 : 89 |



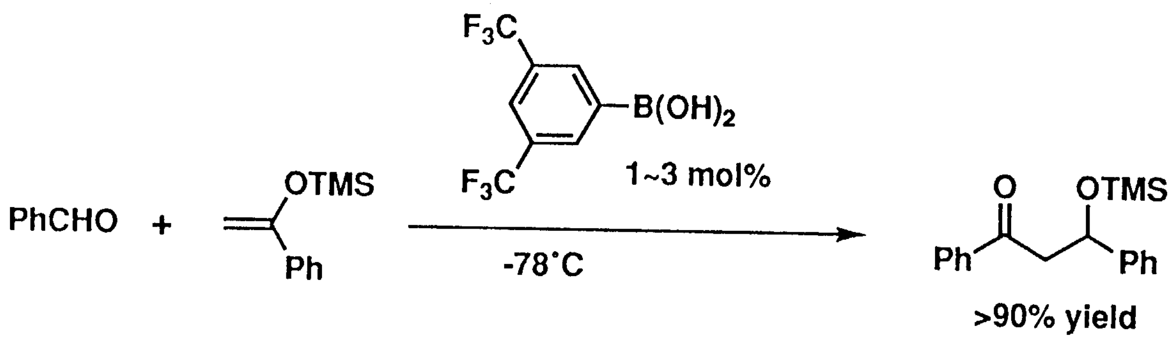

(*R*)-BLA (5-10 mol%)

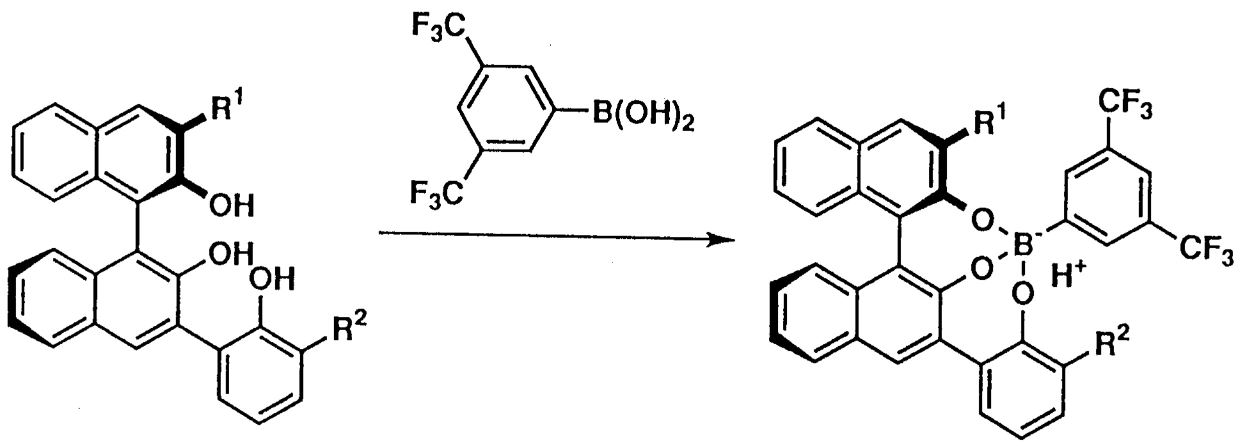
# Design of More Practical and Versatile BLA Catalyst



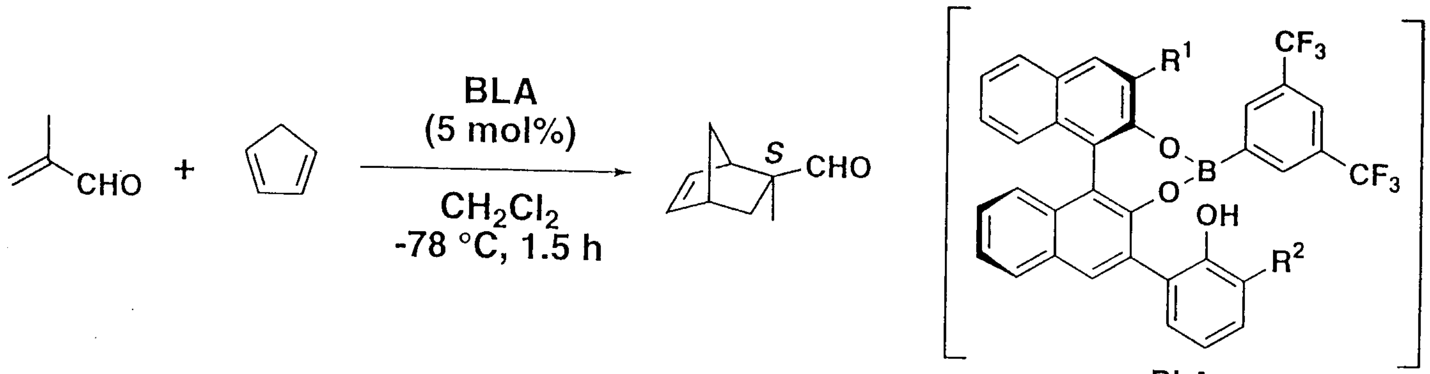

Lewis acid catalyst for

- Diels-Alder reaction
- Mukaiyama aldol reaction
- Sakurai-Hosomi allylation reaction

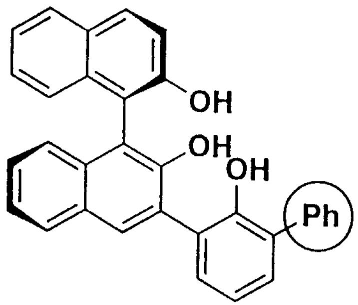


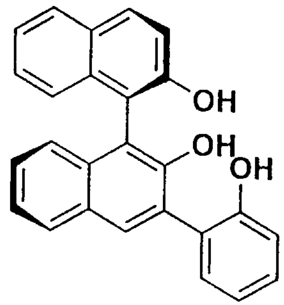
# Substituent Effects of Chiral Terphenol Lignads



