

Società Chimica Italiana - Divisione di Chimica Organica
Università di Napoli Federico II

Ischia Advanced School of Organic Chemistry, VII Session

September 29 - October 4, 1996

Dialkoxy-Cyclopentadienyl-Titanium as Template for Stereoselective Reactions

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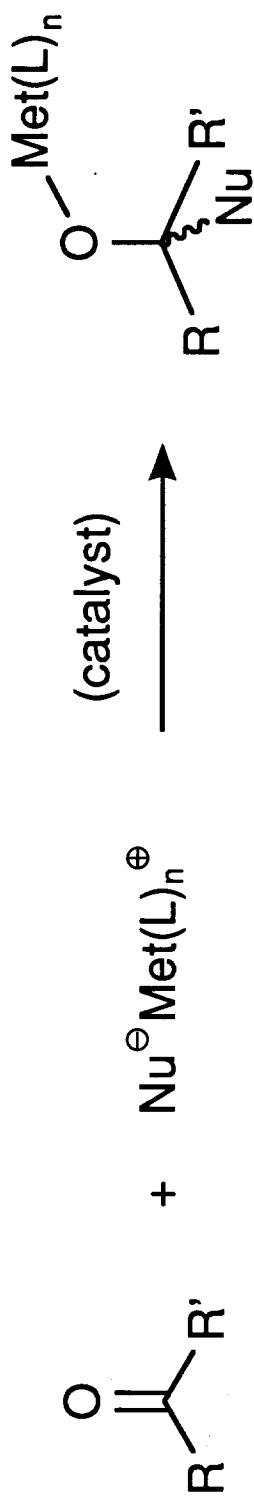
Literature References

Chem. Rev. 1992, 92, 807 - 832.

J. Am. Chem. Soc. 1992, 114, 2321 - 2336.

Pure Appl. Chem. 1992, 64, 1897 - 1910.

Inorg. Chim. Acta 1994, 222, 95 - 113.



Stereocontrol

Chirality

by chiral substrate

R, R'

by chiral reagent

Nu^- $\boxed{\text{Met}(\text{L})_n^+}$

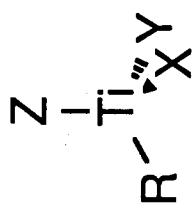
by chiral catalyst

- Well defined, stable metal complexes

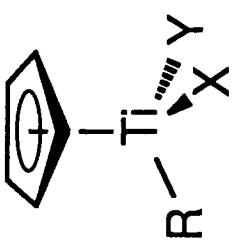
- Non-toxic abundant elements

- Readily available ligands

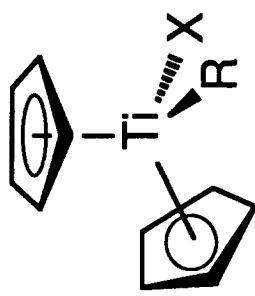
Titanium (Zirconium, Hafnium)



8-electron center



12-electron center



16-electron center

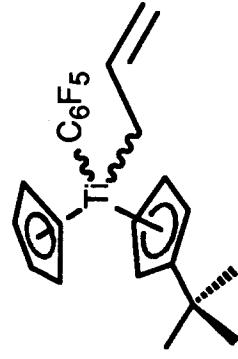
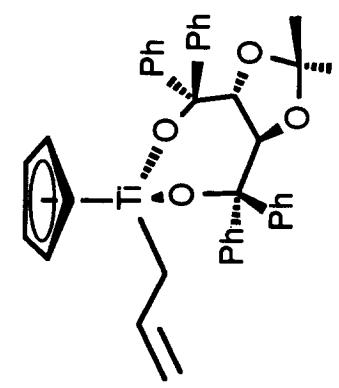
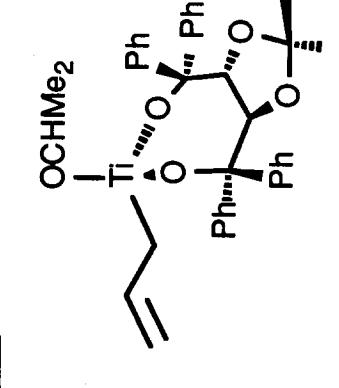
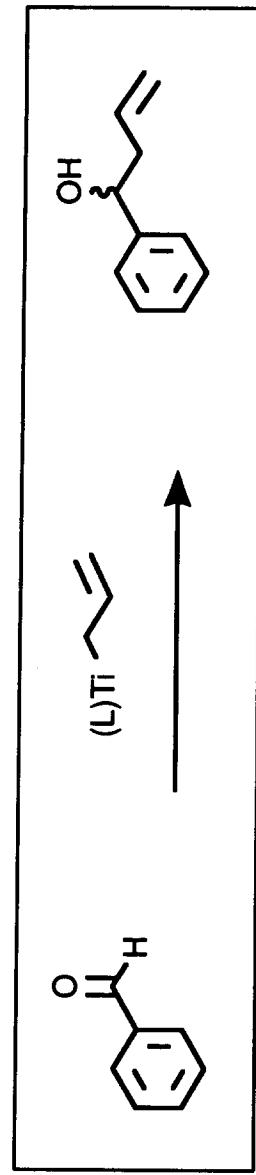
$X, Y, Z:$ Cl, Alkyl, NR₂, OR, Cyclopentadienyl

$X, Y, Z:$

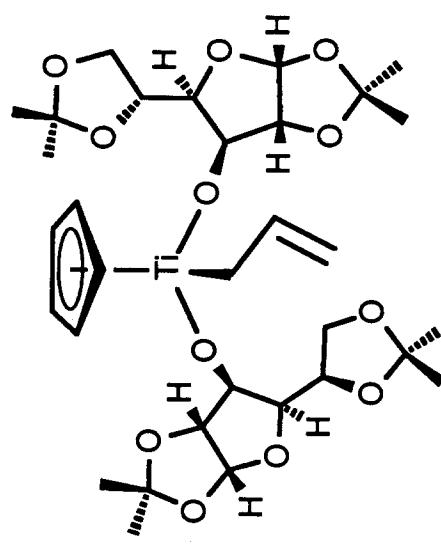
increasing
tendency for aggregation
decreasing

stability
reactivity

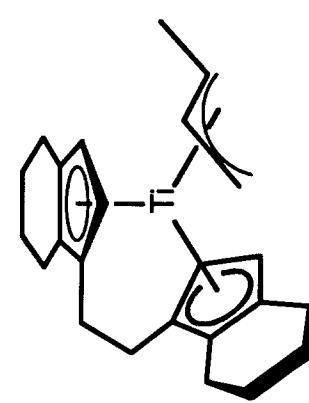
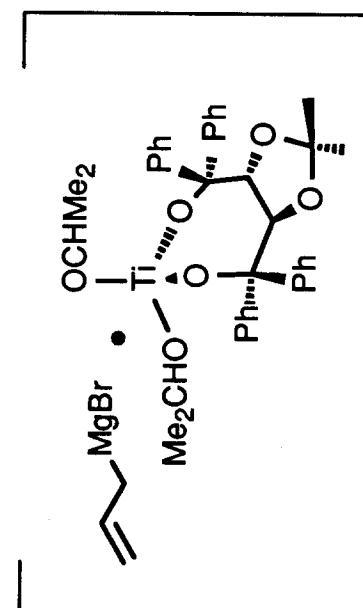
selectivity
monomeric structures
Lewis-acidity



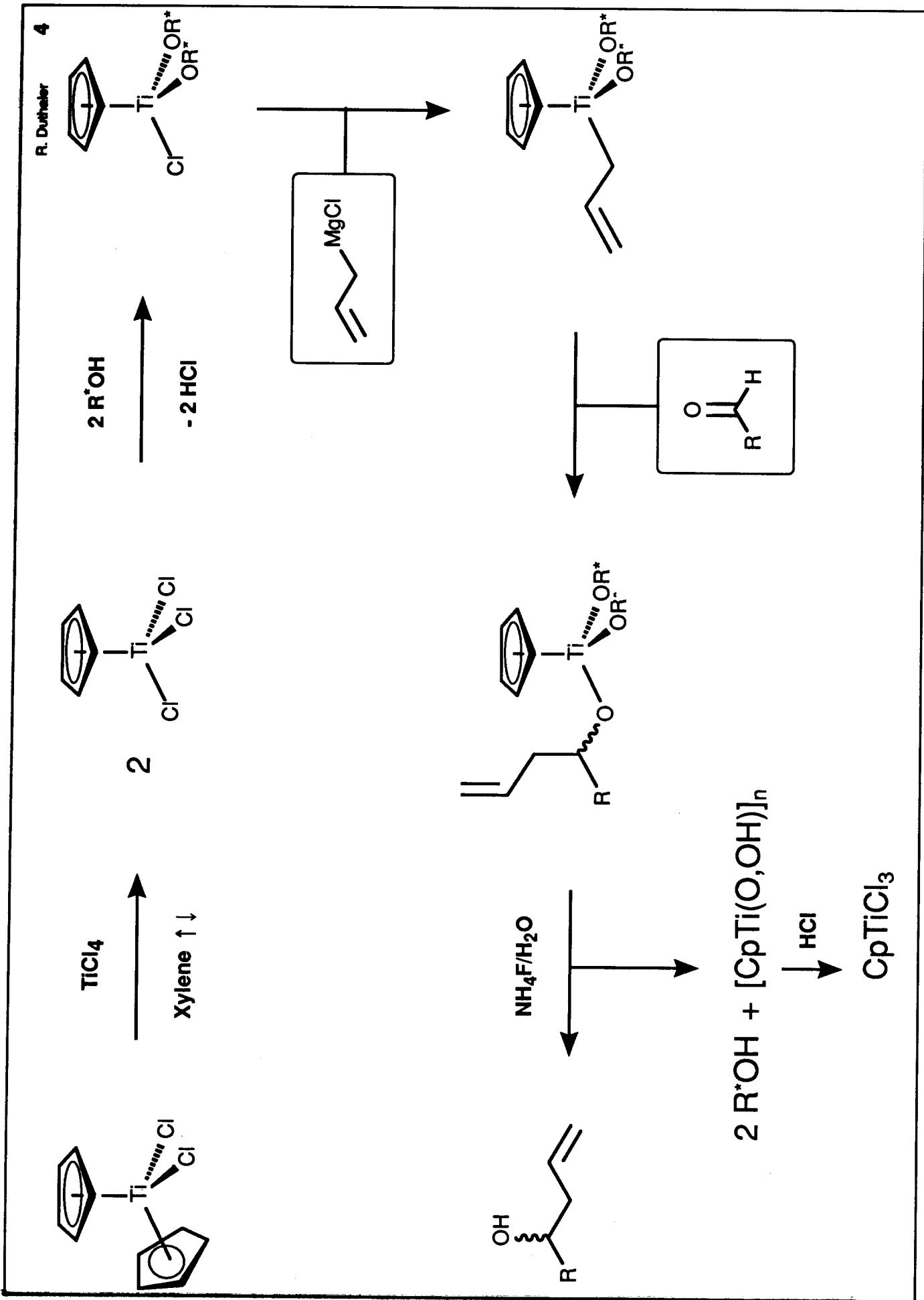
40% de
(M.T. Reetz, 1984)

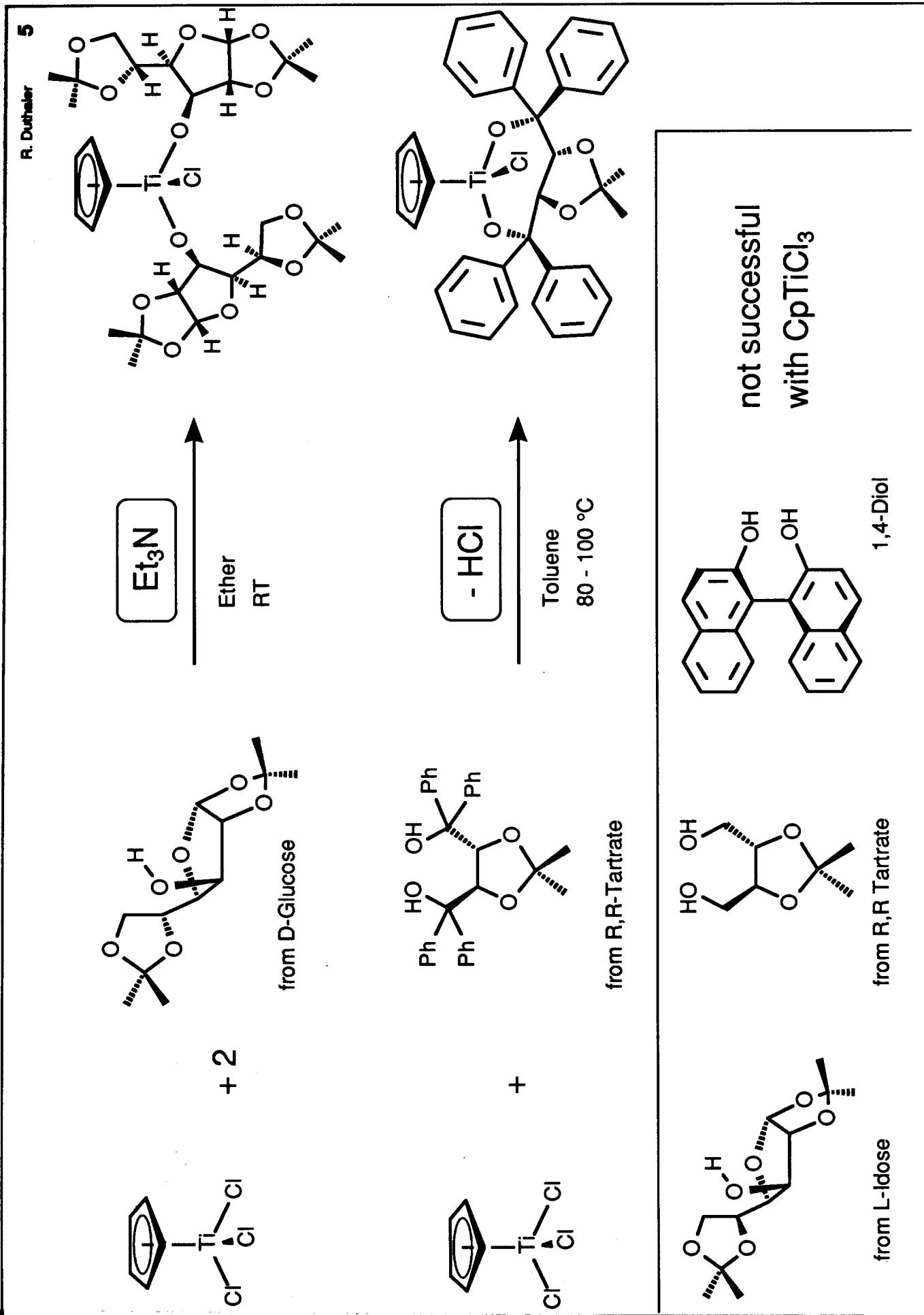


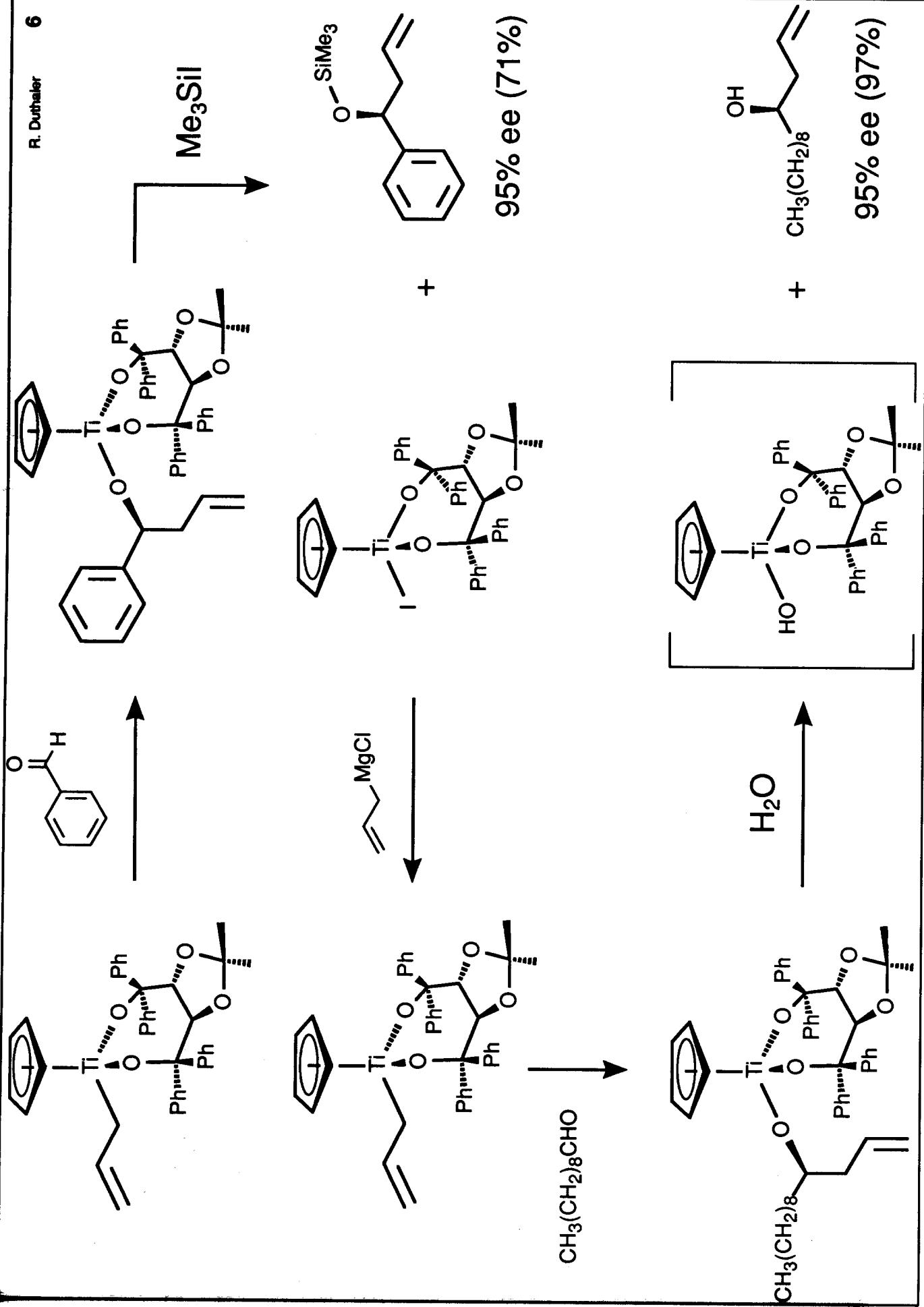
23% ee (R, anti)
(Sc. Collins, 1989)

