Catalytic Asymmetric Synthesis with "Privileged Ligands"

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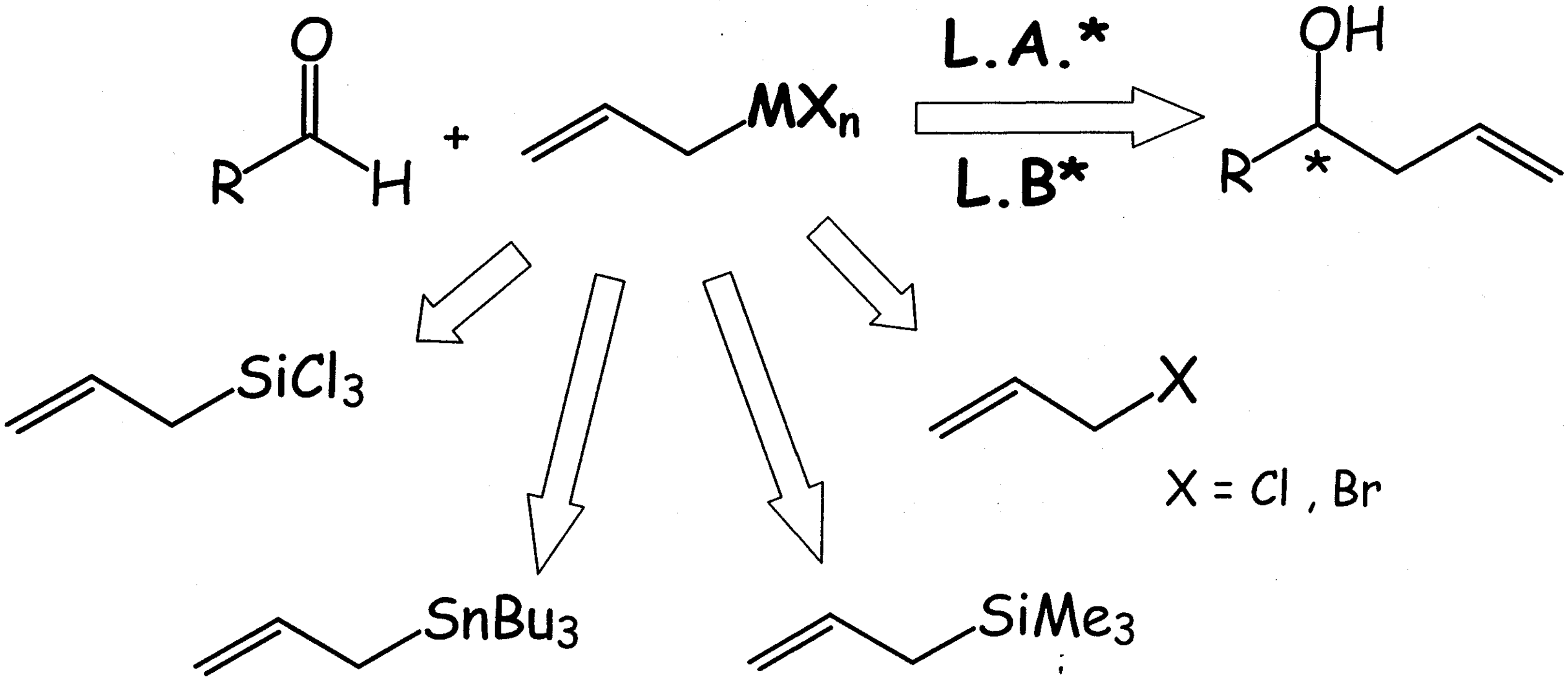
Italy

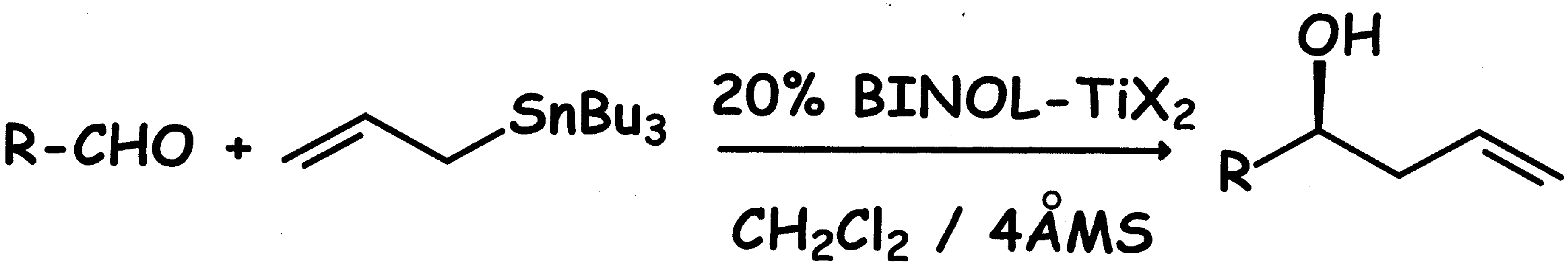
IASOC 2000
Ischia Advanced School of Organic Chemistry