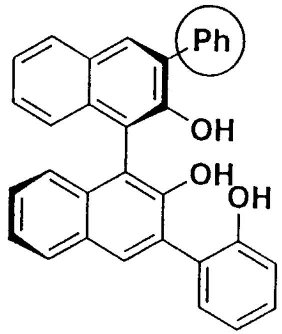

BLA



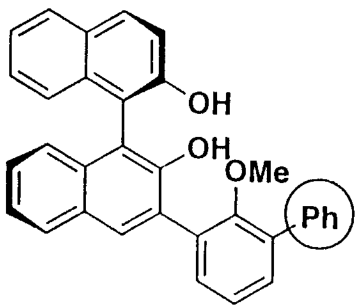

98~99% ee
>95% yield



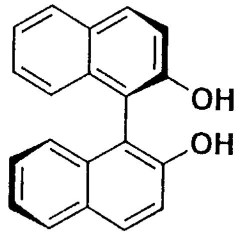

77% ee
>95% yield



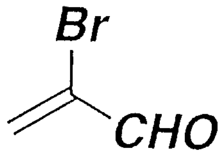

50% ee
89% yield



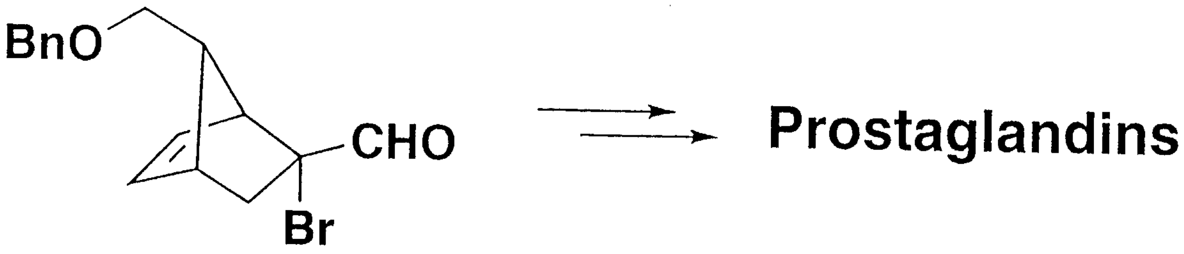

45% ee
9% yield




46% ee
22% yield

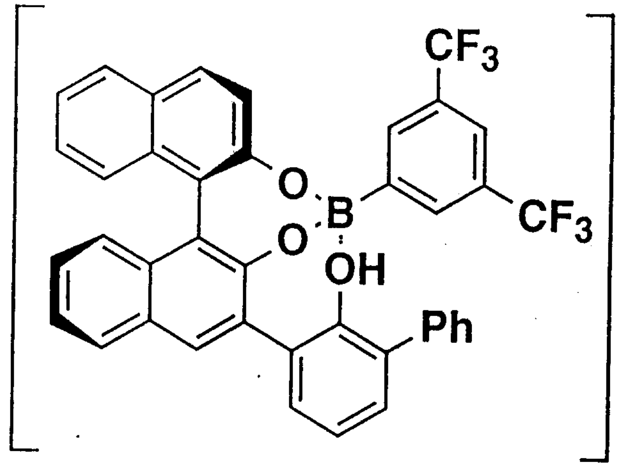
# *Diels-Alder Adducts of* 





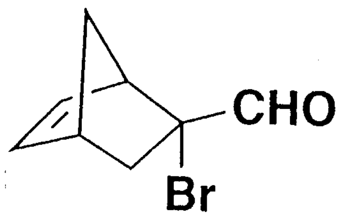


100% yield
>99% ee (*R*)
exo:endo=89:11



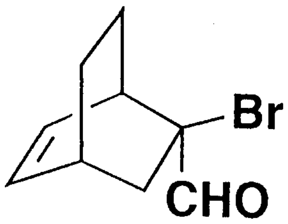


**BLA -2**
(10 mol%)



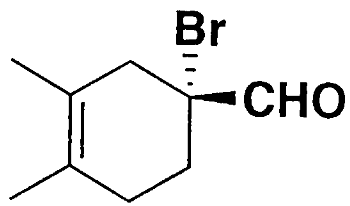


97% yield (1 mol%)
97% ee (*R*)
exo:endo=88:12



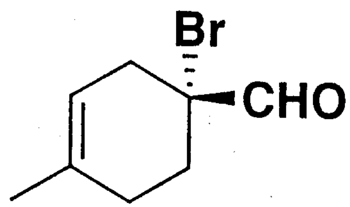


65% yield
95% ee
exo:endo=10:90



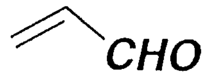


95%yield
91% ee

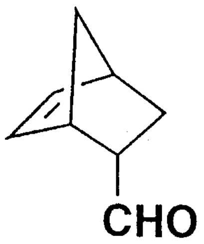




95% yield
>99% ee (*R*)