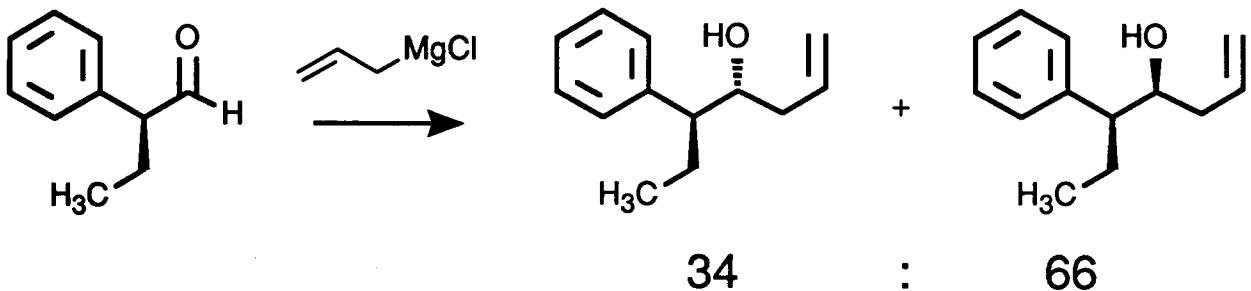
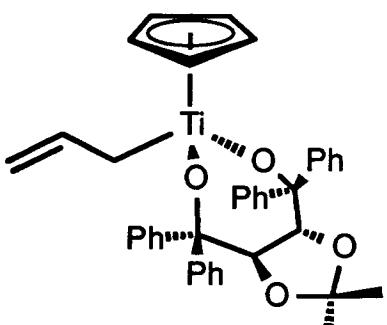


90% ee (R)

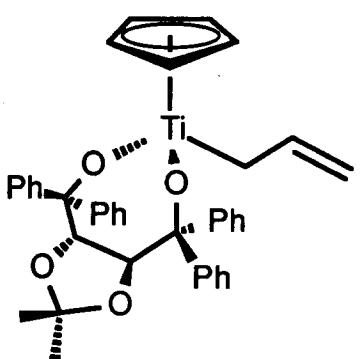




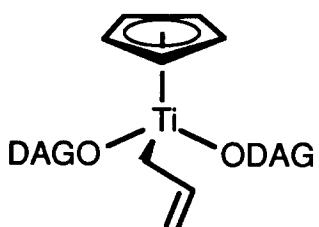


ReagentProduct Ratio

(R,R)-Ligand 0.5 : 99.5



(S,S)-Ligand 95 : 5

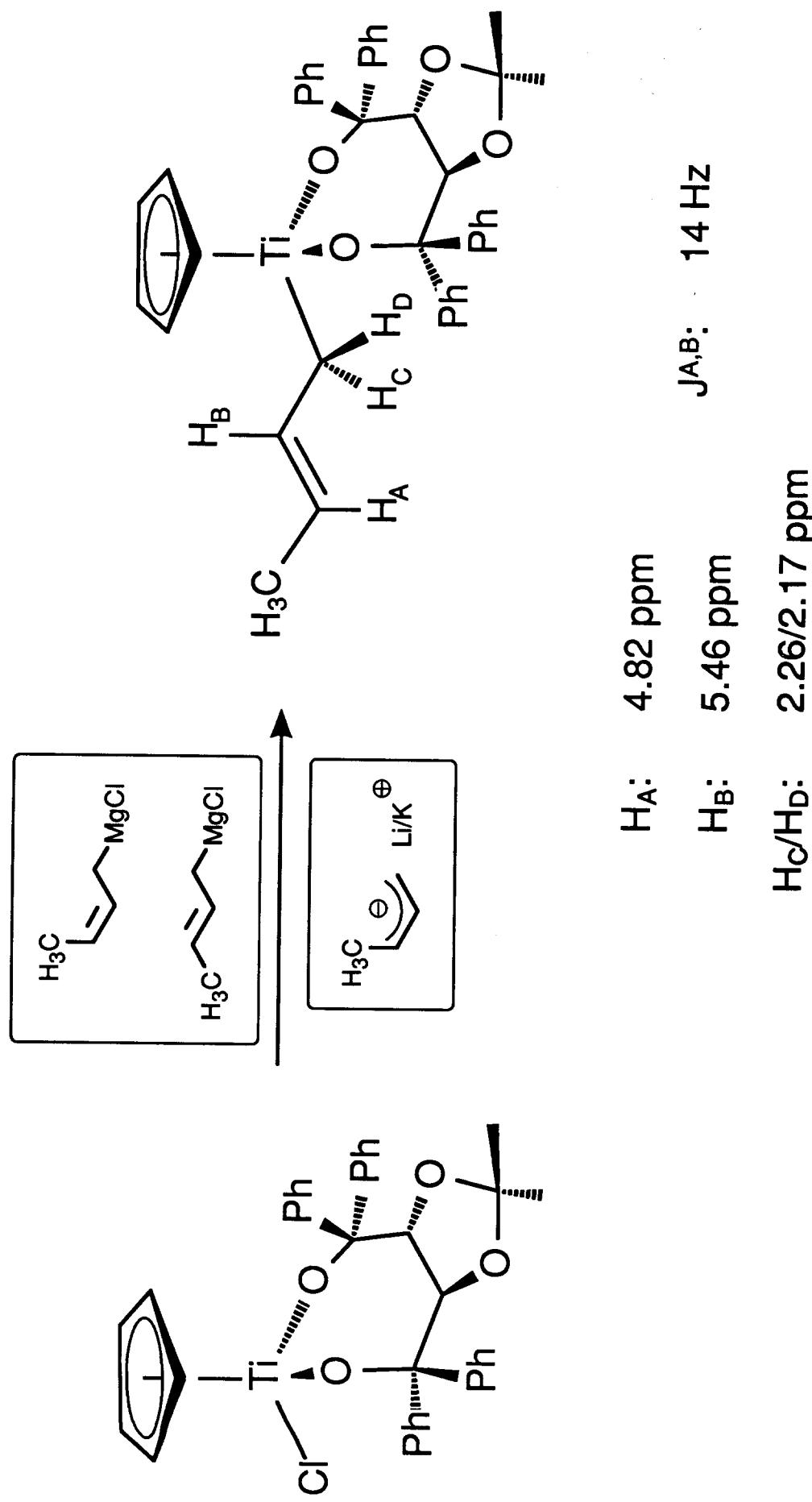


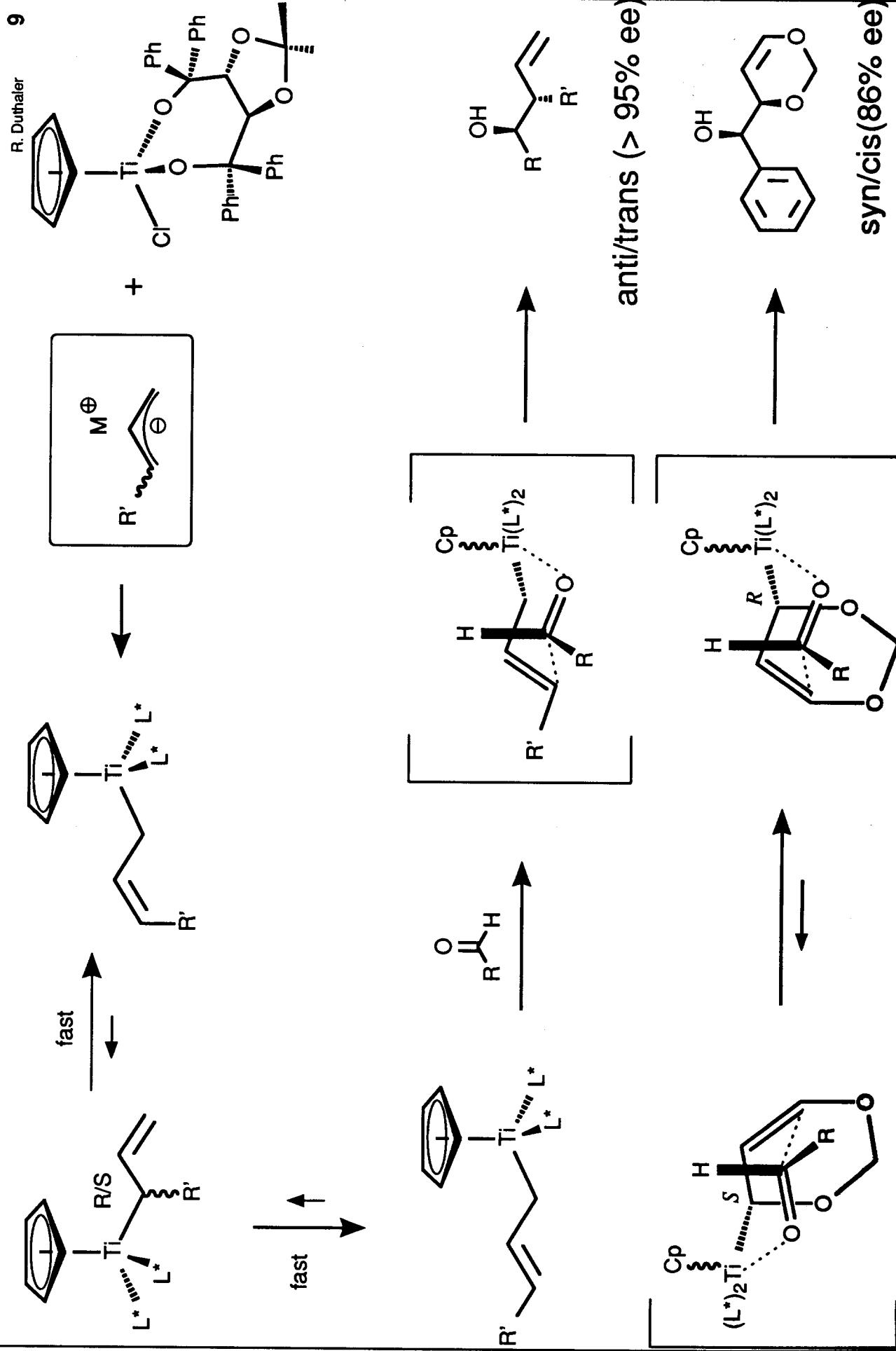
80 : 20

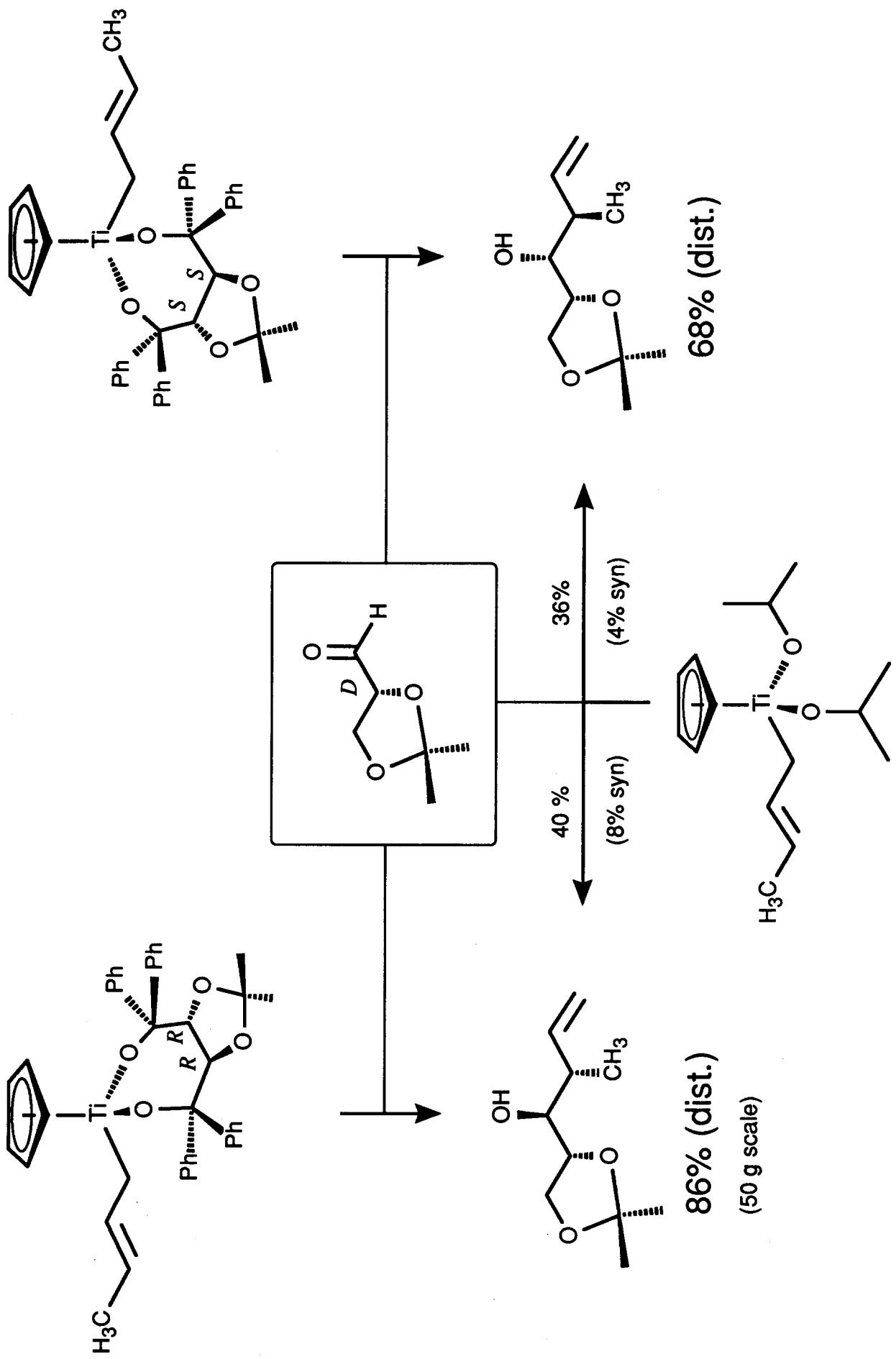
R. Marti

(-)-(Ipc)₂B-CH₂-CH=CH₂ 74 : 26(+)-(Ipc)₂B-CH₂-CH=CH₂ 3 : 97

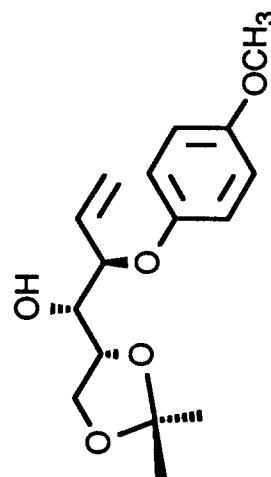
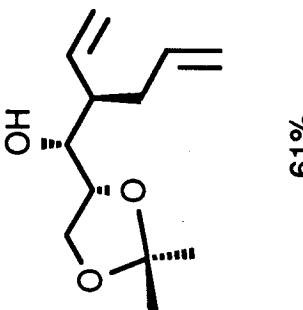
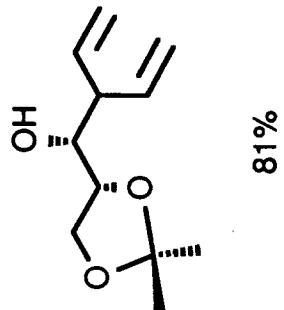
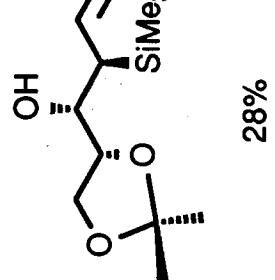
H.C. Brown (1989)



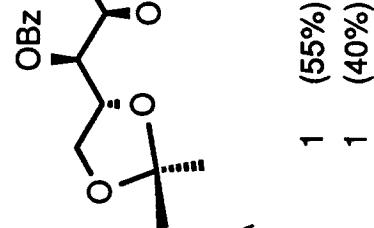
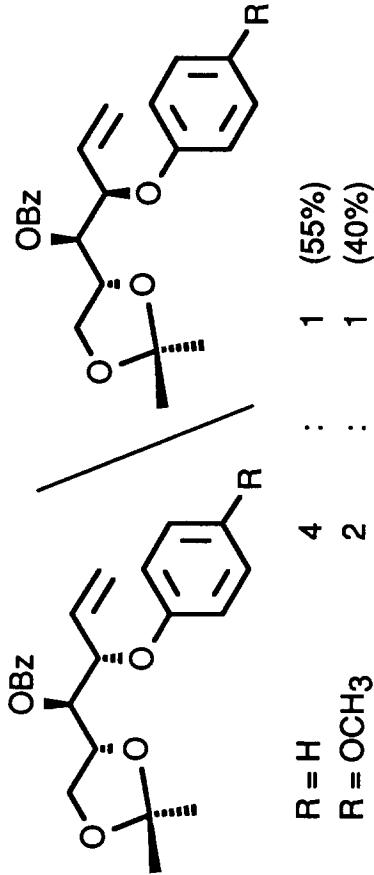
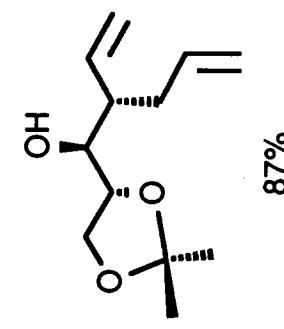
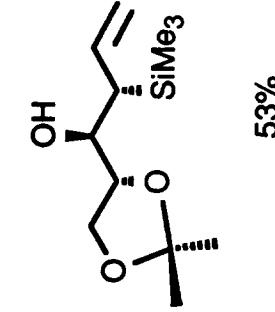
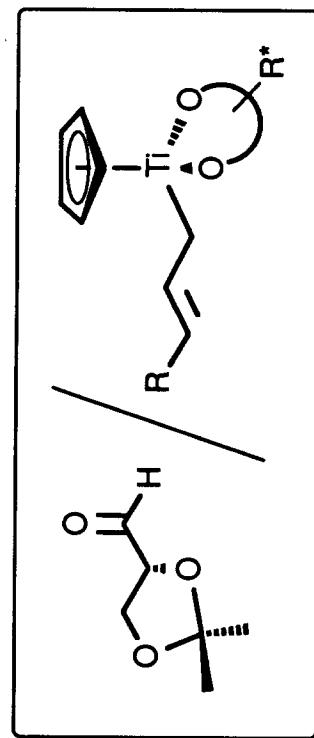
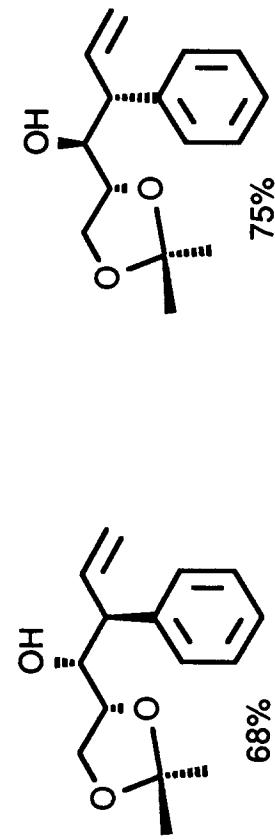