Chiral
Lewis Acid

Substrate + Reagent ⟶ Product

Catalytic Asymmetric Allylation Reaction of Aldehydes

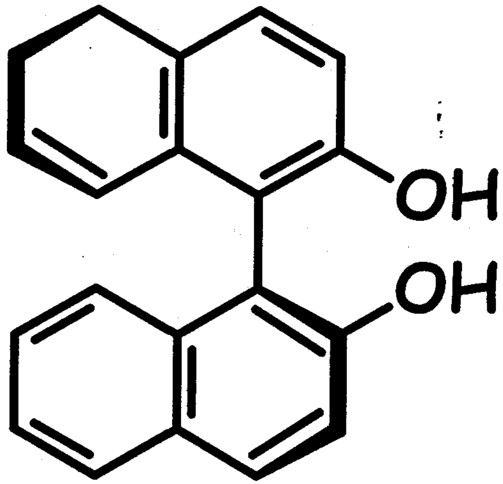




e.e. = 94-97%

yield = 75-80%

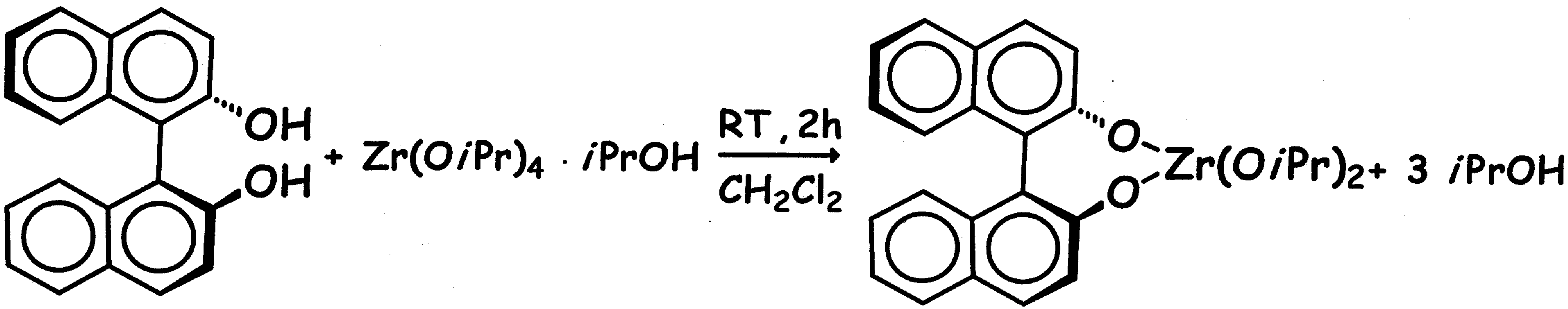
X = Cl , O*i*Pr

BINOL = 

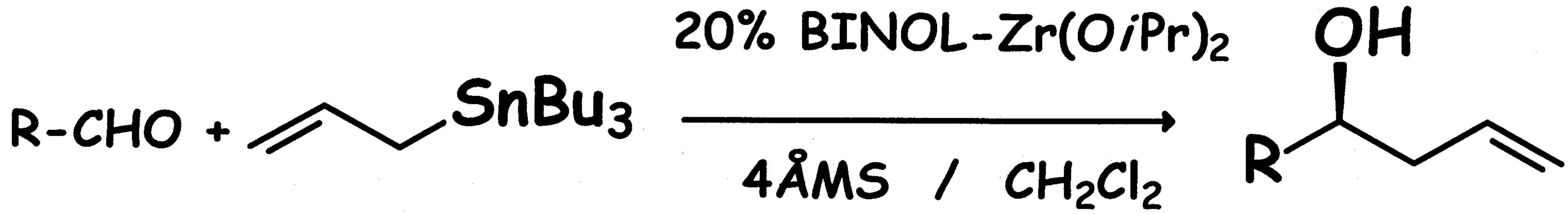
(S)