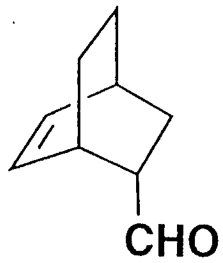
## Diels-Alder Adducts of 





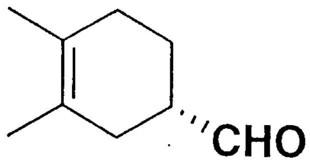


84% yield (5 mol%)
**95**% ee (*S*)
exo:endo=3:97



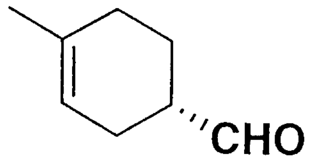


>99% yield (10 mol%)
**96**% ee
exo:endo=<1:99



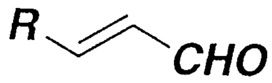


96%yield (10 mol%)
**>99**% ee

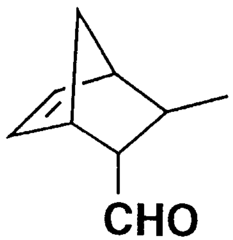




95%yield (10 mol%)
**99**% ee

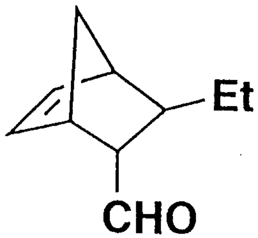
## Diels-Alder Adducts of 





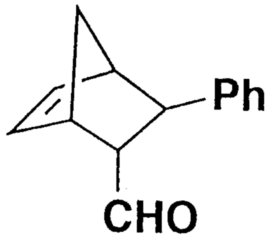


94% yield (20 mol%)
**95**% ee (*S*)
exo:endo=10:90



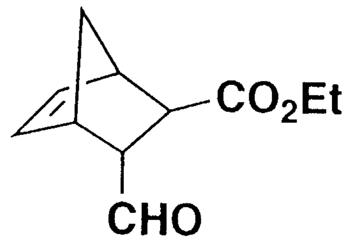


73% yield (20 mol%)
**98**% ee
exo:endo=9:91



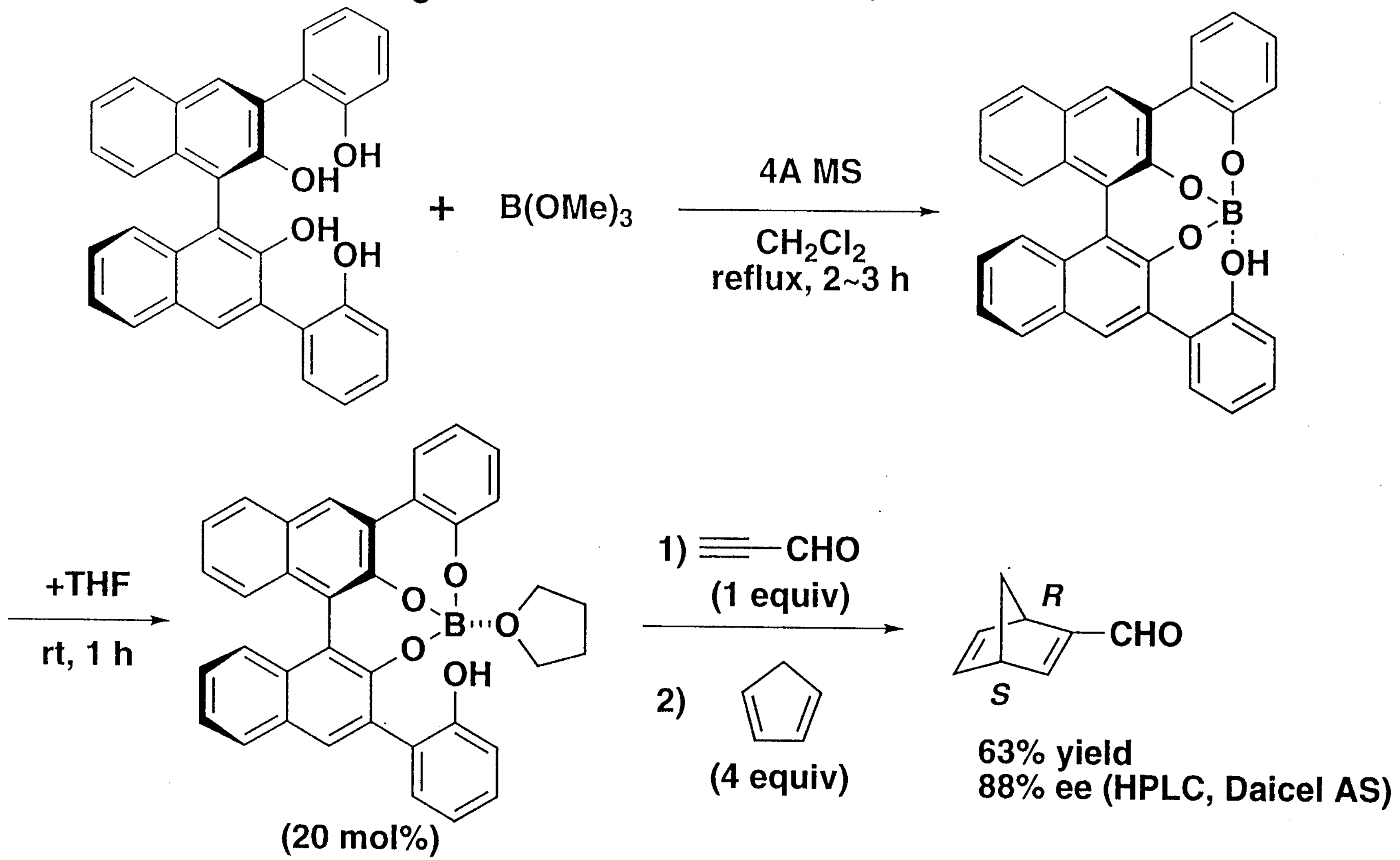


94% yield (20 mol%)
**80**% ee (*R*)
exo:endo=26:74

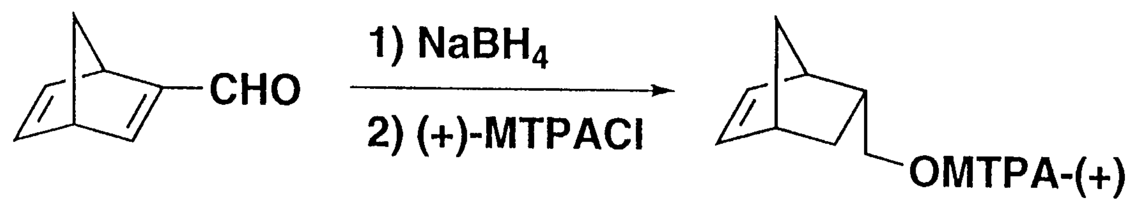


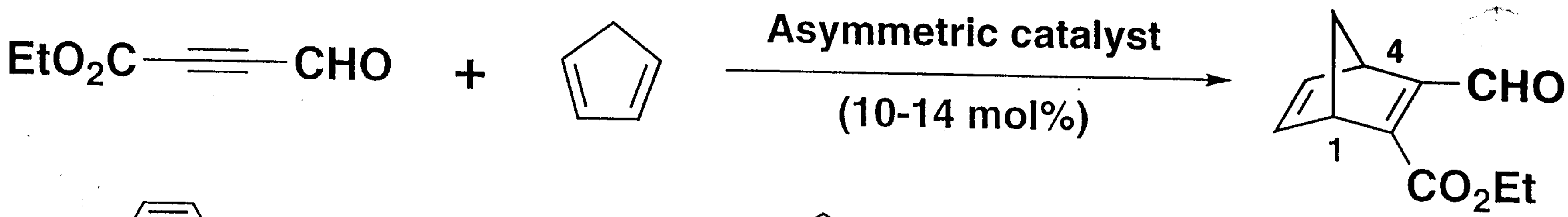


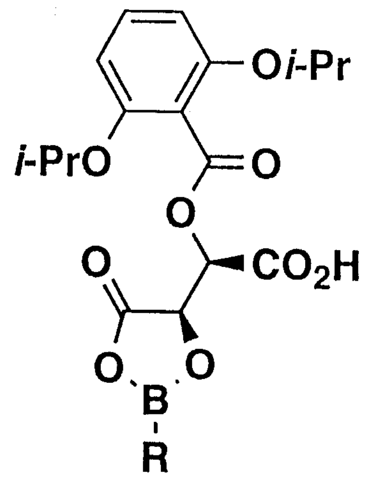
91% yield (5 mol%)
**95**% ee (*R*)
exo:endo=2:98




## Determination of absolute configuration

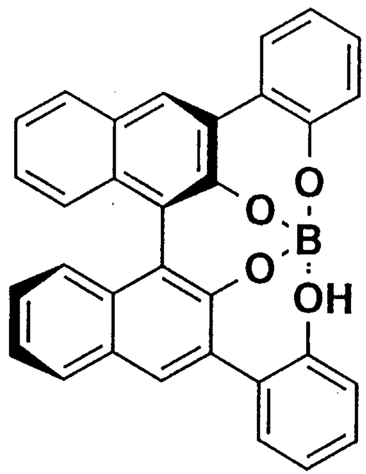




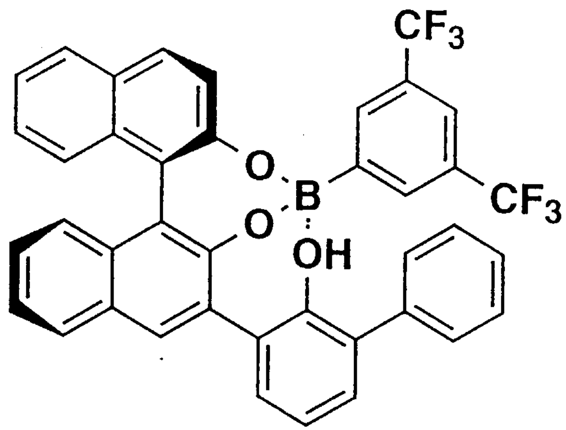

CAB (10 mol%)

78% ee (1*S*,4*R*)
99% yield




BLA 1 (10 mol%)

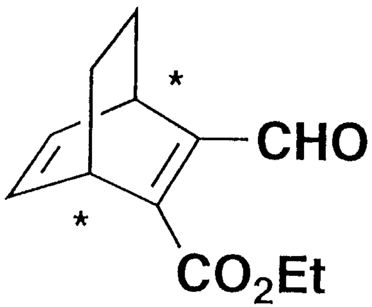
95% ee (1*S*,4*R*)
97% yield




BLA 2 (14 mol%)