Lyxo-config. (S,S)-reagent



Ribo-config. (R,R)-reagent

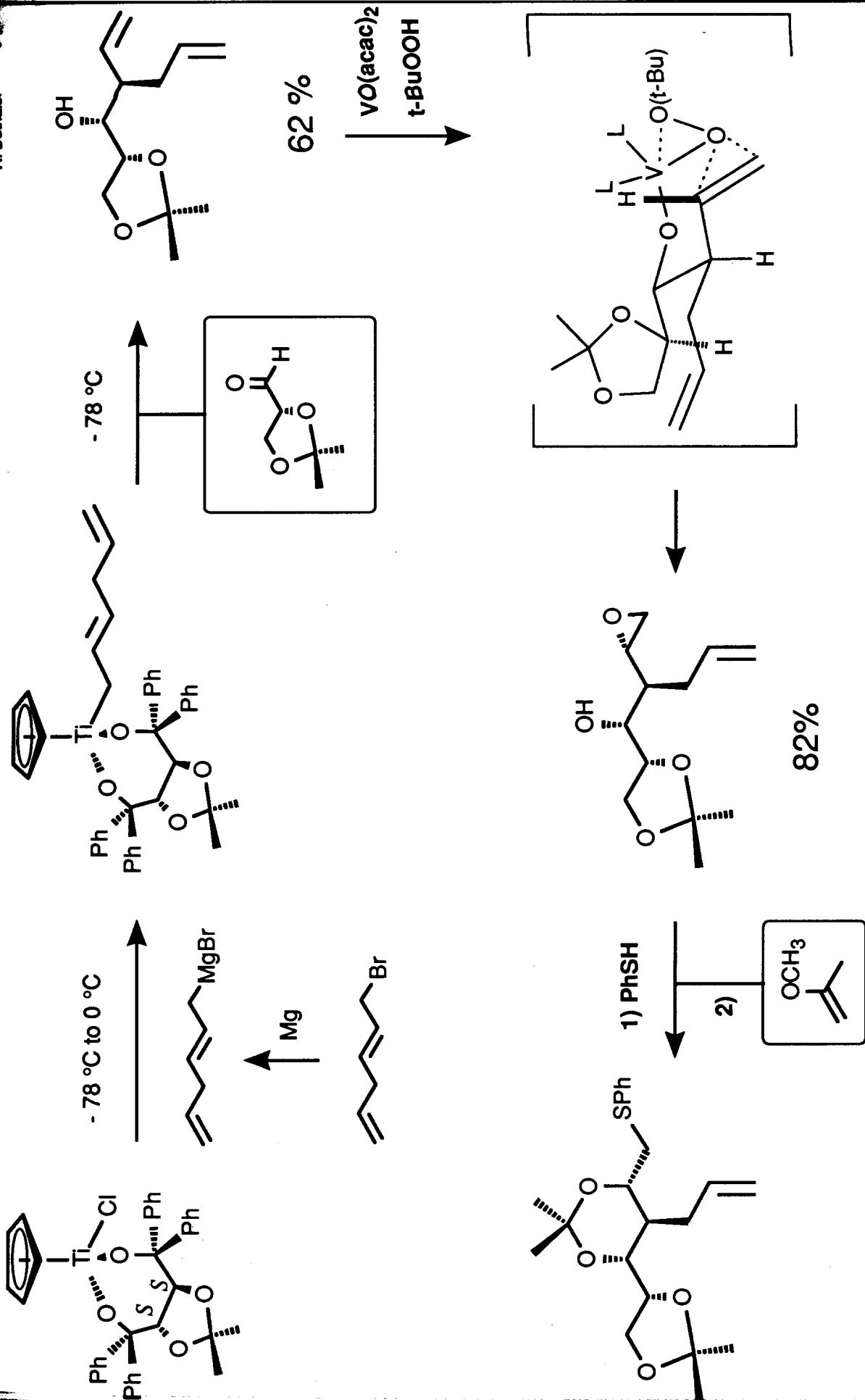


$R = H$
 $R = OCH_3$

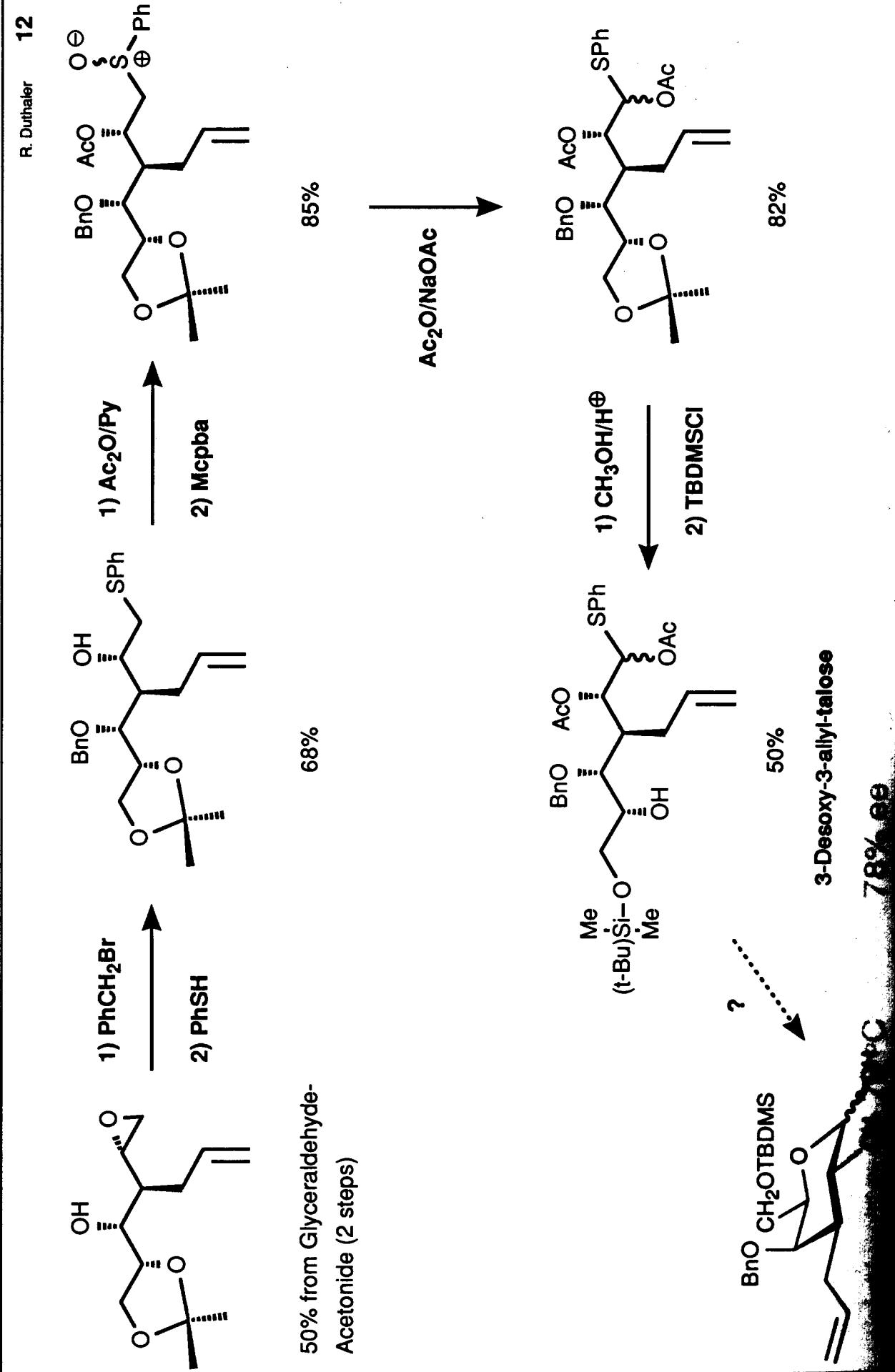
4 : 2

1 : 1

R. Duthaler

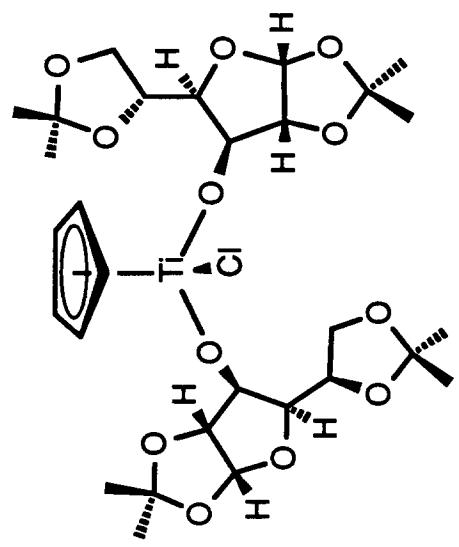


R. Wietzke, F. Niemann

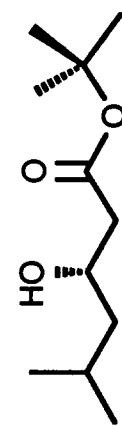
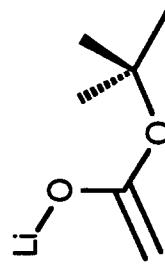
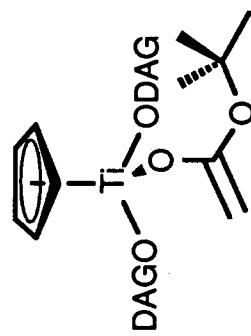
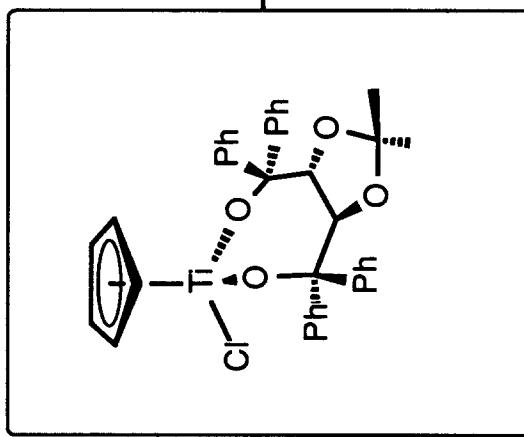


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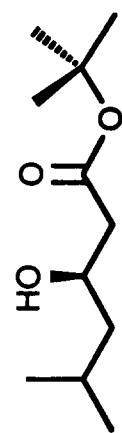
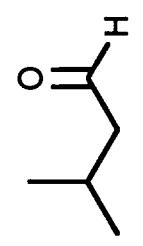
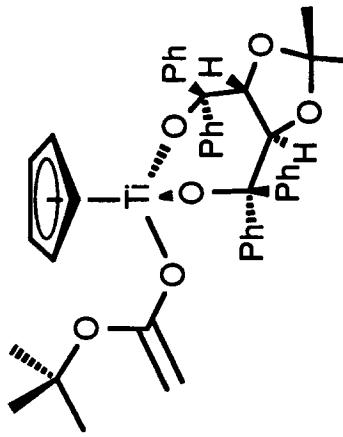
R. Duthaler



3h - 30 °C

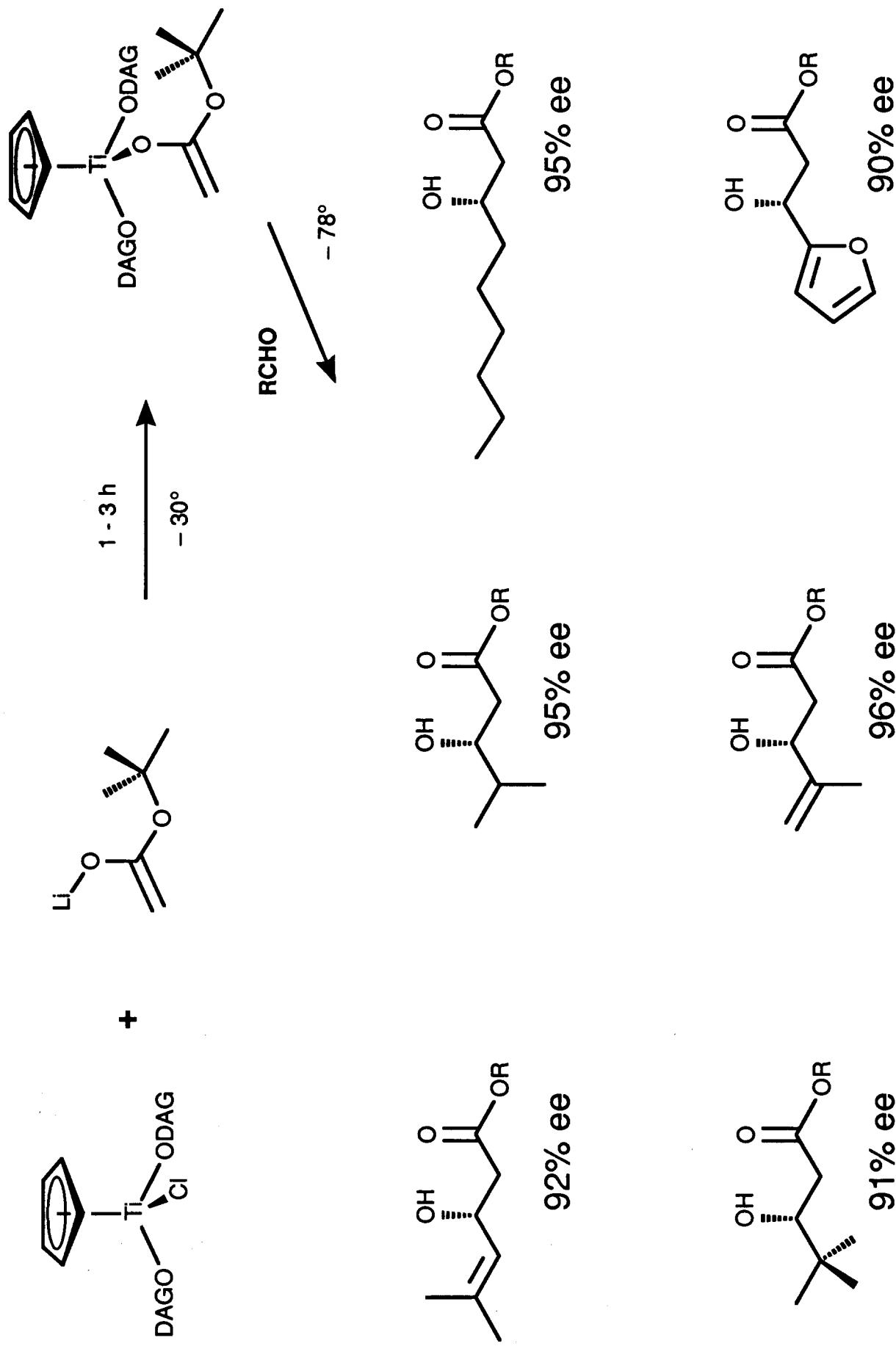
94% ee
95% ee

3h - 30 °C

78% ee
78% ee

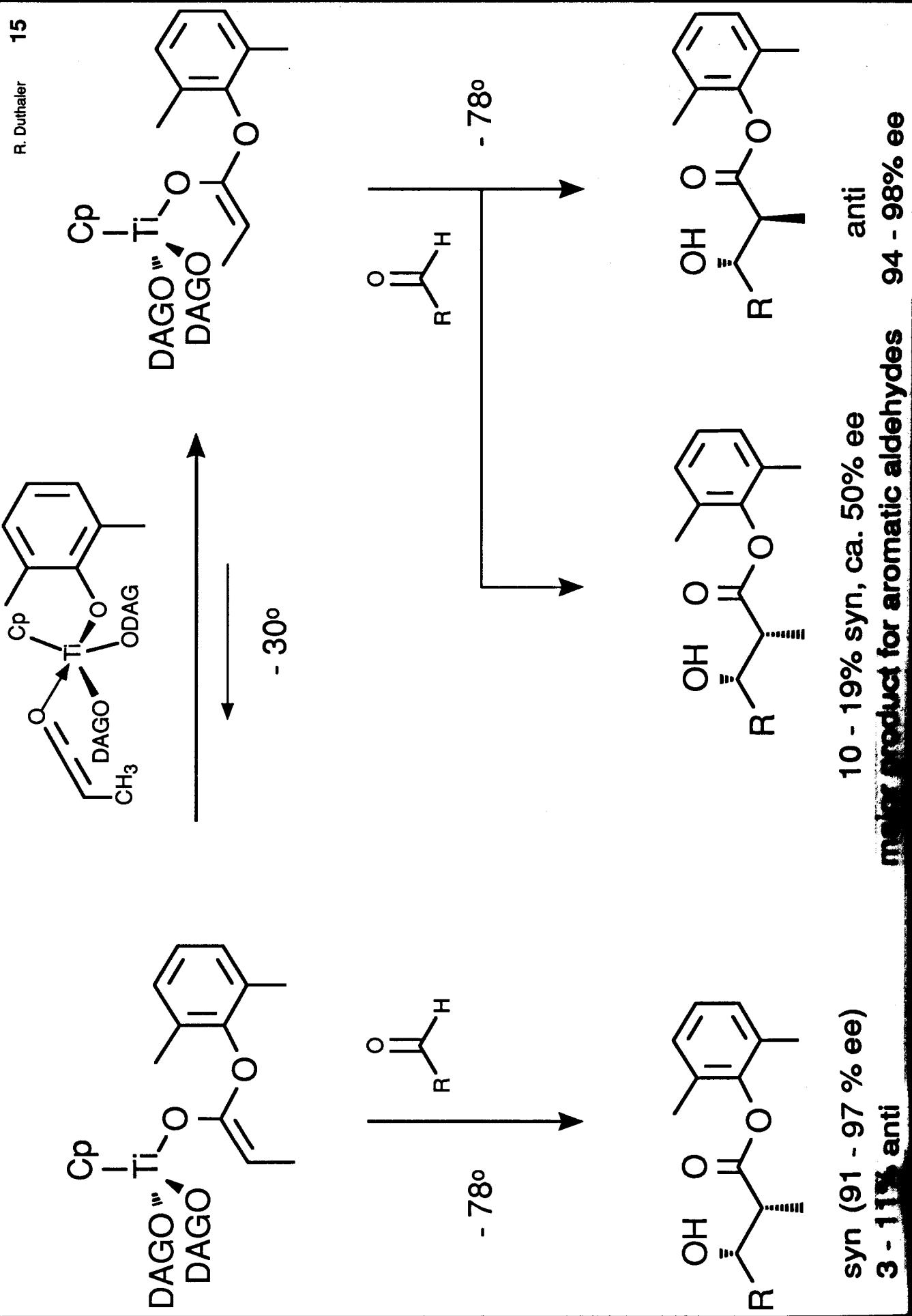
- 78 °C

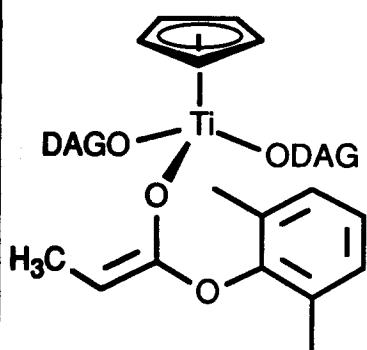
DEAUS 23-000000000000



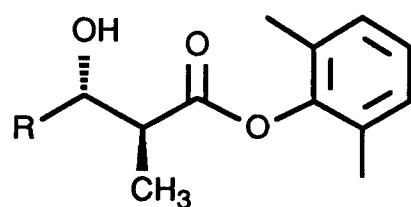
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R. Duthaler



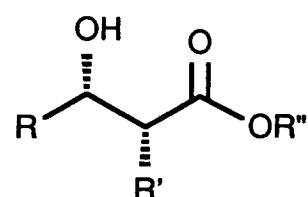
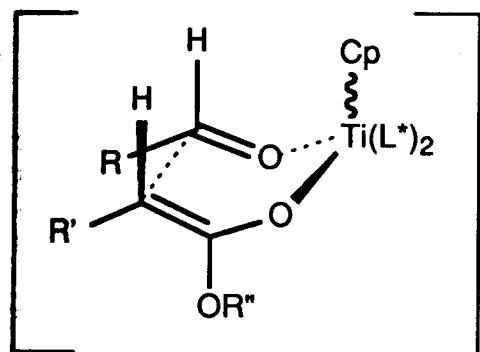


RCHO
- 78 °C

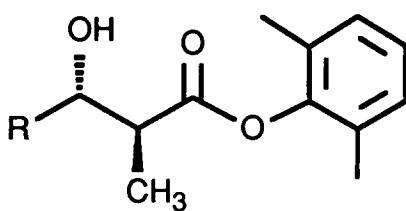
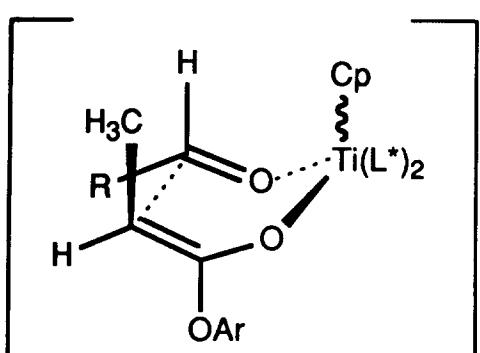


anti (23 - 90%) 94 - 98% ee
syn (10 - 77%) 47 - 98% ee

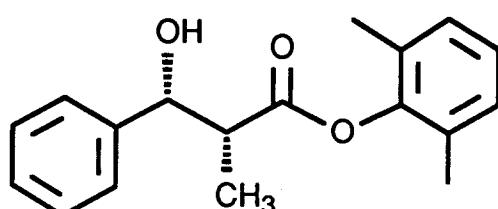
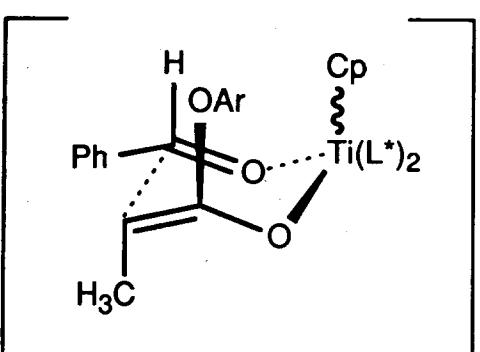
Helv. Chim. Acta. 1992, 73, 659.