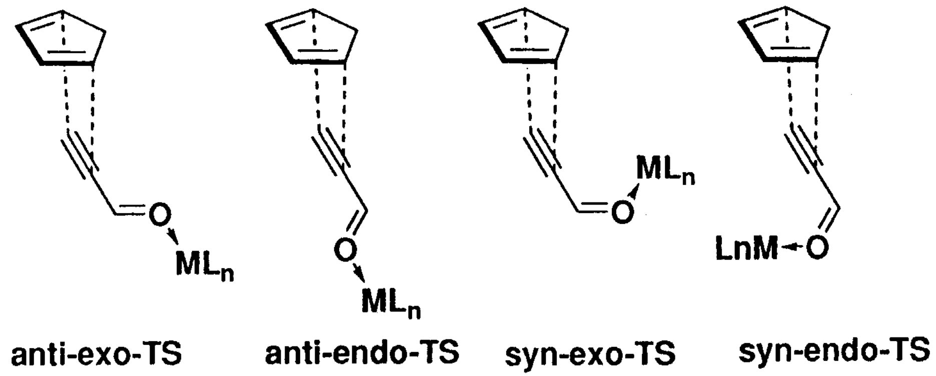
63% ee (1*R*,4*S*)
98% yield

---



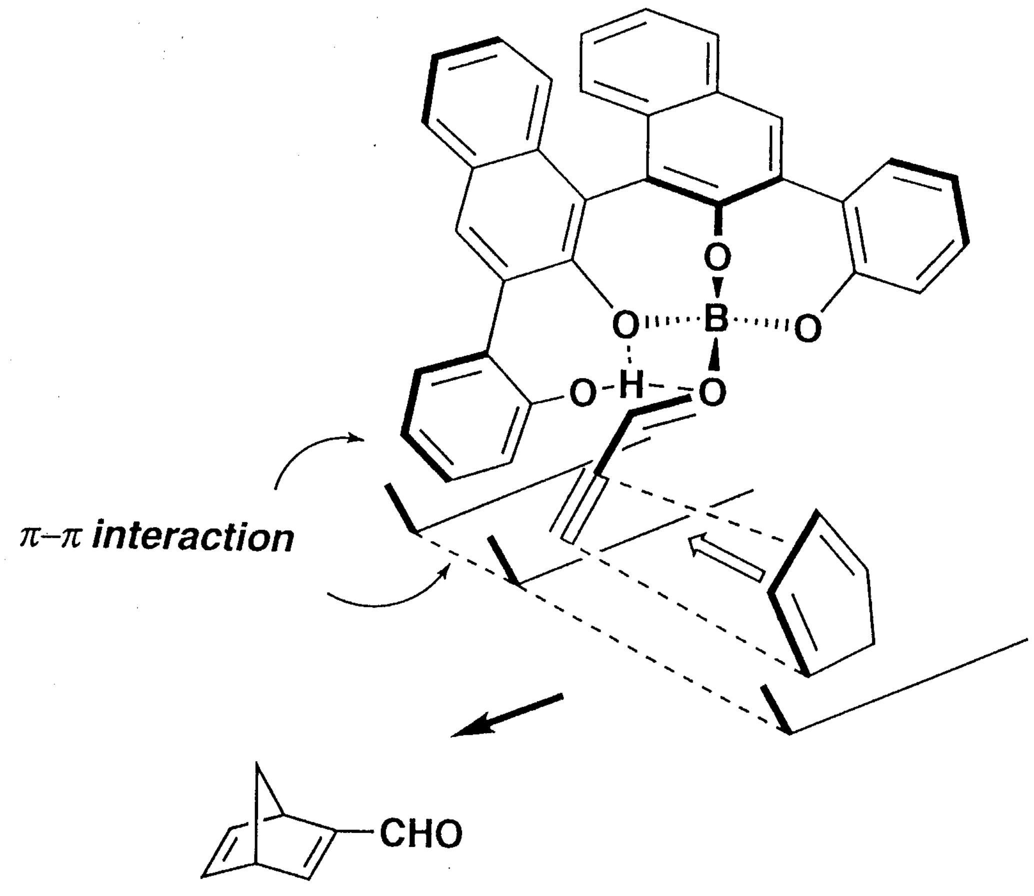

BLA 1 (20 mol%)

84% ee
81% yield

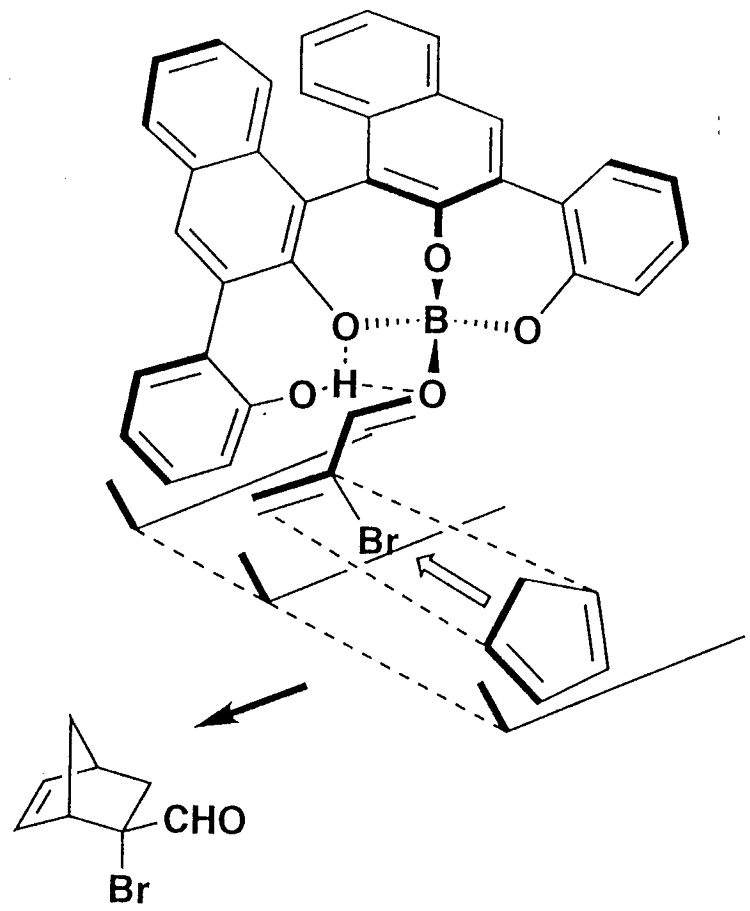



*The four possible transition structures in the Diels-Alder reaction of propiolaldehyde and cyclopentadiene promoted by Lewis acid. $ML_n$=Lewis acid.*

# Proposed Transition-State Model

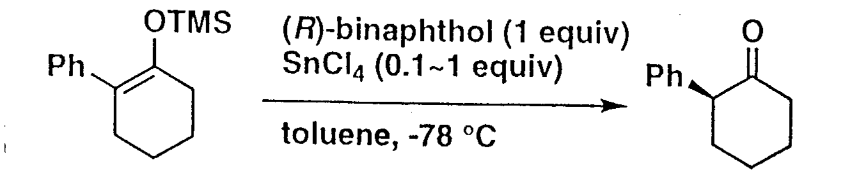



Major enantiomer



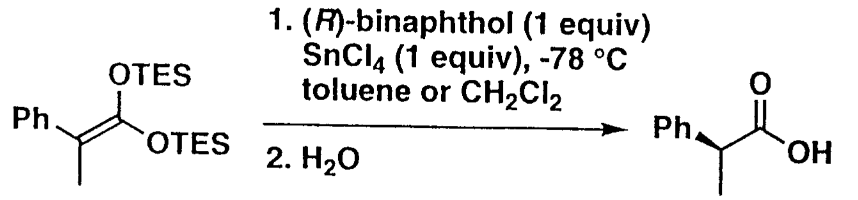
# Highly Enantioselective Protonation
# Using *Lewis Acid Assisted Chiral Brφnsted Acid (LBA)*

## Silyl Enol Ethers

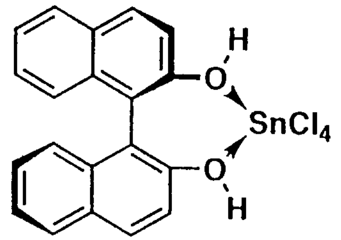



>95% yield, 97% ee (*S*)

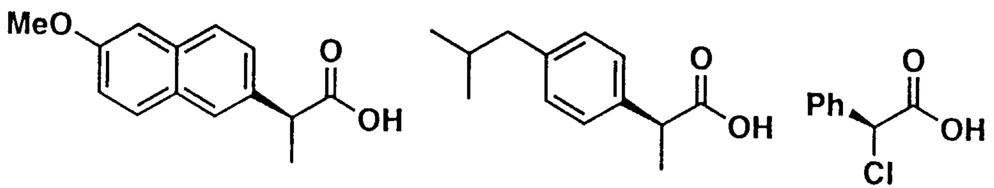
## Ketene Bis(silyl) Acetals




>95% yield, 96% ee (*S*)