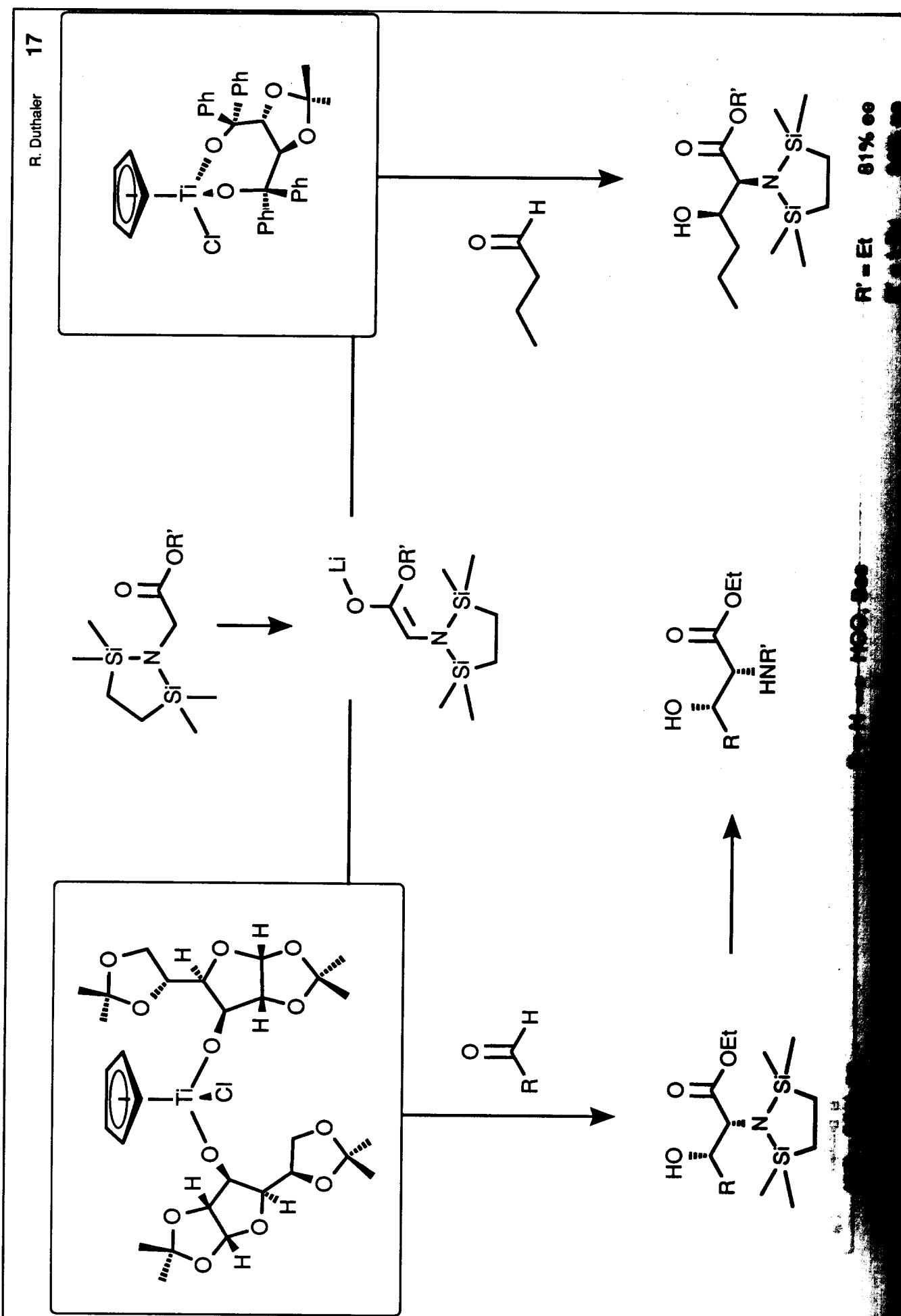
R': CH₃, N(SiMe₂CH₂)₂
syn high enant. excess

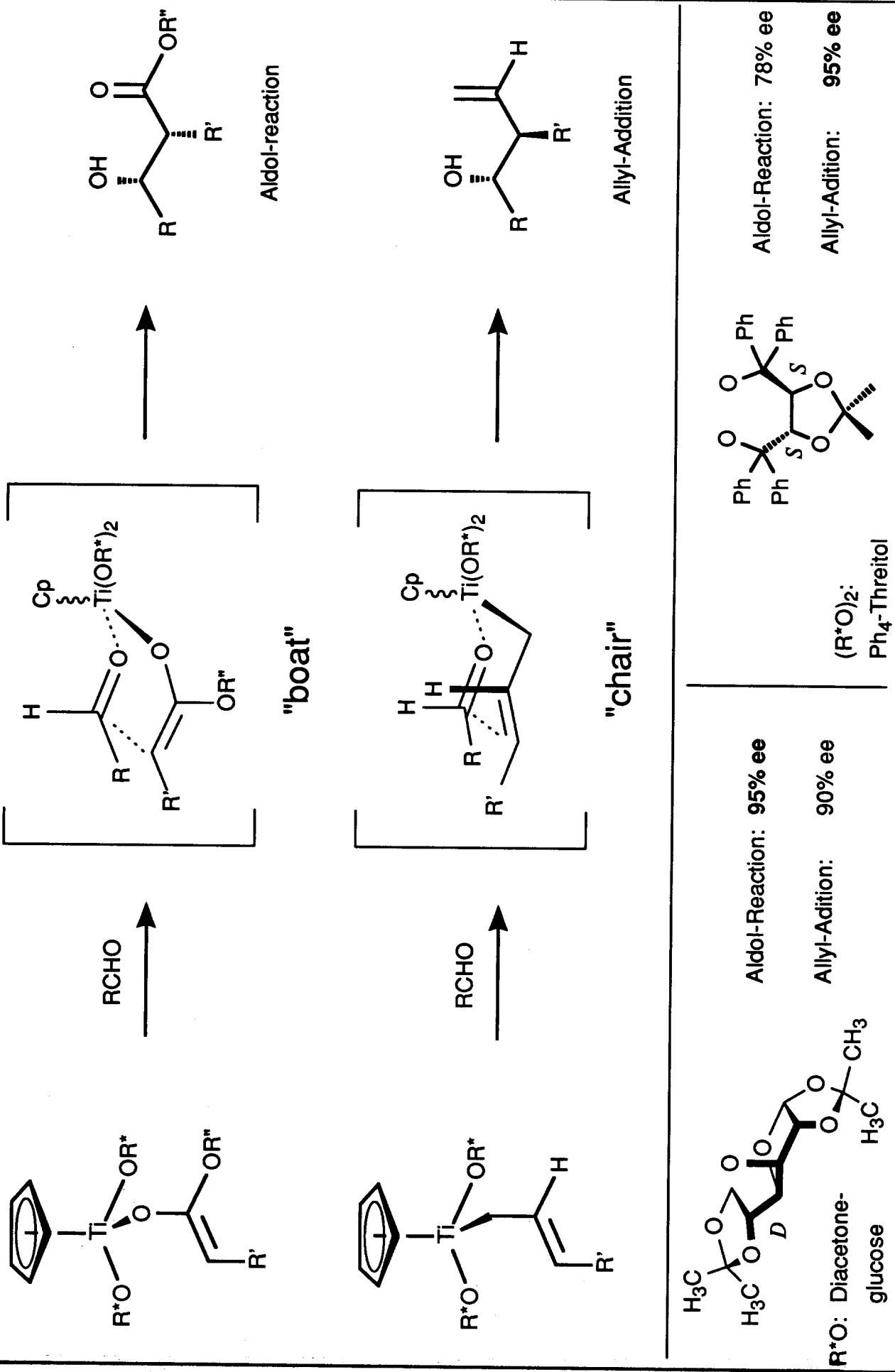


anti high enant. excess

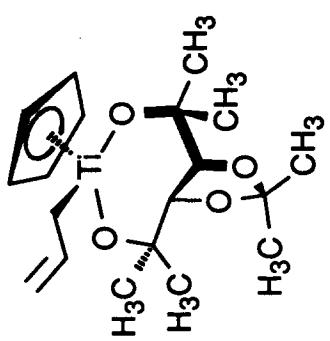


syn 47 % enant. excess

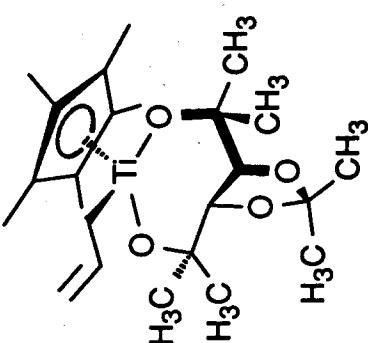




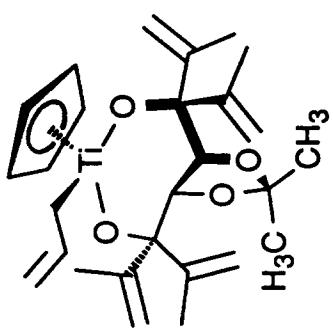
**Allyltitanation of Benzaldehyde
Ligand Influence**



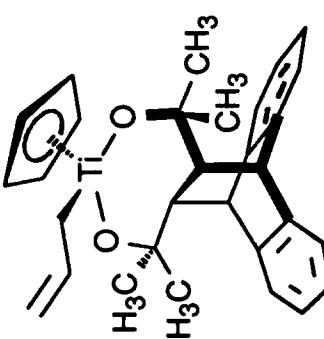
12% ee



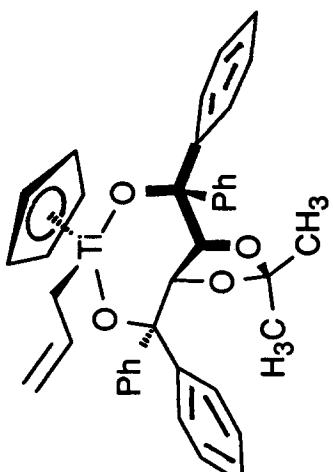
88% ee



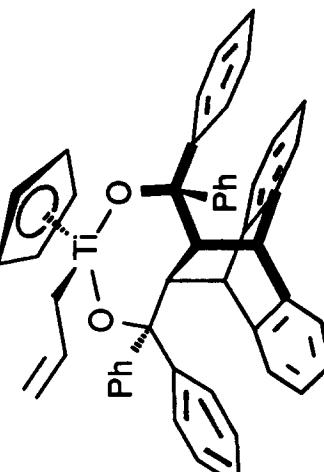
71% ee



5% ee

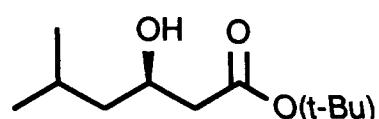
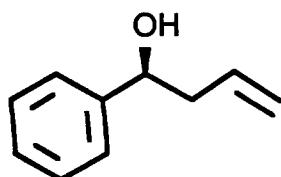
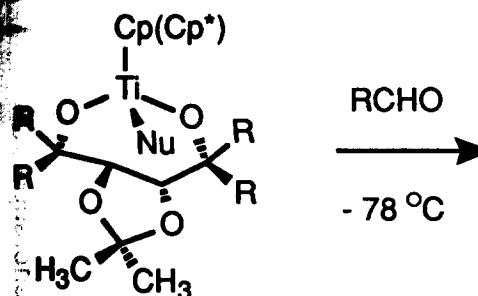


95% ee



87% ee

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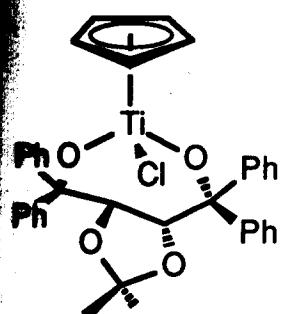


$\text{Cp}(\text{Cp}^*)\text{Ti}(\text{OR}^*)_2\text{Cl}$

optical purity of products

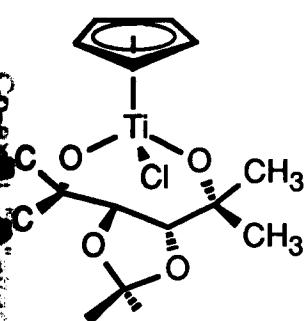
Allyltitanation

Ti-Aldol



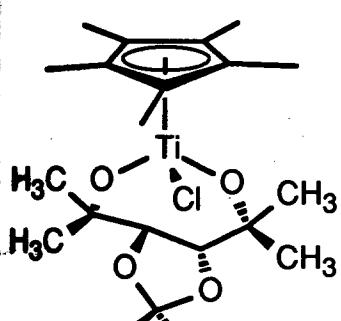
95% ee

78% ee



12% ee

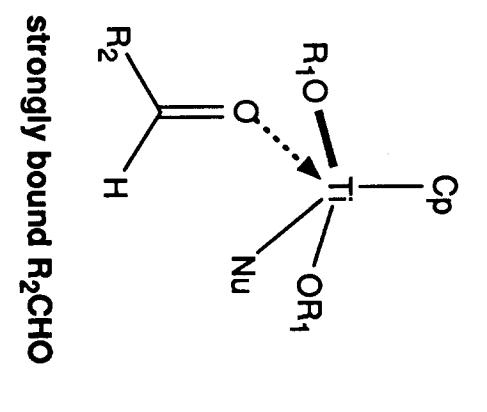
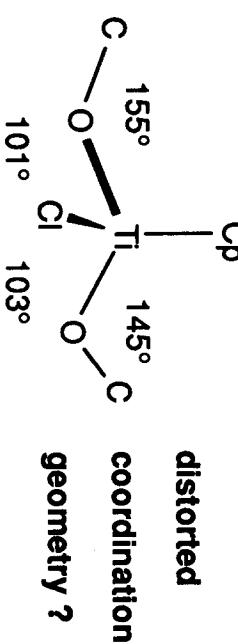
42% ee



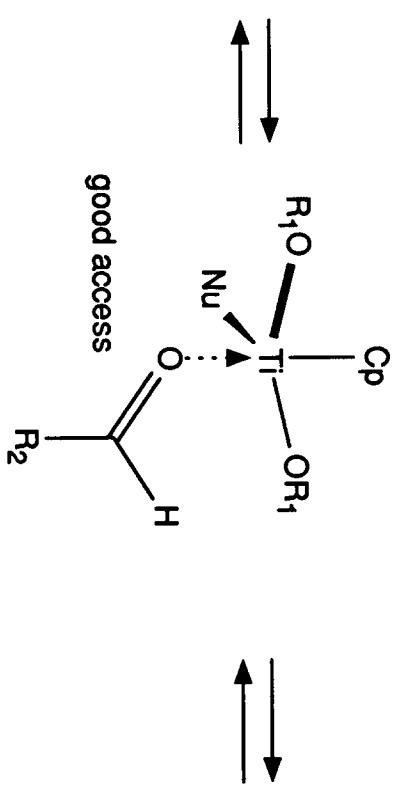
88% ee

57% ee

distorted
coordination
geometry?