(*R*)-LBA

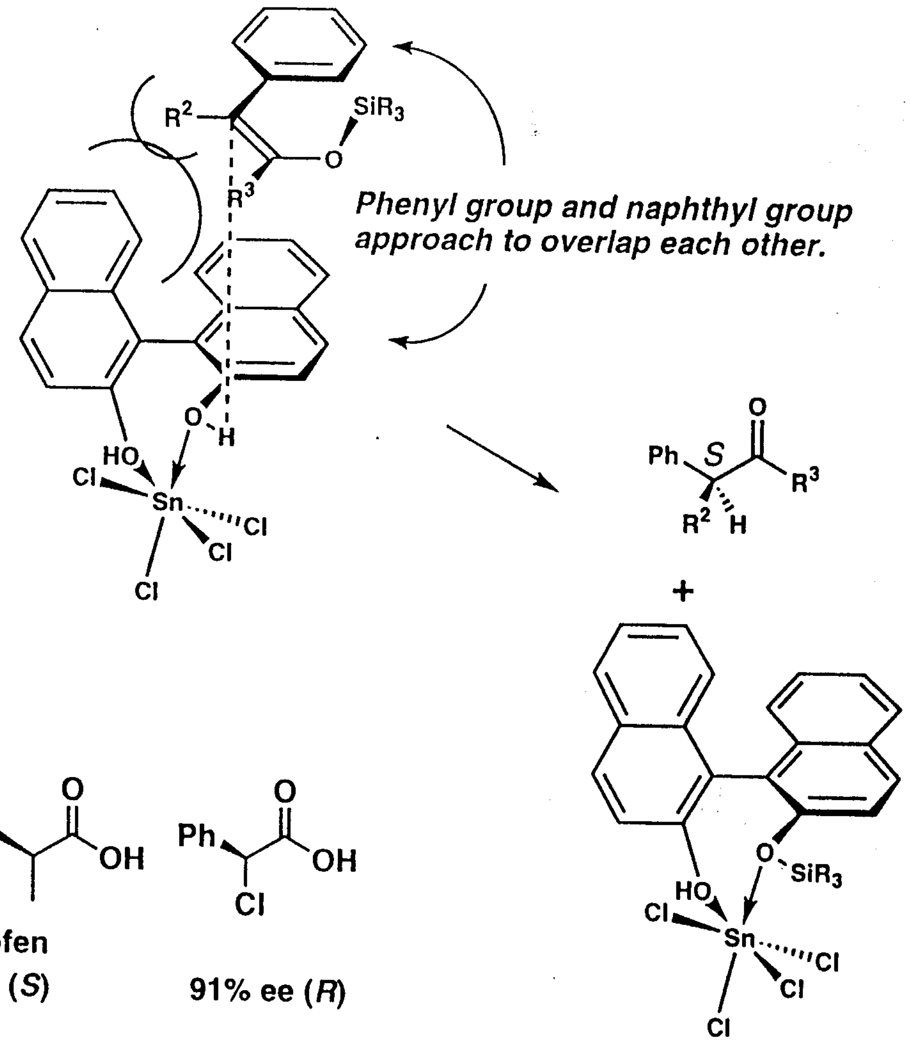



naproxen 92% ee (*S*)

ibuprofen 94% ee (*S*)

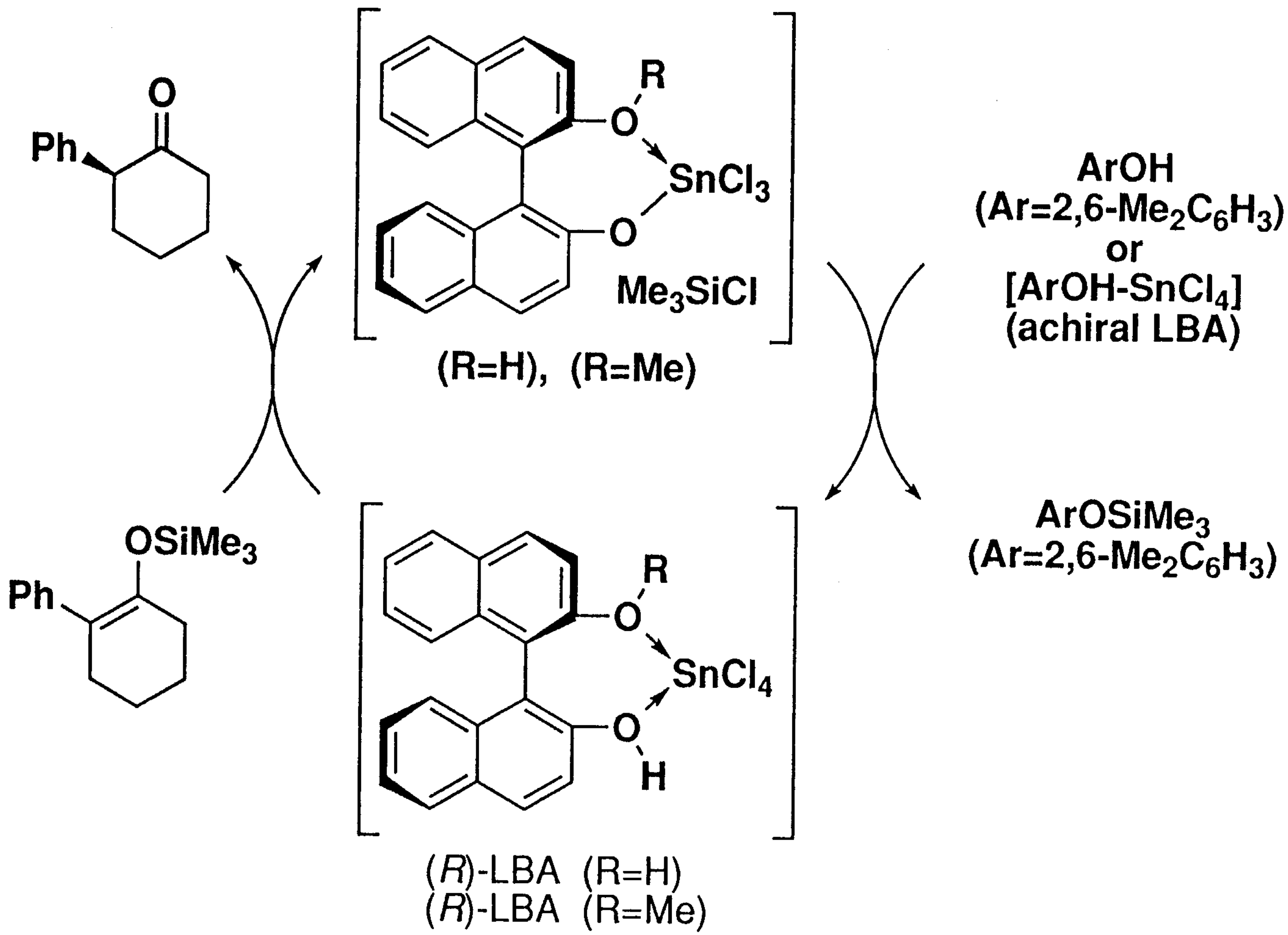
91% ee (*R*)

## Proposed Transition State Model

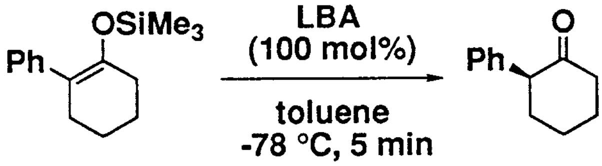


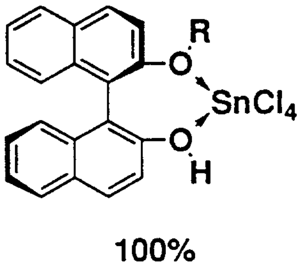

Ishihara, K.; Kaneeda, M.; Yamamoto, H. *JACS* **1994**, *116*,11179.
Ishihara, K.; Nakamura, S.; Yamamoto, H. *Croat. Chem. Acta*, in press.

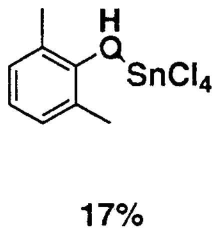
### *Proposed Catalytic Cycle for the Enantioselective Protonation of Silyl Enol Ethers Catalyzed by LBA 1 or 3*



*Comparison of the Reactivities of LBAs in the Protonation of Enol Ether at -78˚C for 5 min*



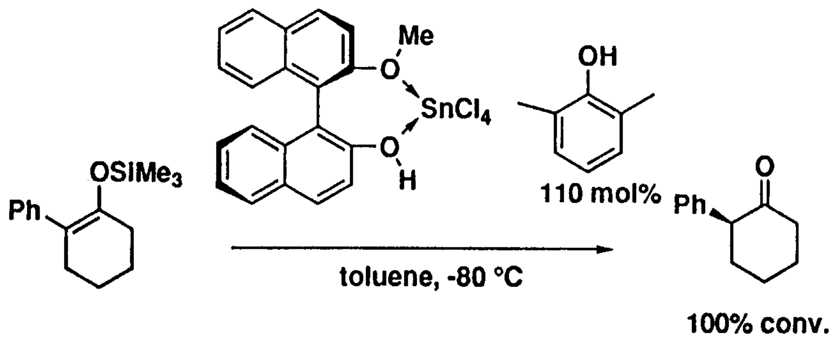




$SnCl_4$

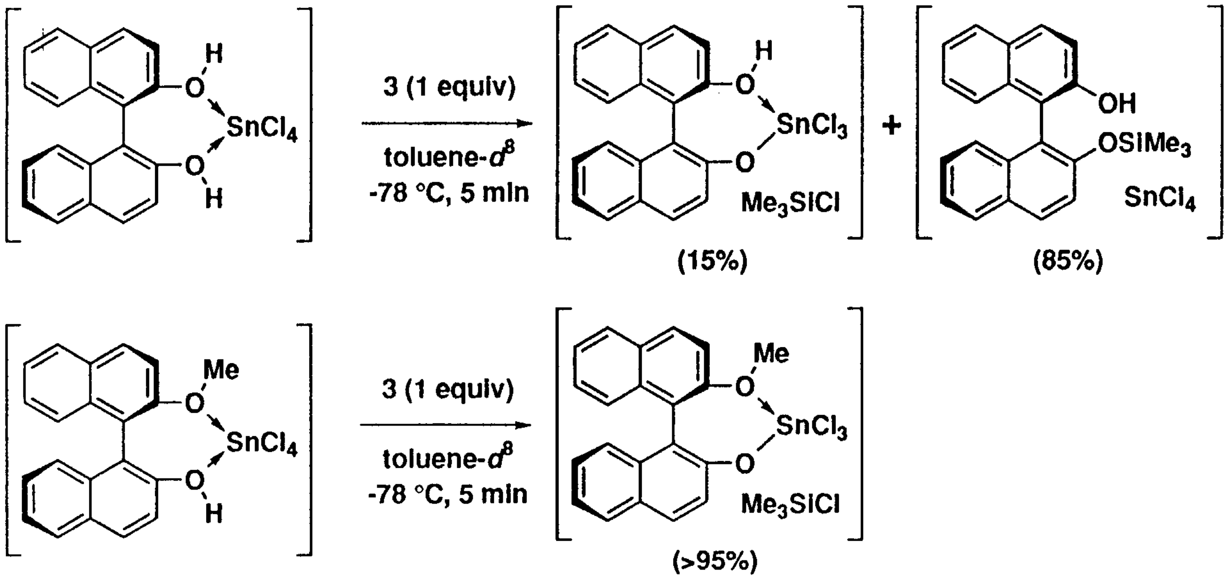
0%

## *LBA Catalyzed Enantioselective Protonation*

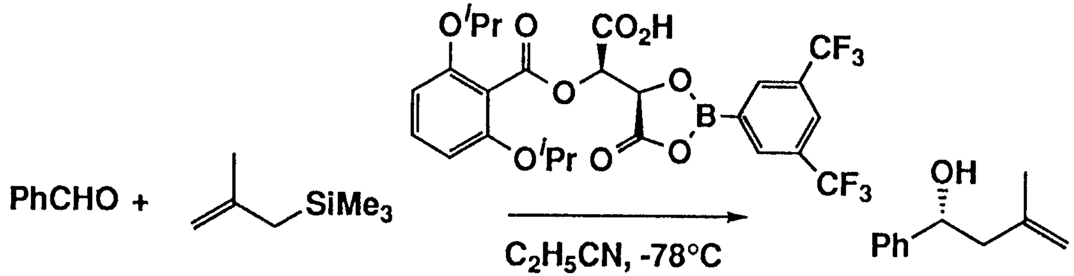



| entry | (*R*)-BINOL-Me (mol%) | $SnCl_4$ (mol%) | time (h) | optical yield (% ee) |
|---|---|---|---|---|
| 1 | 2 | 50 | 2 | 90 |
| 2 | 2 | 110 | 1 | 90 |
| 3 | 5 | 110 | 0.5 | 91 |
| 4 | 20 | 16 | 1 | 0 |

*Tin Aryloxide Intermediates Predicted by ¹H NMR Analyses*

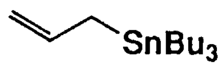


# Chiral Lewis Acid Catalyzed Allylation



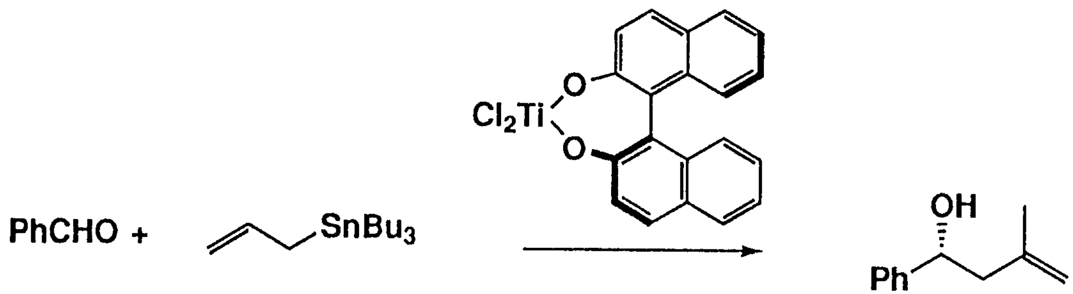

99%, 88% ee ( *R* )

*Synlett*, 1991, 561




with CAB catalyst

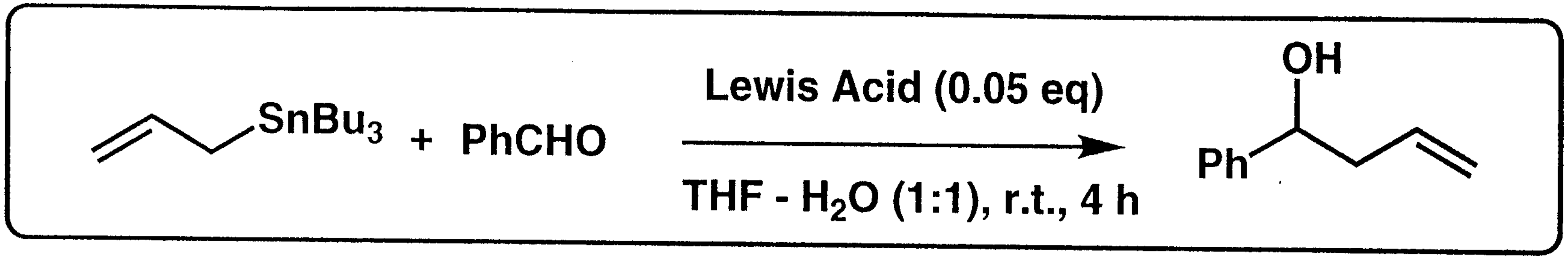
J. A. Marshall, Y. Tng, *Synlett*, 1992, 653



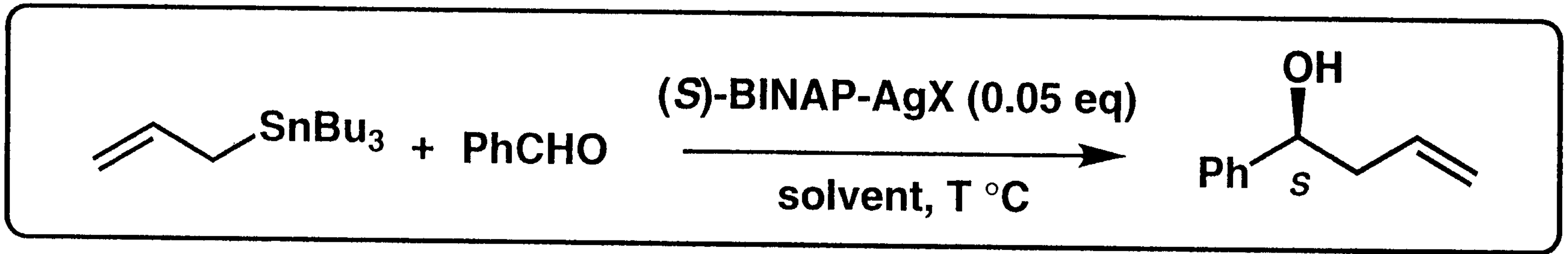

88~95%, 92~95% ee ( *R* )

G. E. Keck, K. H. Tarbet, L. S. Geraci, *J. Am. Chem. Soc.*, 115, 8467 (1993); A. L. Costa, M. G. Piazza, W. Tagliavini, C. Trombiani, A. Umani-Ronchi, *J. Am. Chem. Soc.*, 115, 7001 (1993).