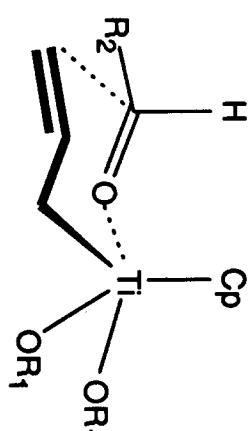


good access

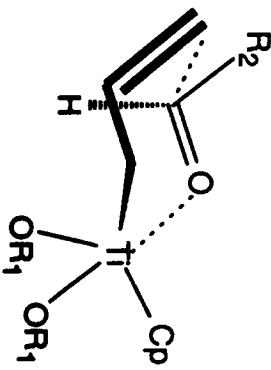


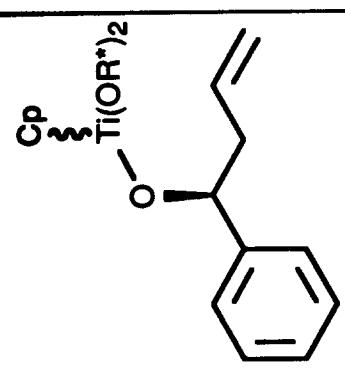
strongly bound nucleophile

ring-inversion

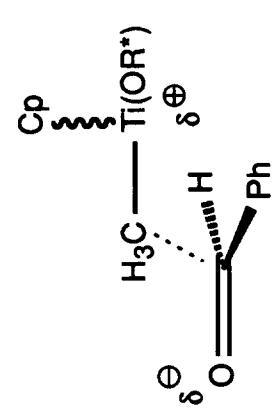
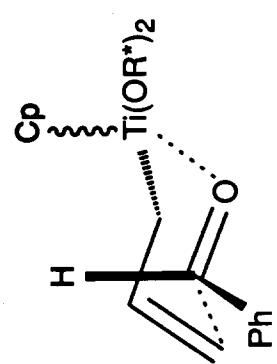
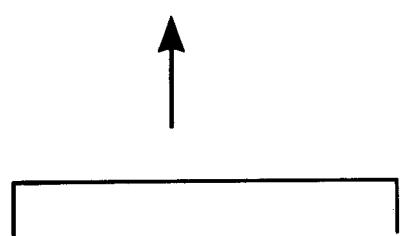


Co-ord. "in" attack

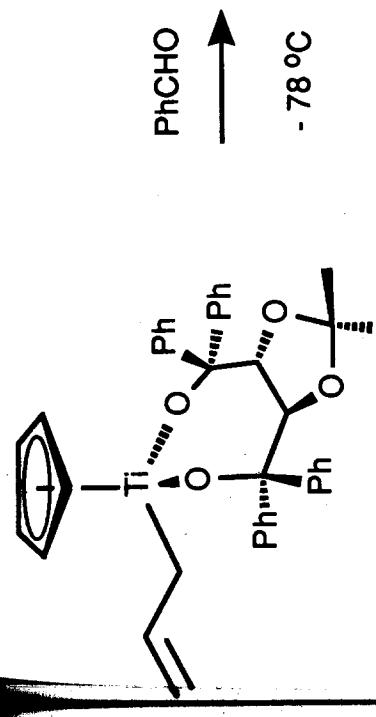




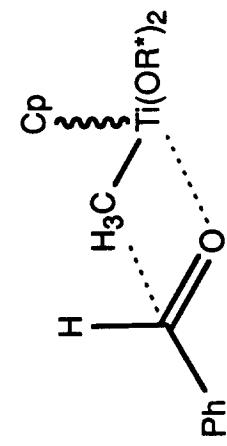
95 % ee



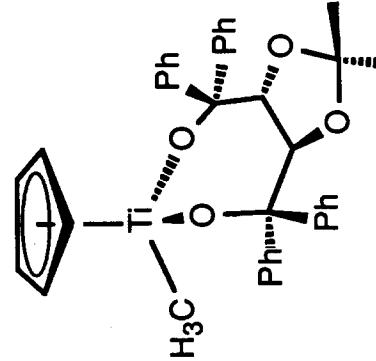
unlikely



bimolecular

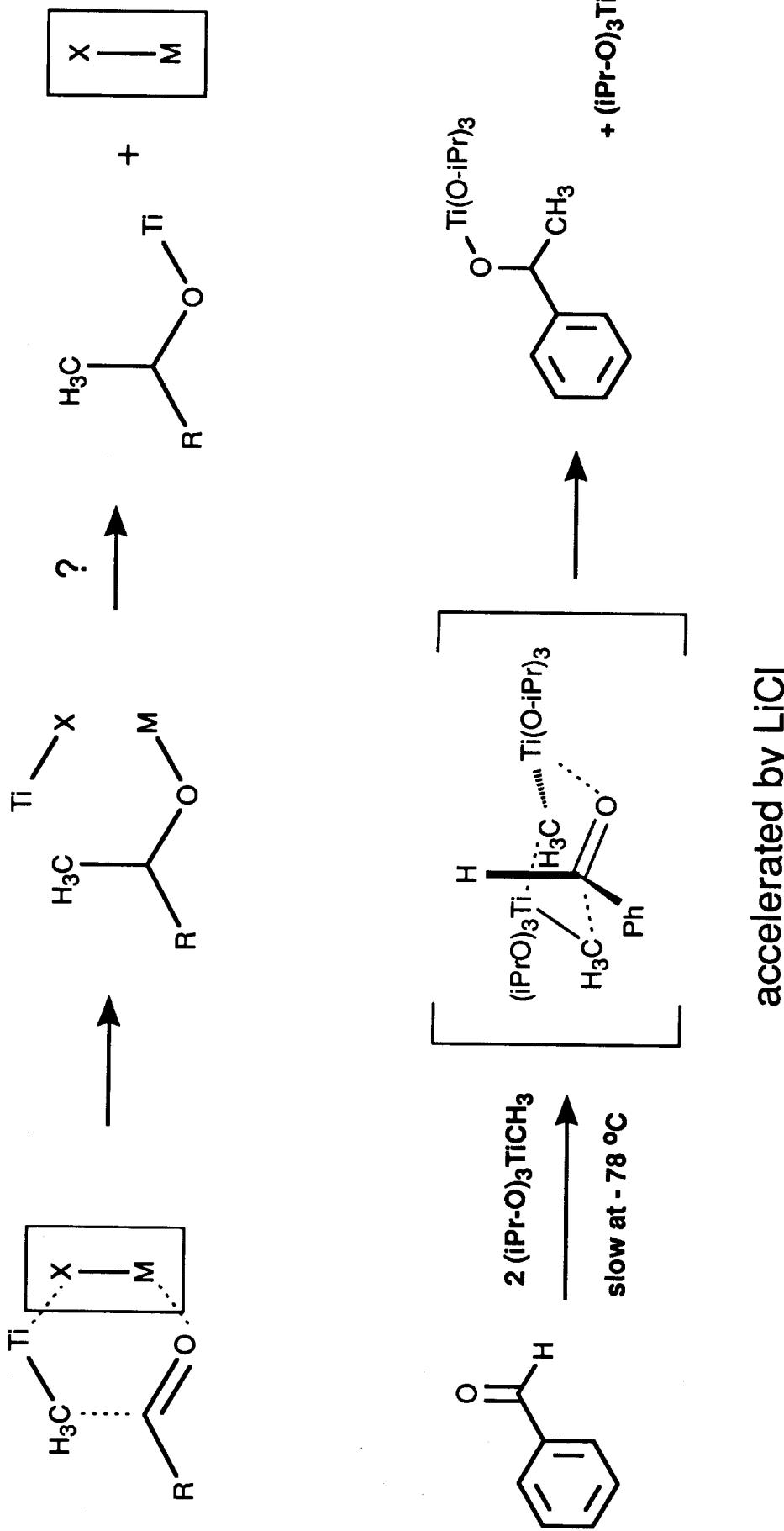


unreactive

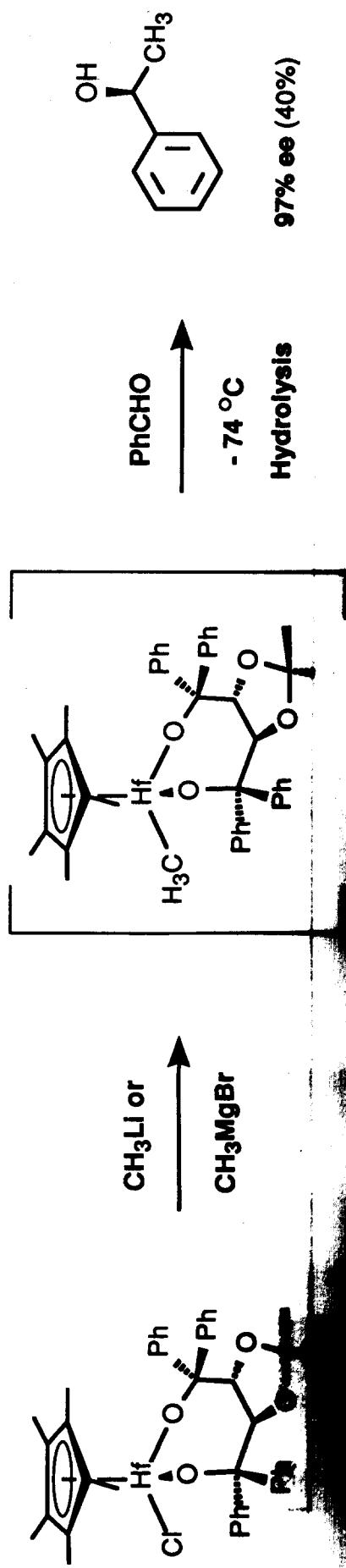
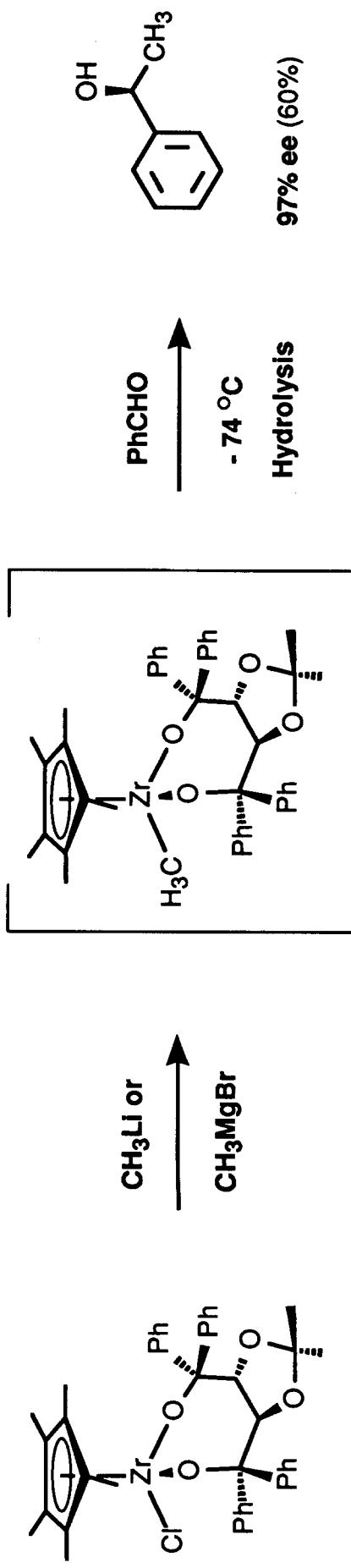


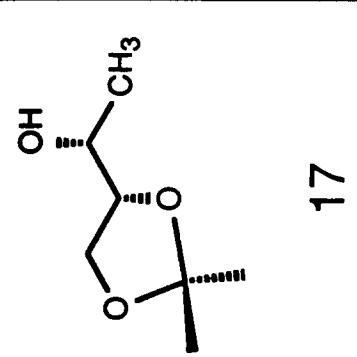
Unreactive Organometallics \Rightarrow Possibility for Catalysis

R. Duthaler 23

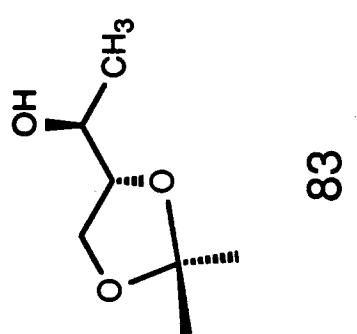


Zr and Hf have a higher tendency for aggregation than Ti





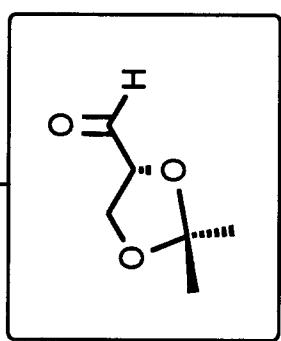
17



83

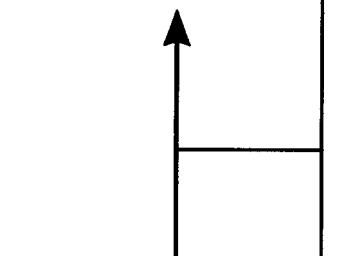
47

16

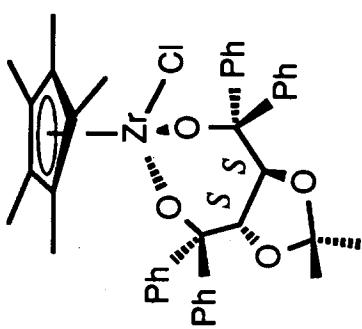
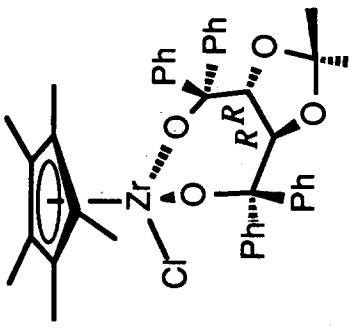


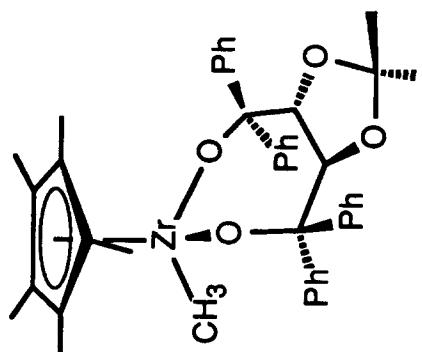
53

84


 CH_3Li
 $\xrightarrow{\text{Et}_2\text{O}}$

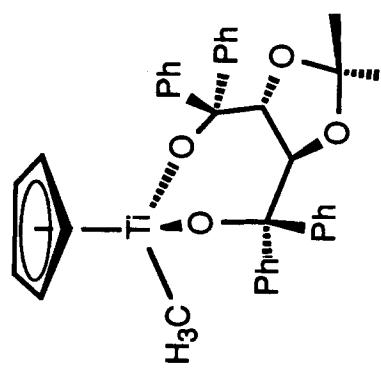
 CH_3Li
 $\xrightarrow{\text{Et}_2\text{O}}$

 CH_3MgBr


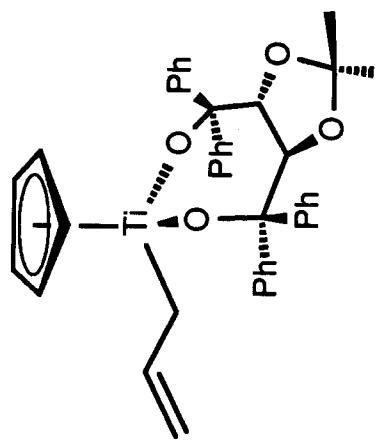


good results with
benzaldehyde only (97% ee)

80 - 83% ee with aliphatic
aldehydes



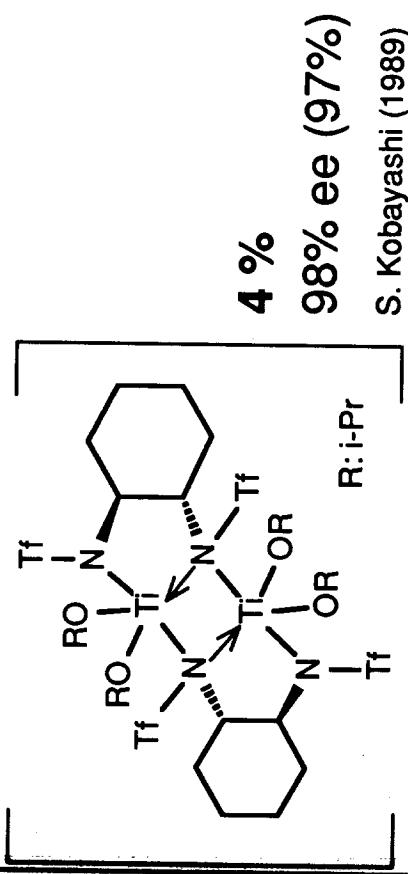
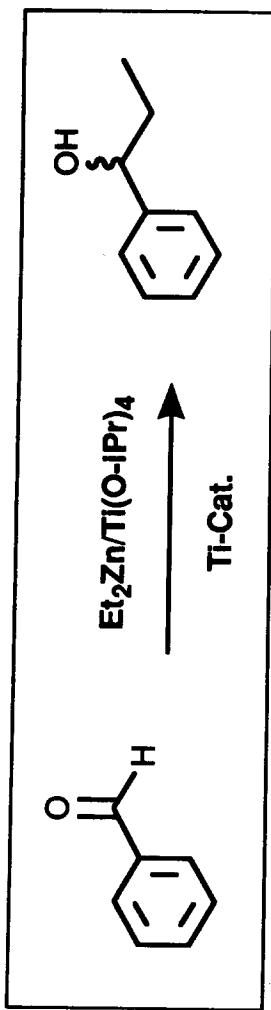
unreactive



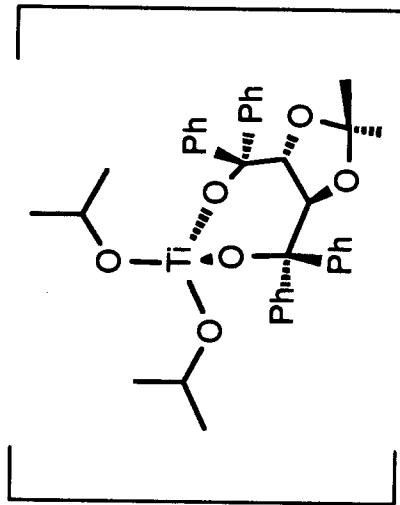
good results (95% ee)
with many substrates
including chiral aldehydes

find catalyst
for unreactive Ti-reagent

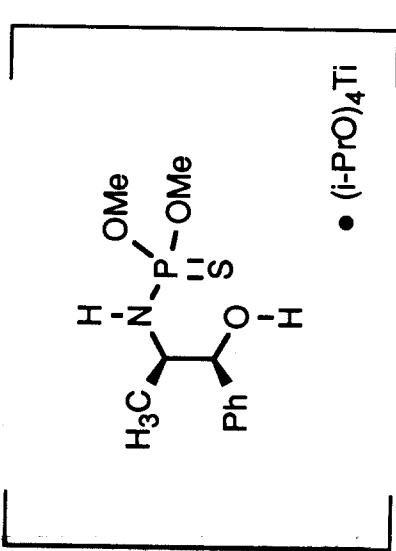
look for catalytic properties
of chiral Cp-Ti(Zr)-system



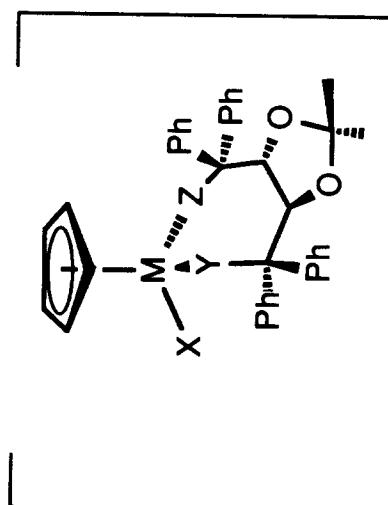
4 %
98% ee (97%)
S. Kobayashi (1989)



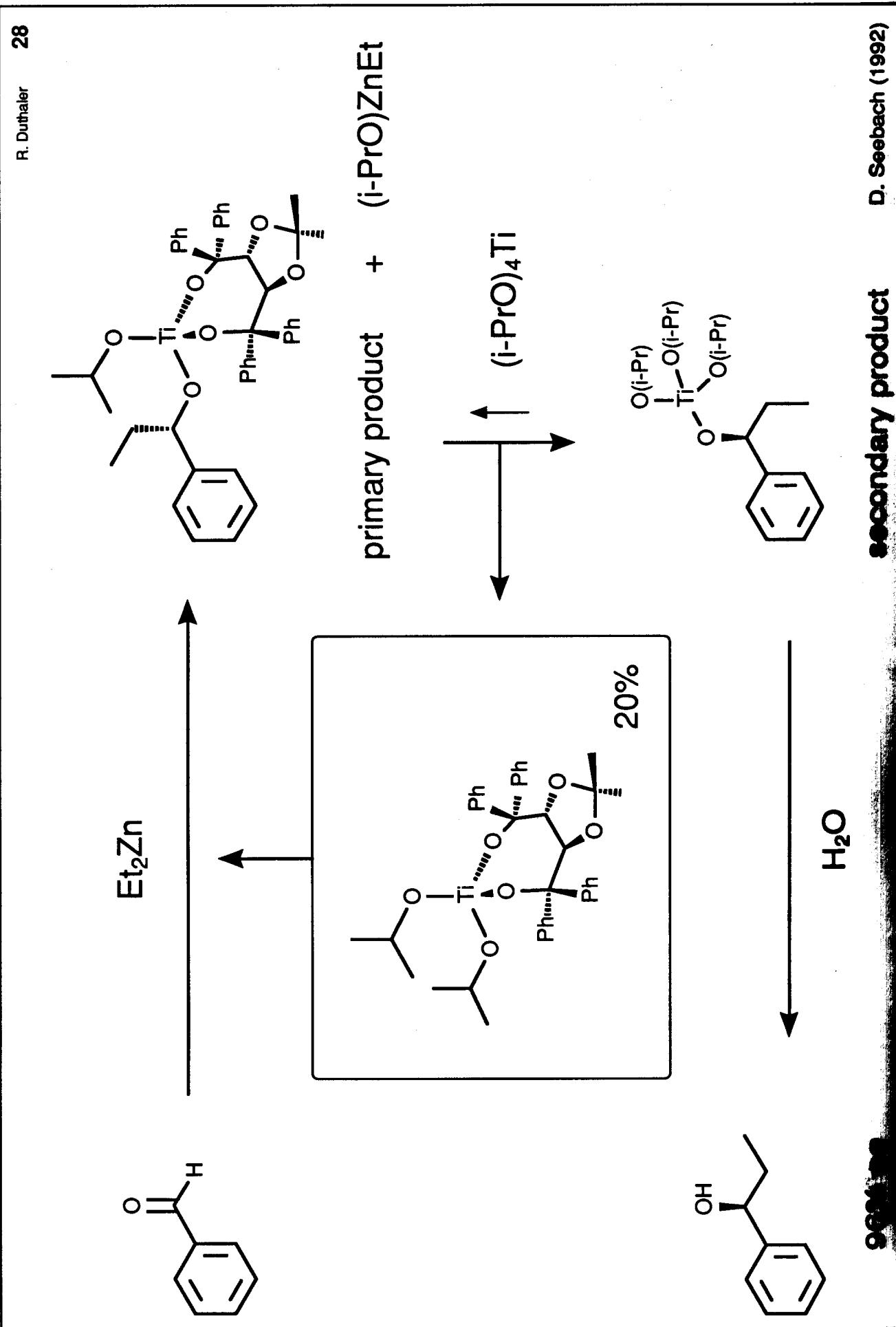
20 %
99% ee (75%)
D. Seebach (1990)