# Silver(I) Catalyzed Allylation of Aldehyde with Allyltributyltin in Aqueous Media

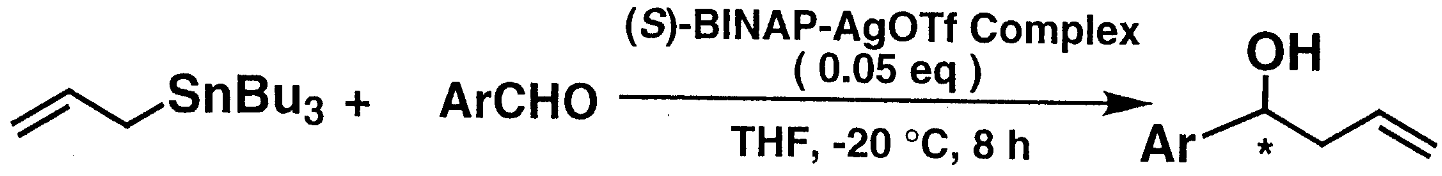



| Lewis Acid | yield, % |
|---|---|
| — | <1 |
| $AgOCOCF_3$, AgOTf, $AgNO_3$ | 48~44 |
| $AgOCOCF_3$•$2PPh_3$ | 92 |

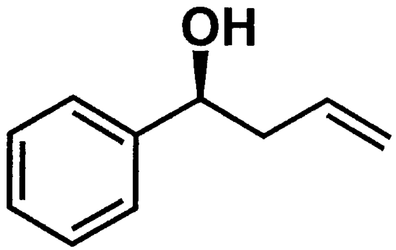



| AgX | solvent | T °C | yield, % | % ee |
|---|---|---|---|---|
| $AgOCOCF_3$ | THF - $H_2O$ (1:1) | r.t. | 96 | 30 |
| AgOTf | THF - $H_2O$ (1:1) | 0 | 46 | 60 |
| AgOTf | THF | -20 | 88 | 96 |

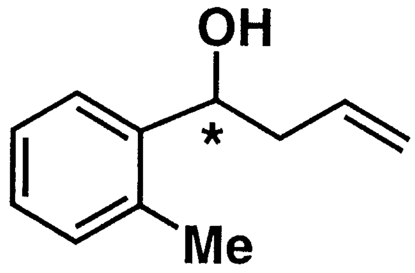
# Asymmetric Allylation of Various Aldehydes Catalyzed by (*S*)-BINAP·AgOTf Complex ( Part 1 )



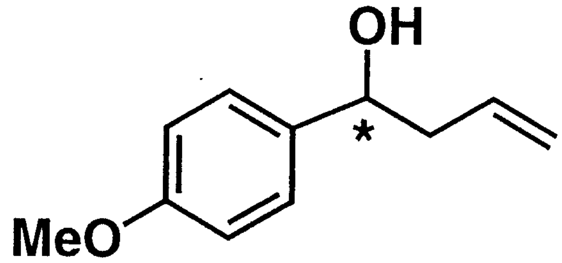

## Product ( yield, enantioselectivity, configuration )



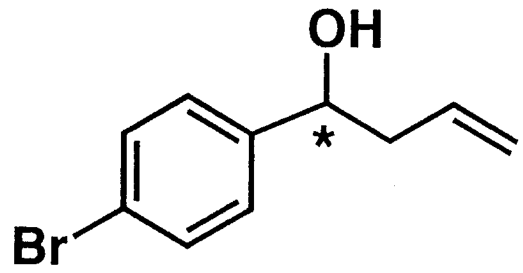

( 88%, 96% ee (*S*) )



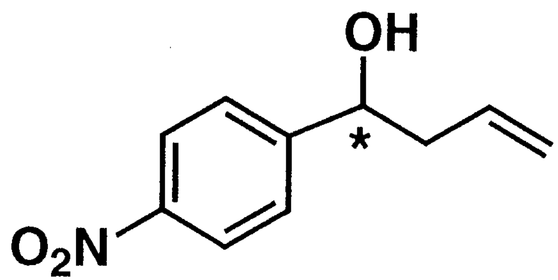

( 85%, 97% ee )




( 59%, 97% ee )

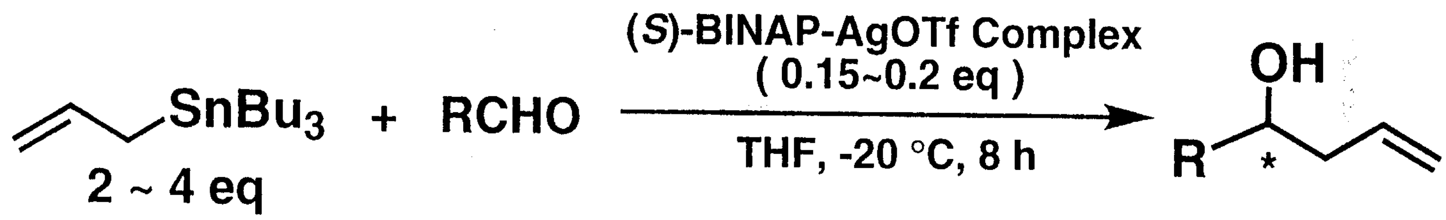



( 95%, 96% ee )

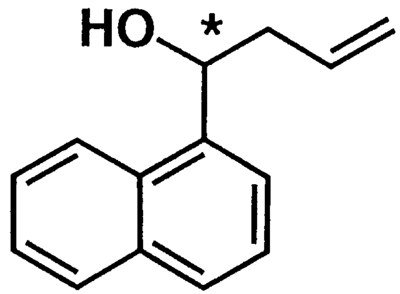



( 80%, 61% ee )

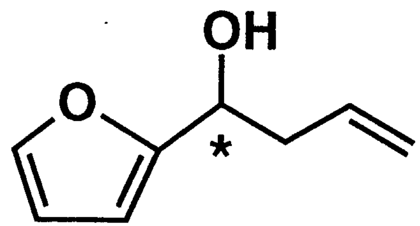
# Asymmetric Allylation of Various Aldehydes Catalyzed by (*S*)-BINAP·AgOTf Complex ( Part 2 )



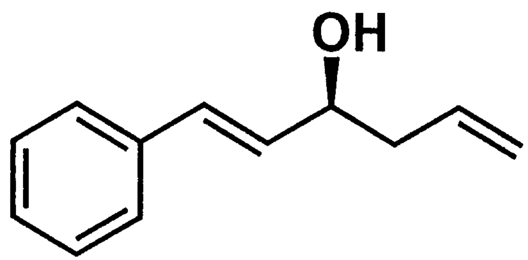

**Product ( yield, enantioselectivity, configuration )**



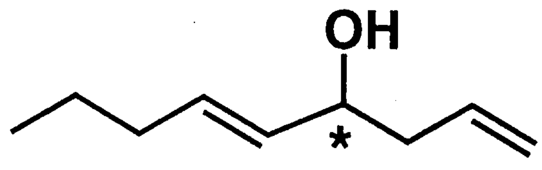

( 89%, 97% ee )




( 94%, 93% ee )