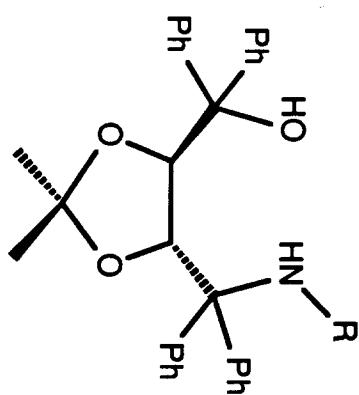
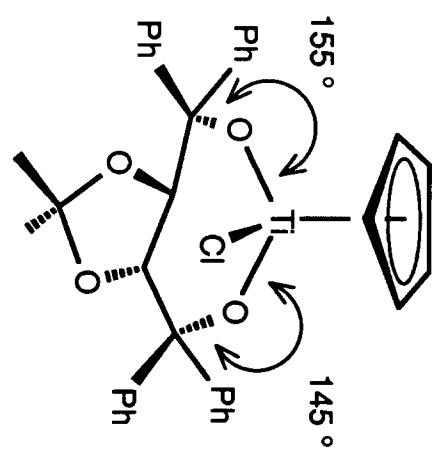


5 %
95% ee (93%)
K. Soai (1993)



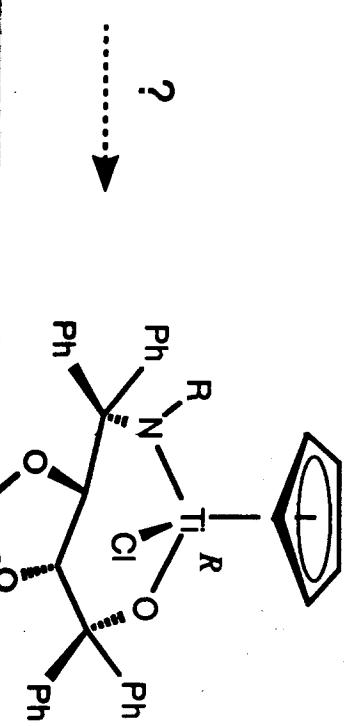
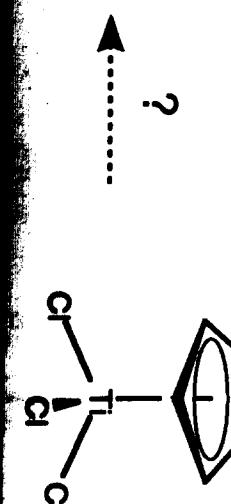
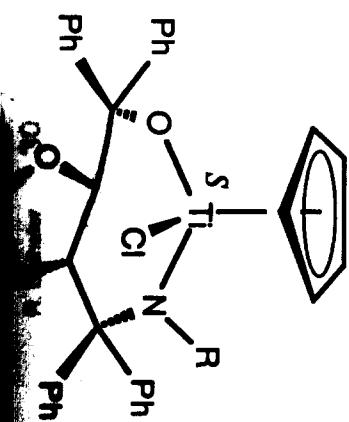
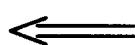
M: Ti, Zr, Hf
 X: ?
 Y, Z: O, NR

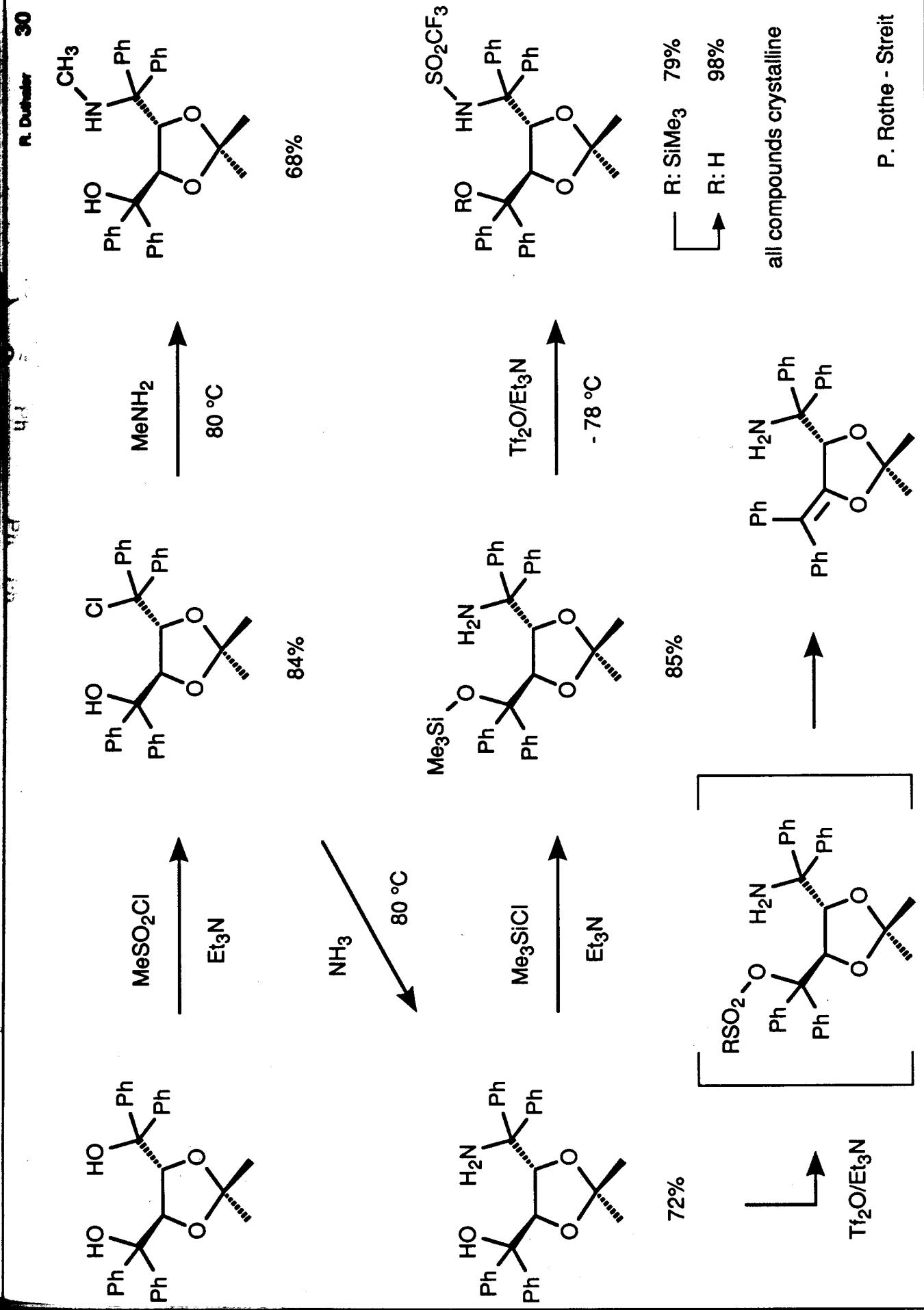


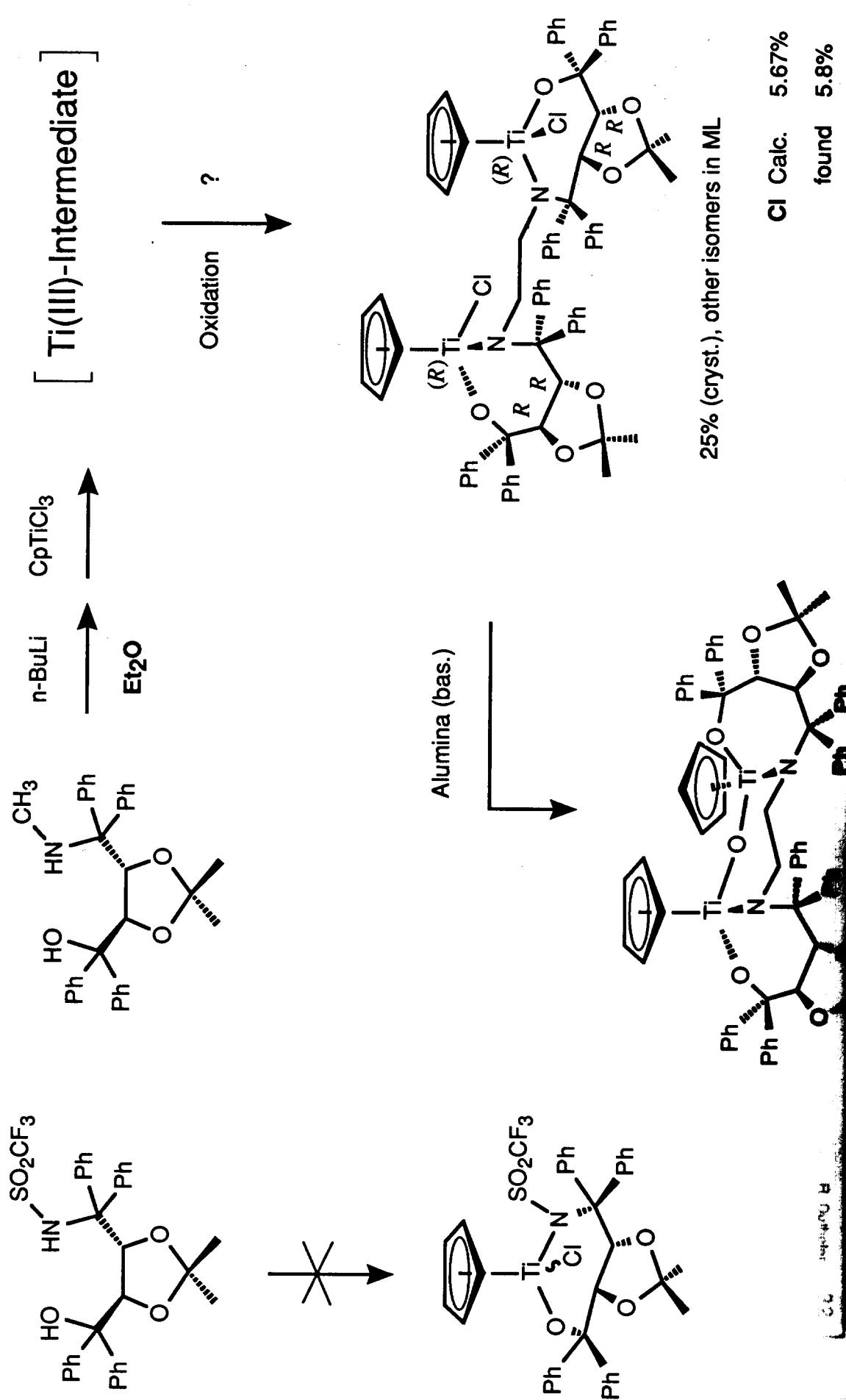


$\text{R-NH-SO}_2\text{CF}_3$
 ≈ 7
 OH
 R-NH-CH_3
 ≈ 18
 ≥ 30

$\text{R: CH}_3, \text{CF}_3\text{SO}_2,$
 not H

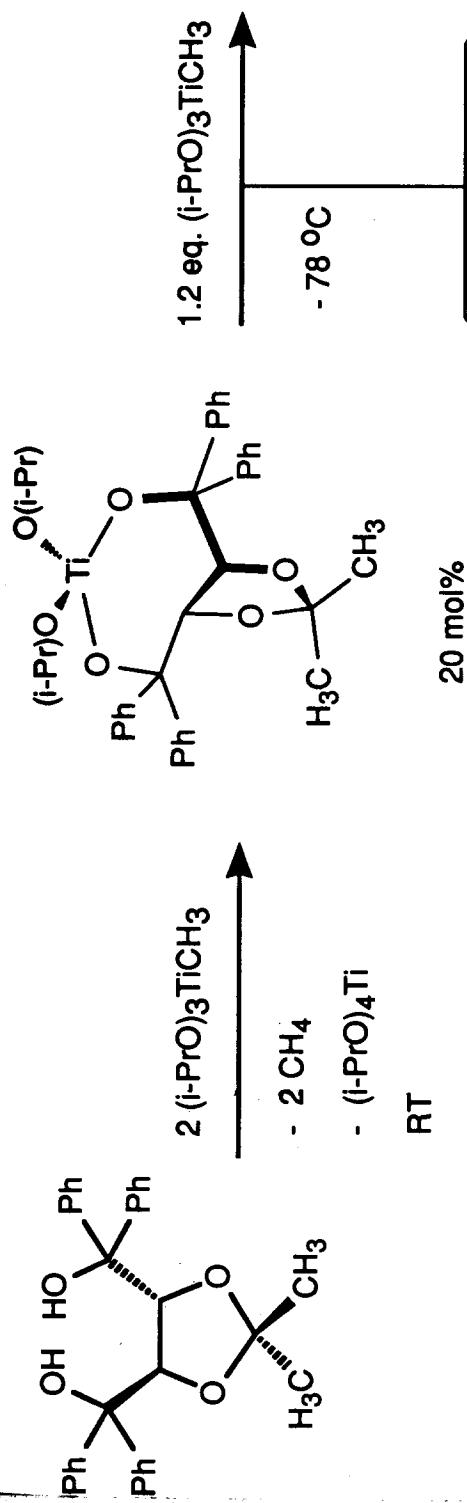






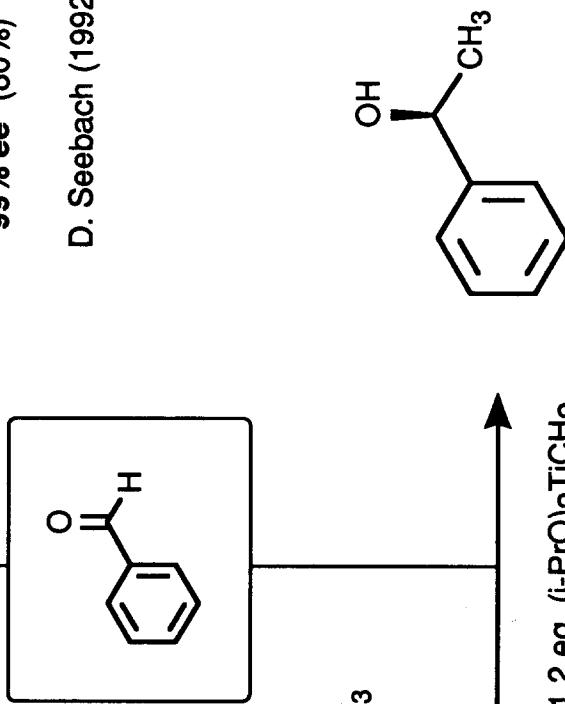
32

R. Dauter



99% ee (80%)

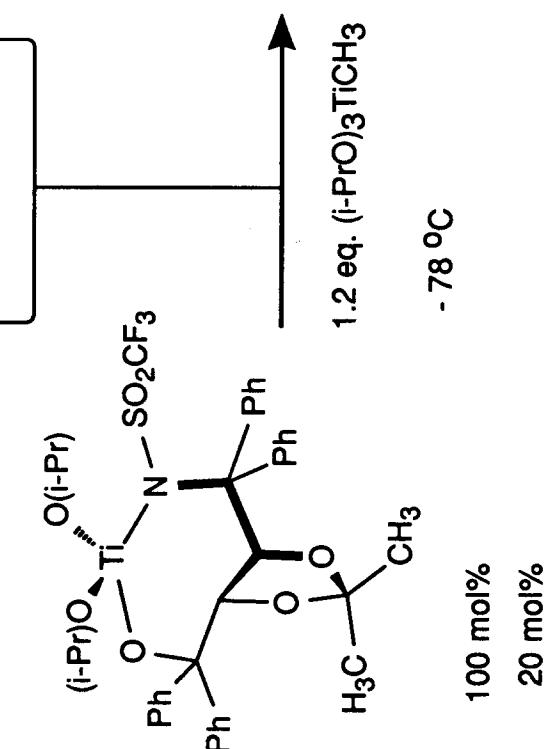
D. Seebach (1992)



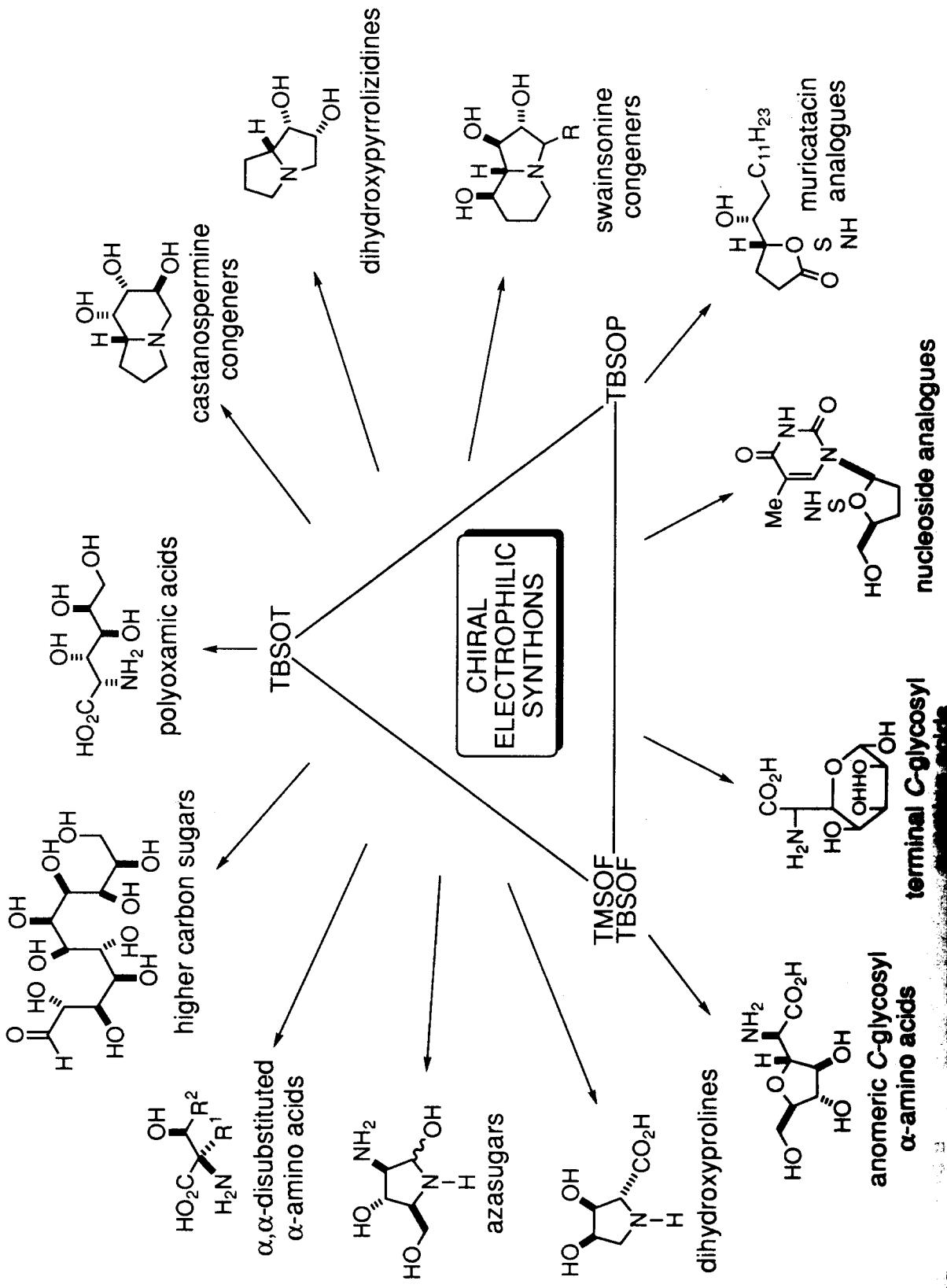
94% ee (70%)

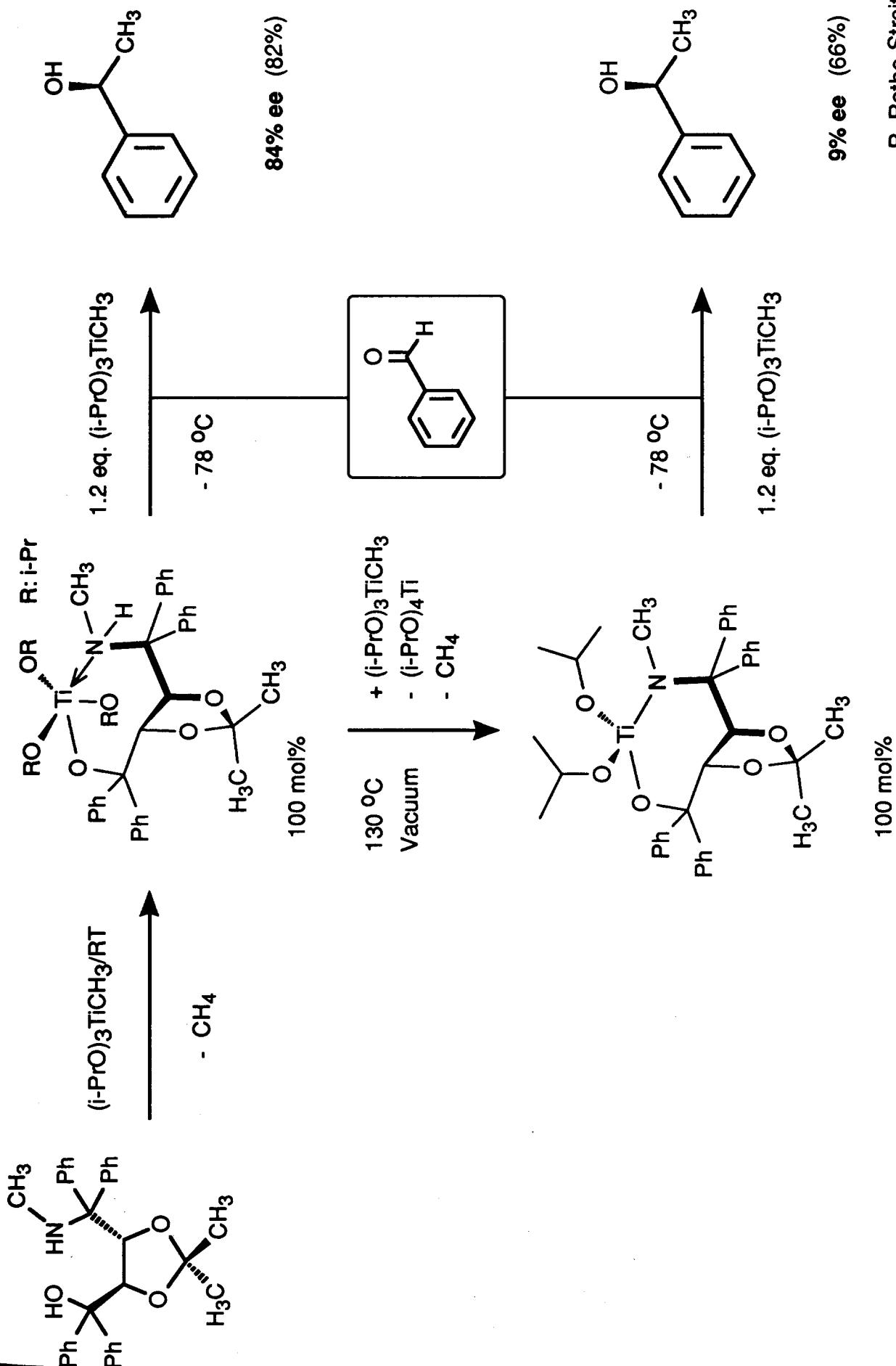
11% ee (75%)

P. Rothe-Streit



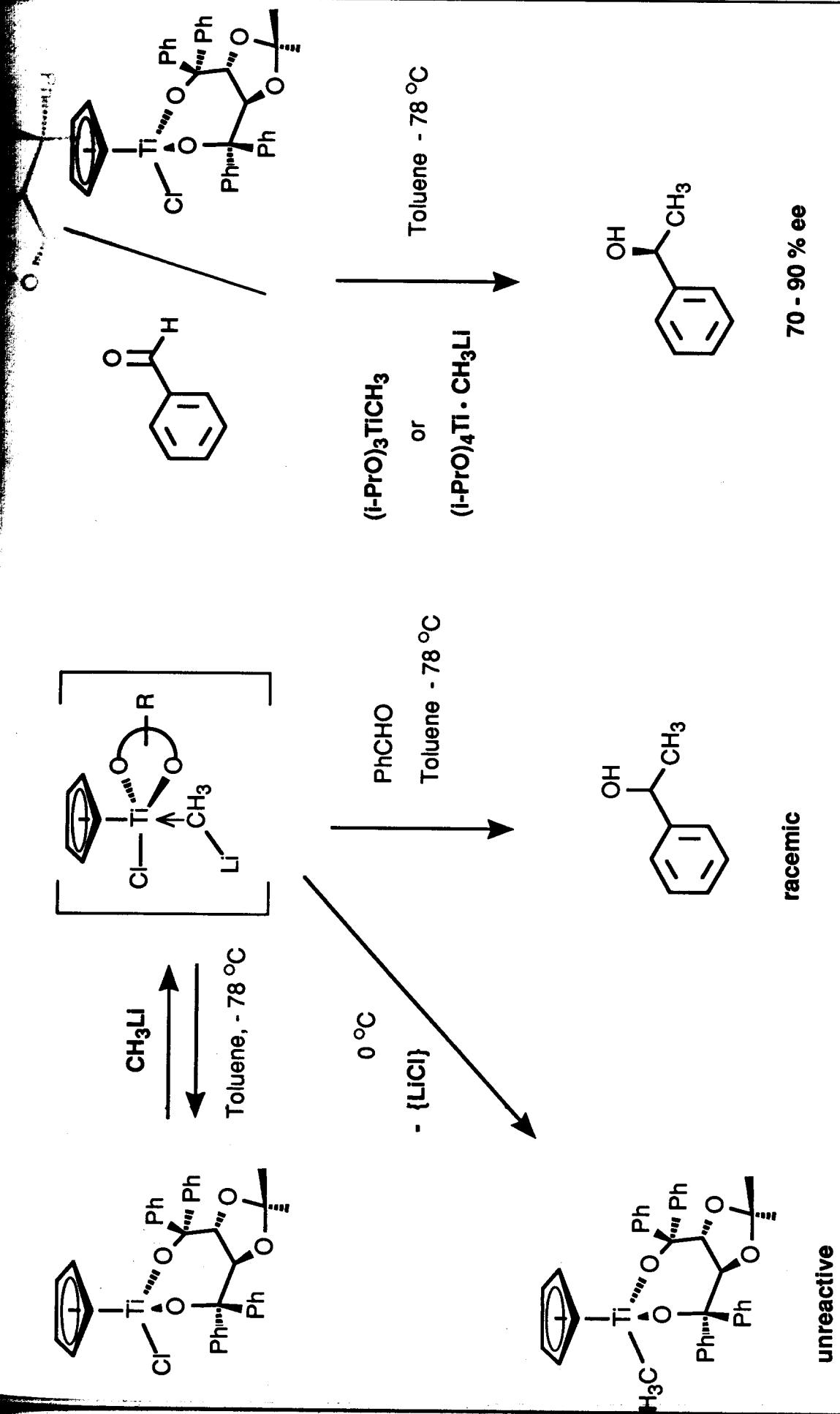
THE SILOXYDIENE ROUTE: ACHIEVEMENTS

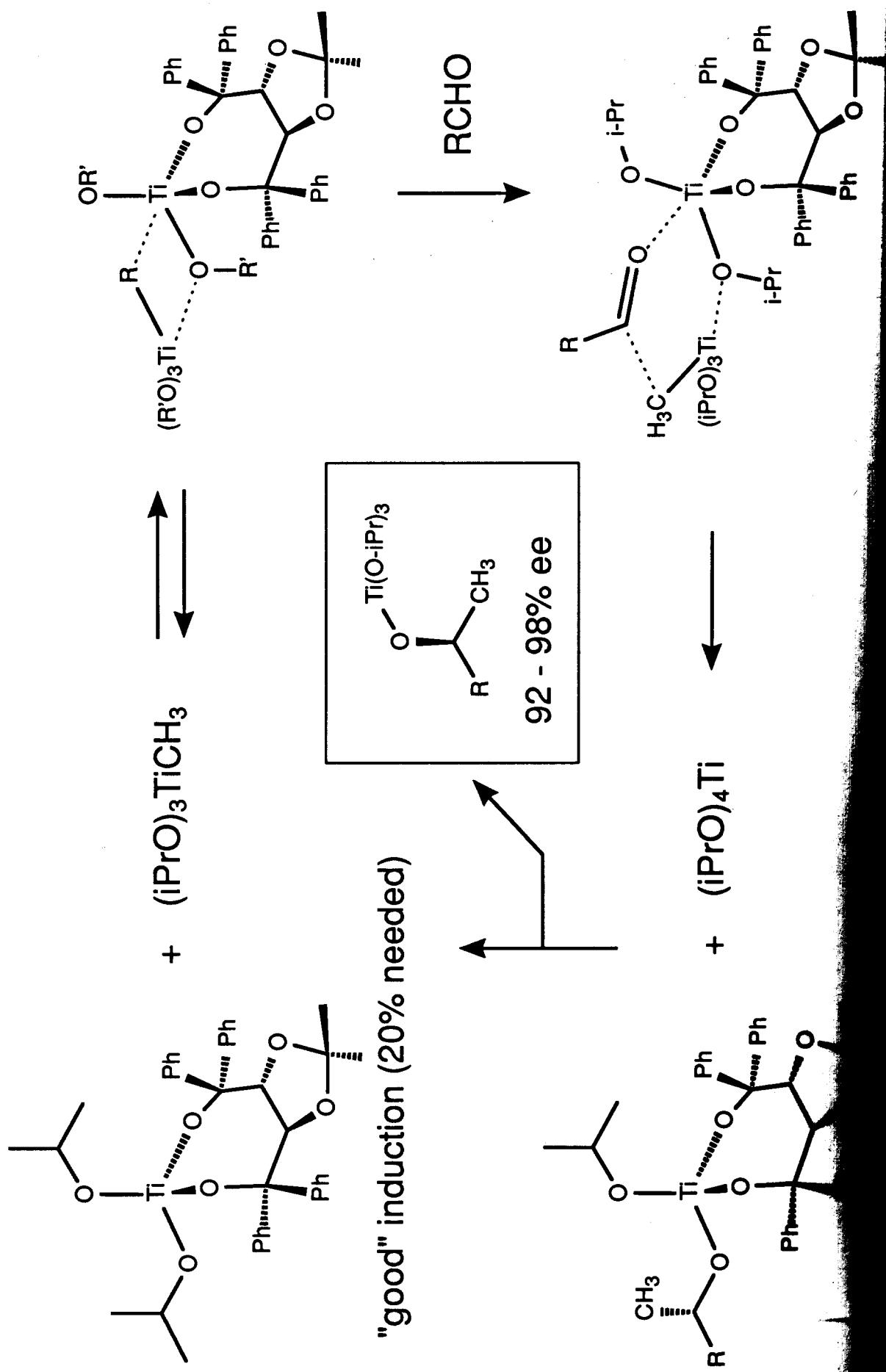


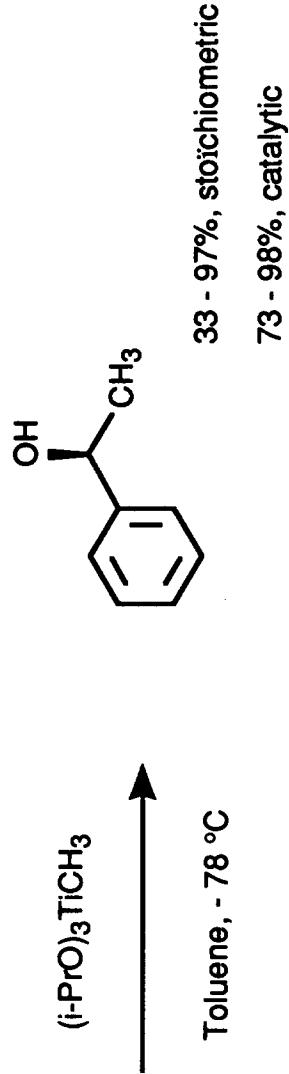
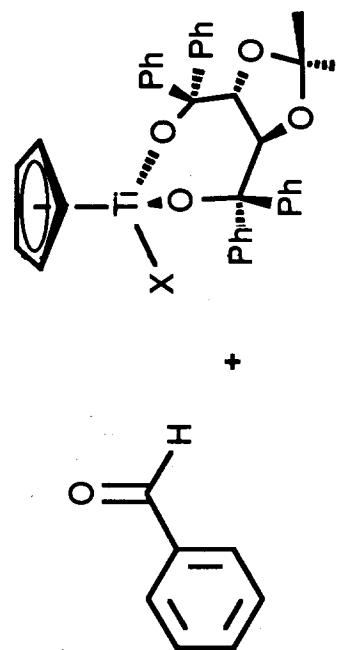


P. Rothe-Streit

P.L. Alsters







0.1 equiv. (1 equivalent)

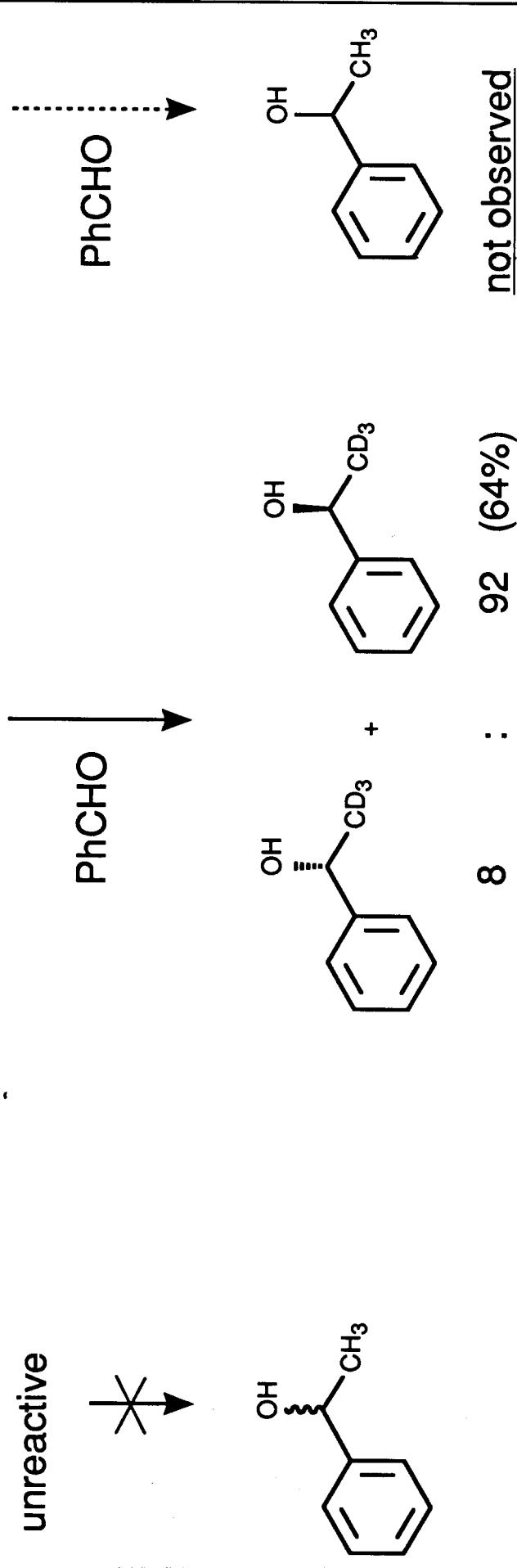
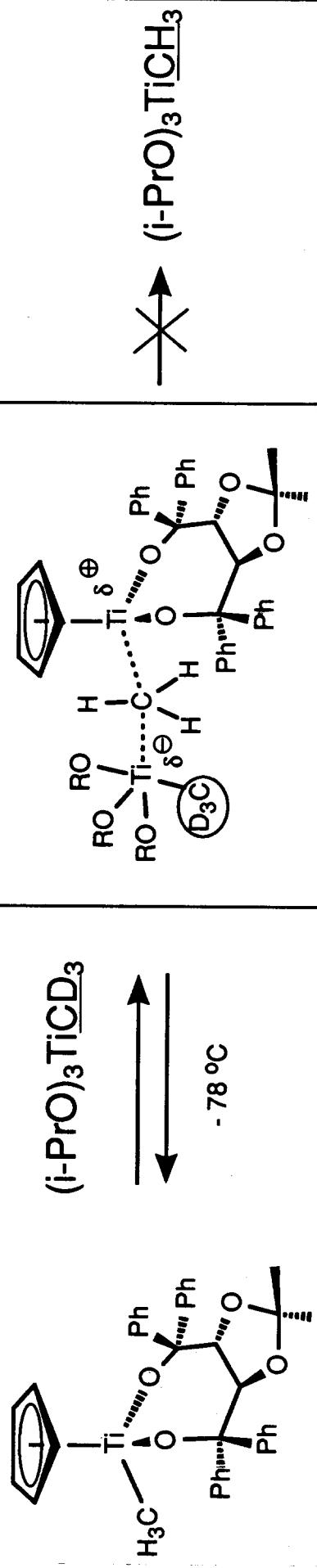
0.1 equiv.