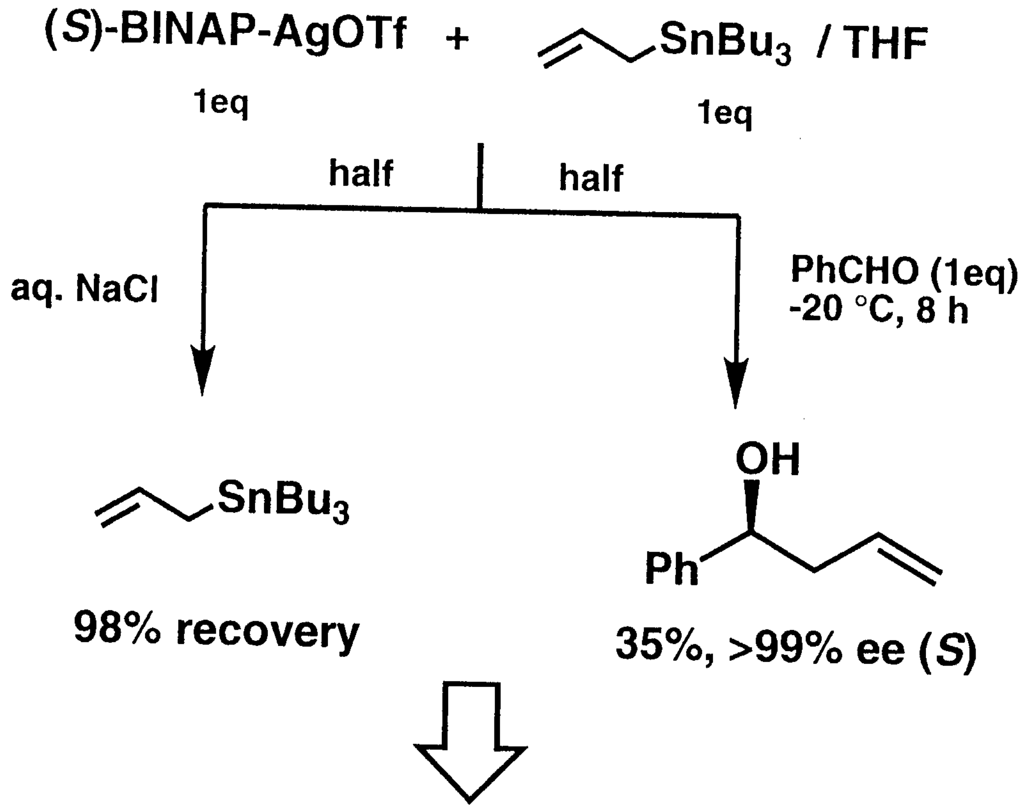



( 83%, 88% ee (*S*) )



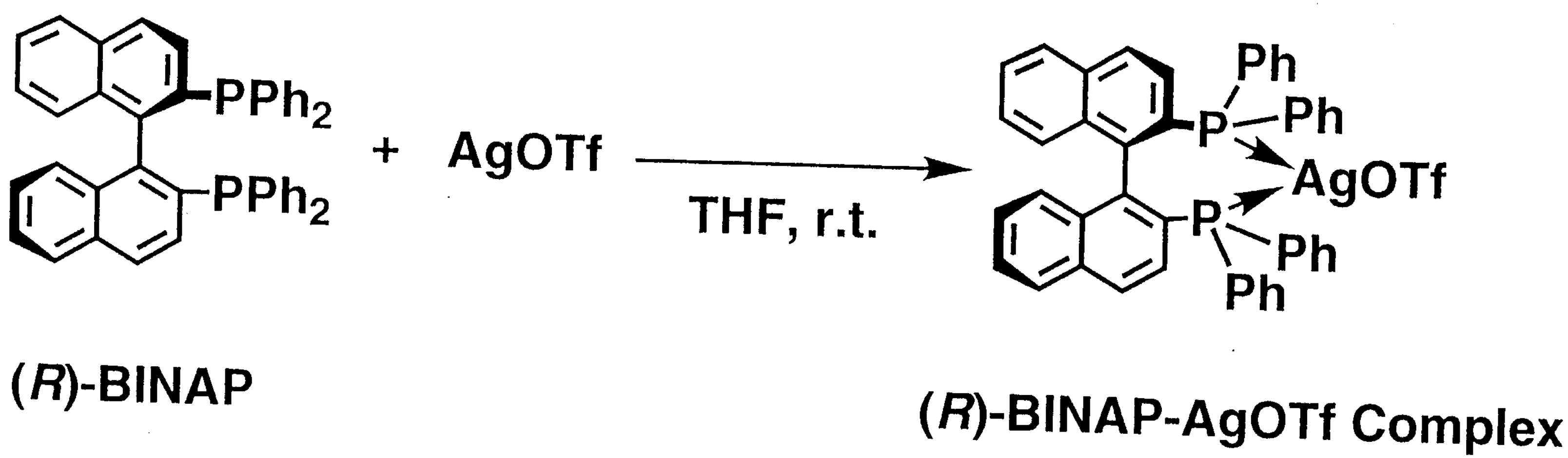

( 72%, 93% ee )

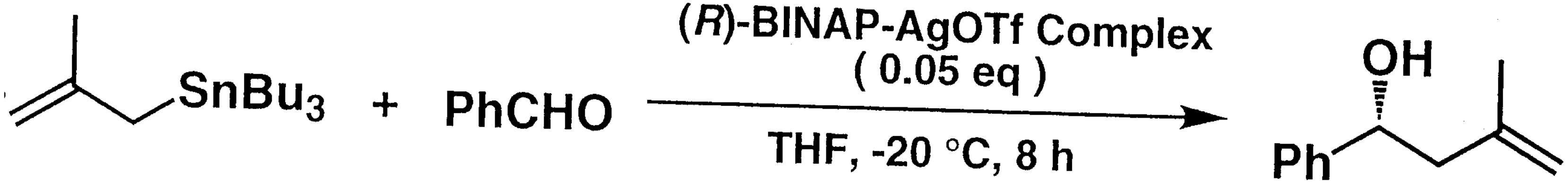
# Possibility of Transmetallation Mechanism



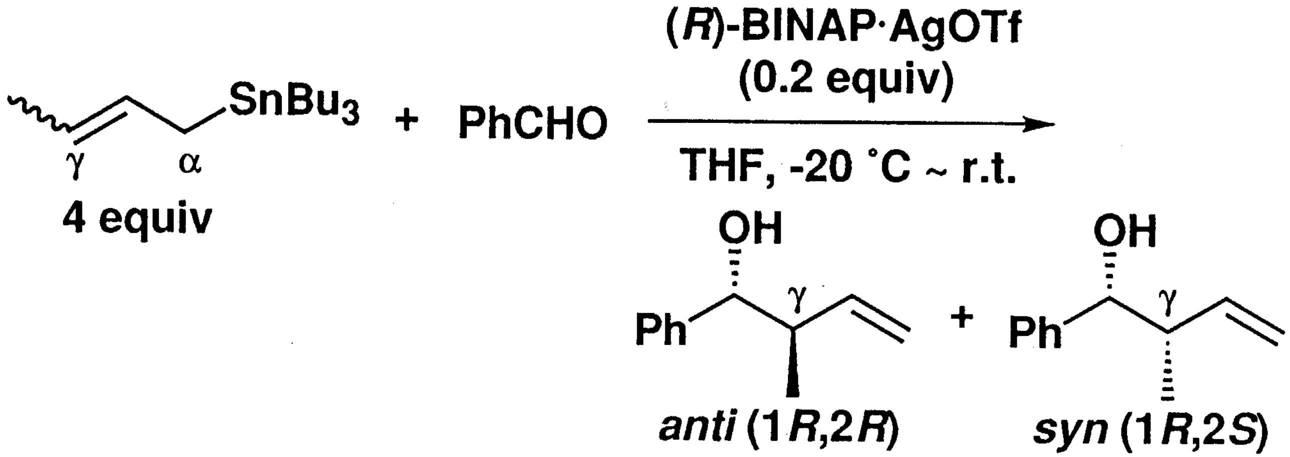

**Transmetallation does not occur before addition of benzaldehyde**

# Enantioselective Addition of Methallylstannane to Benzaldehyde Catalyzed by (*R*)-BINAP-AgOTf Complex




75% yield, 92% ee (*R*)




| *E:Z* ratio of crotyltin | Yield (%) | *anti* (% ee) : *syn* (% ee) |
|---|---|---|
| 95 : 5 | 56 | 85 (94) : 15 (64) |
| 2 : 98 | 72 | 85 (91) : 15 (50) |
| 53 : 47 | 45 | 85 (94) : 15 (57) |

## Plausible acyclic and cyclic transition-state structures