X

0.1 equiv.

premixed

<chem>CH3</chem>	51% ee	(84% ee)
<chem>i-PrO</chem>	37% ee	(85% ee)
<chem>Cl</chem>	56% ee	(90% ee)
<chem>CF3SO3</chem>	60% ee	-

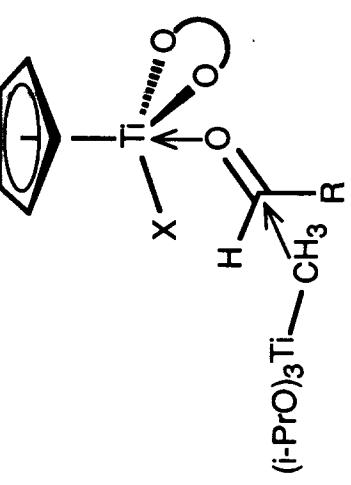


potential for catalysis

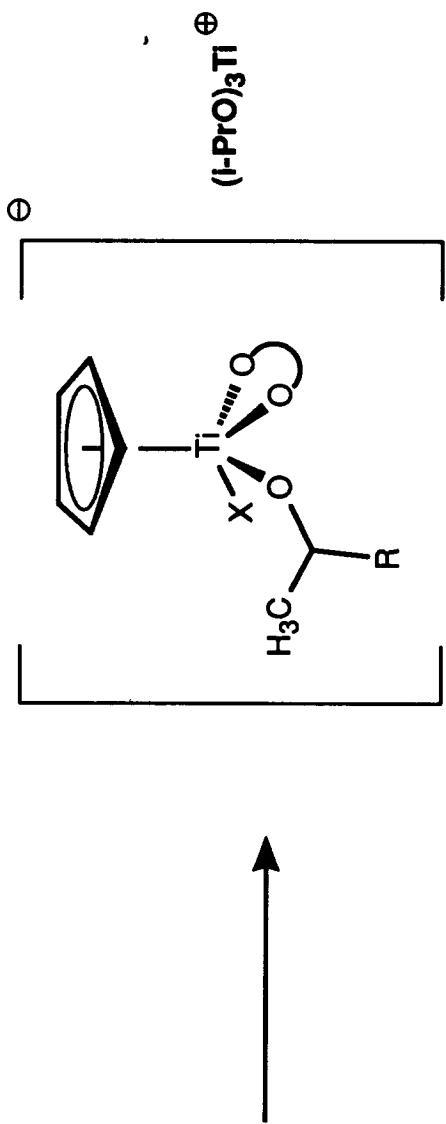
Two mechanistic Possibilities

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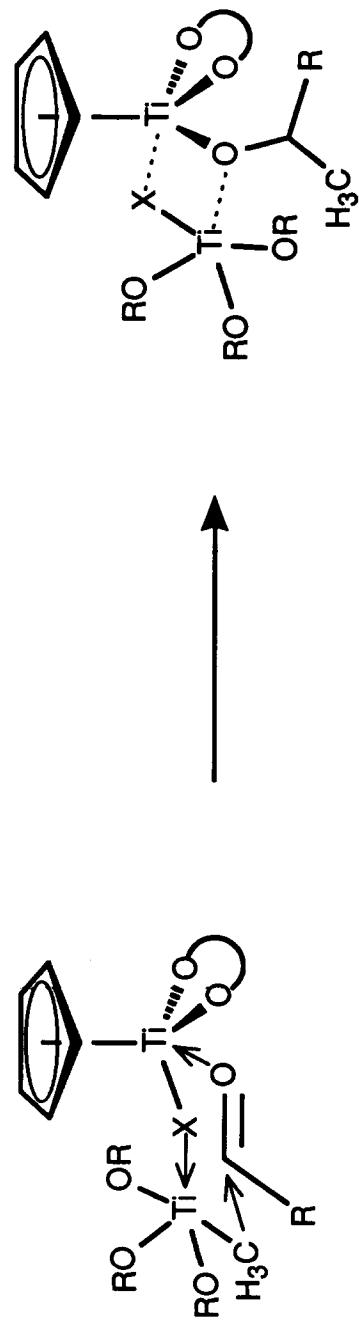
R. Duthaler



activation of RCHO



X: CF_3SO_3 best

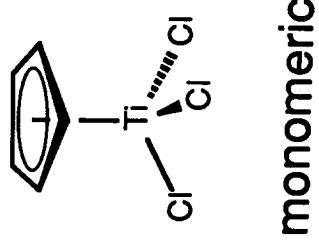
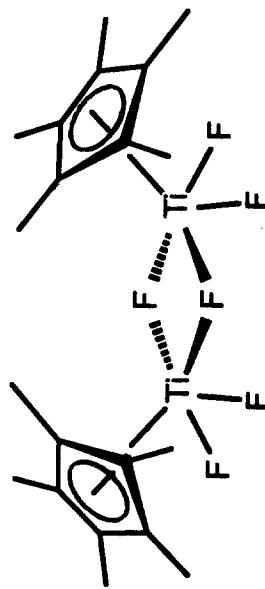
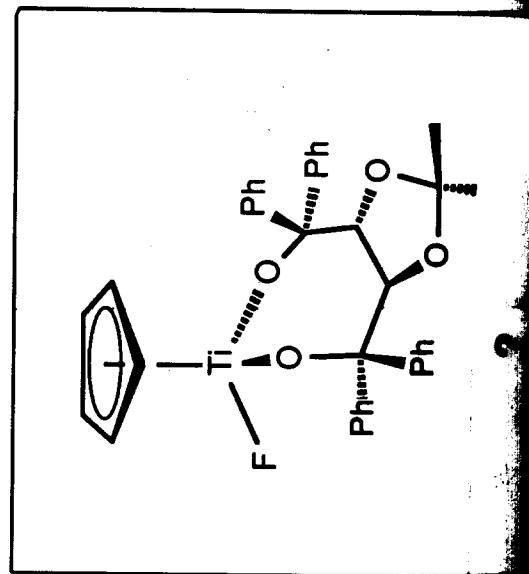


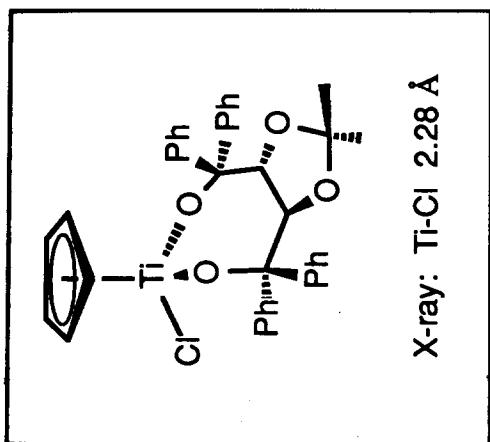
X: F best

Fluoride - strongly bridging ligand for Ti



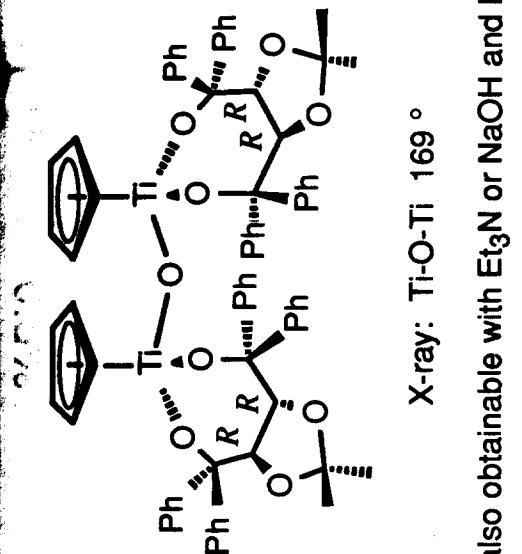
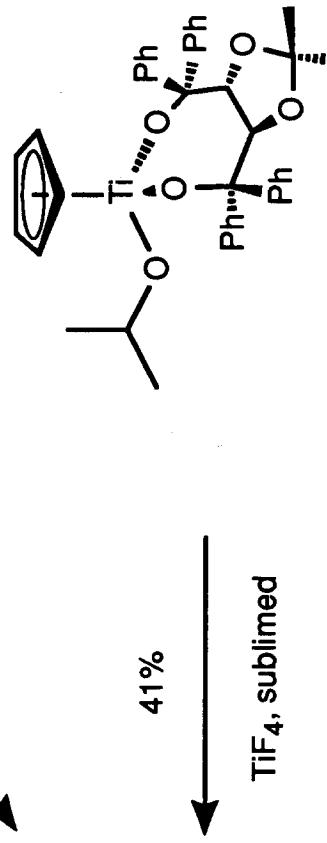
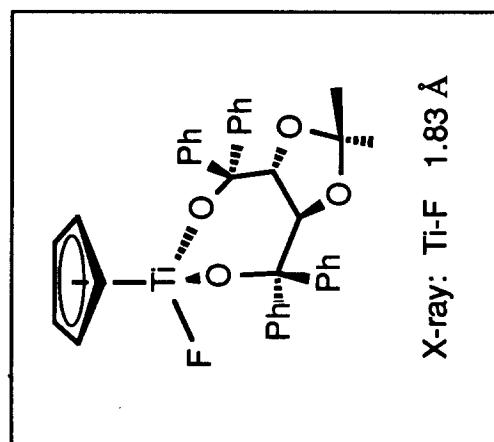
volatile liquid

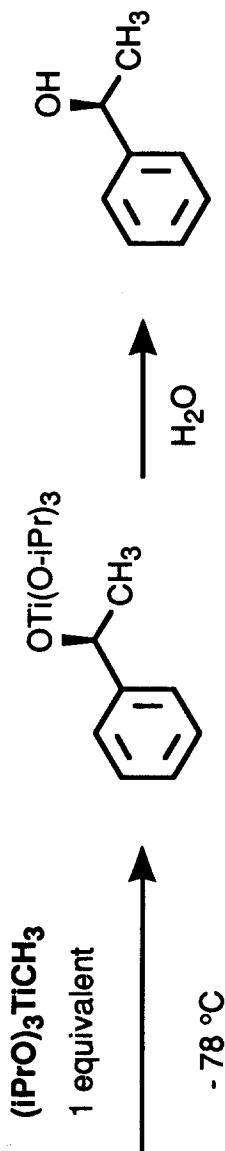
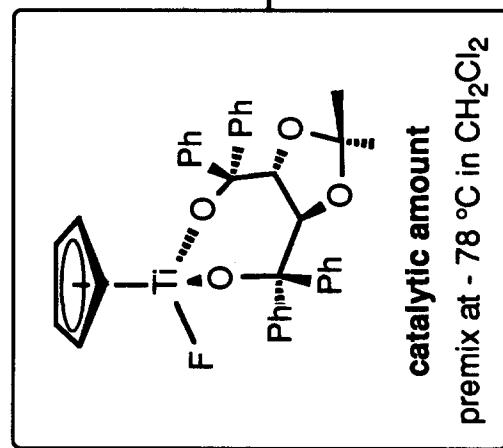




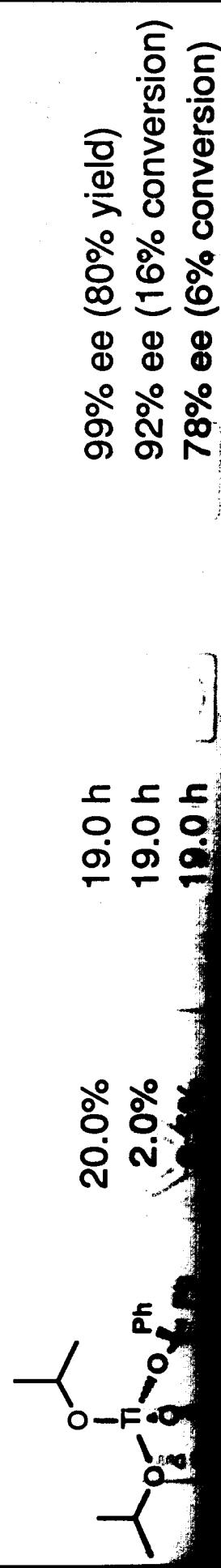
method of
H.W. Roesky (1994)

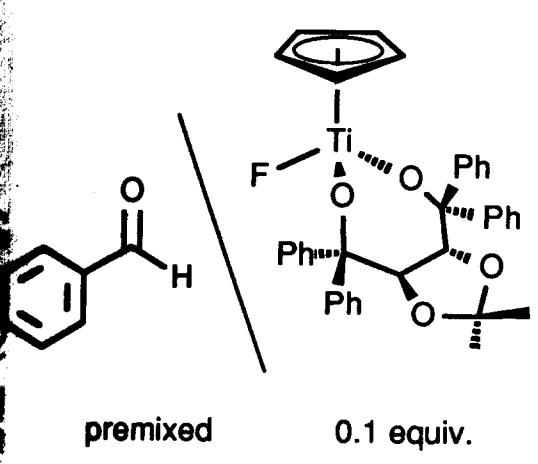
Me₃SnF
- Me₃SnCl, volatile
quantitative





2.0%	1.5 h	95% ee (35% conversion)
0.5%	1.5 h	93% ee (77 % conversion)
	19.0 h	87% ee (12% conversion)
	19.0 h	78% ee (60% conversion)





R-Met

Conv. Induction

(i-PrO) ₃ TiCH ₃	distilled	97%	90% ee
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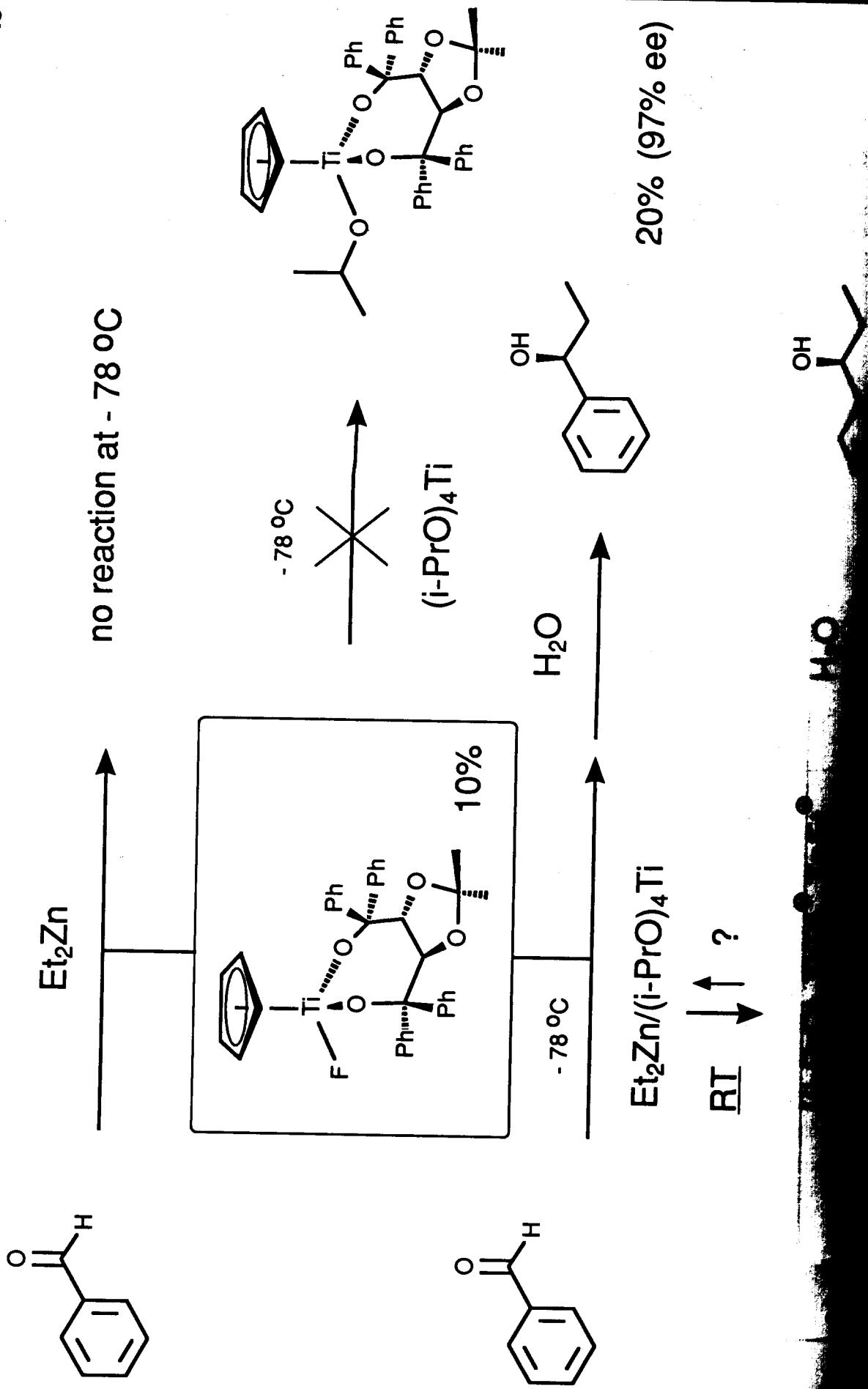
(i-PrO) ₃ TiCH ₃ • LiCl	in situ	97%	41% ee
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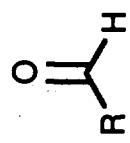
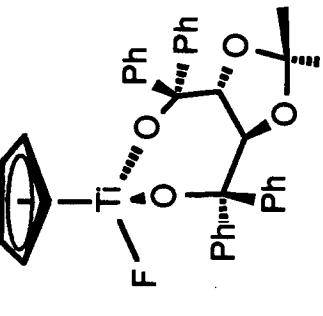
(i-PrO) ₄ Ti • CH ₃ Li	premixed	40%	90% ee
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(i-PrO) ₄ Ti • n-BuLi	premixed	5%	28% ee
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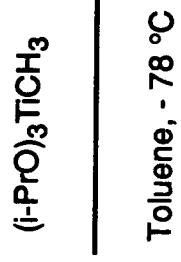
(i-PrO) ₄ Ti • Et ₂ Zn	premixed at - 78 °C	20%	97% ee
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(i-PrO) ₄ Ti • Et ₂ Zn	premixed at RT	70%	97% ee
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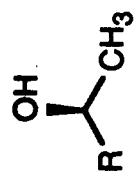




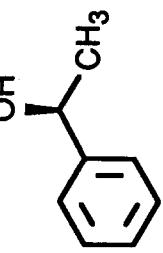
premixed



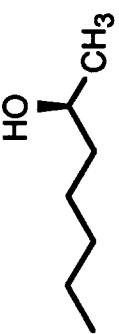
0.1 equiv.



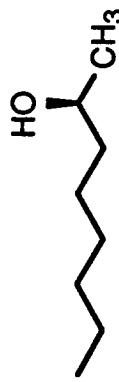
55 - 97%



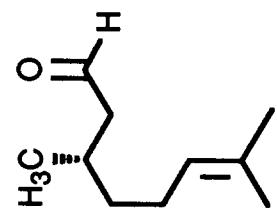
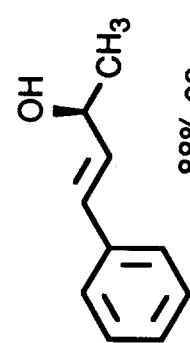
91 - 95% ee



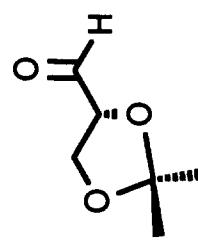
89% ee



88% ee



low conversion



low conversion

P. Alsters