Catalytic allylation of aldehydes

R	T(°C)	t(h)	Yield%	e.e.%	Conf.
C_7H_{15}	-20	24	83	97.4	R
C_5H_{11}	-20	24	75	98.4	R
c-C_6H_{11}	-20	90	36	89.1	S
c-C_6H_{11}	RT	24	75	92.6	S
PhCH=CH	-20	90	38	94.0	S
PhCH=CH	RT	24	85	88.8	S
Ph	RT	48	96	82.0	S

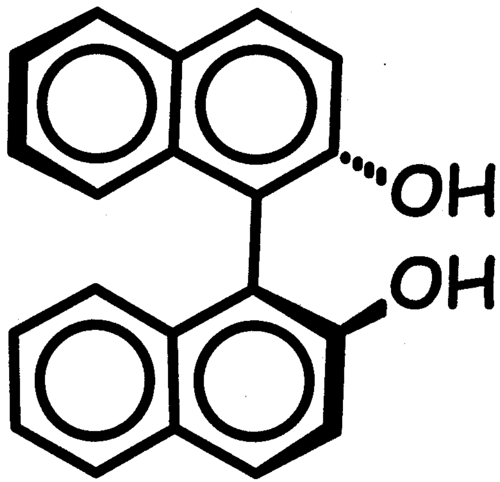


(S)

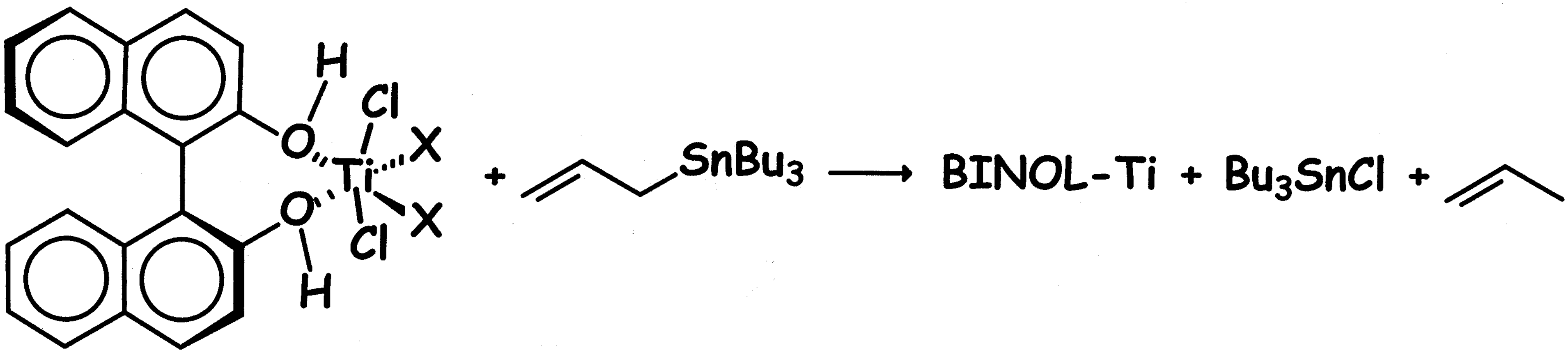


e.e. = 85-93%
yield = 60-80%

BINOL =

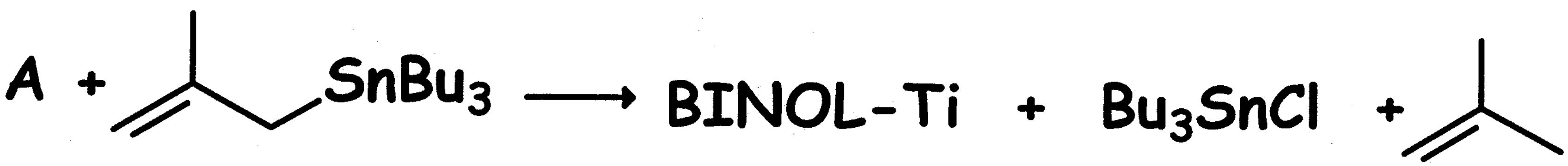


(S)

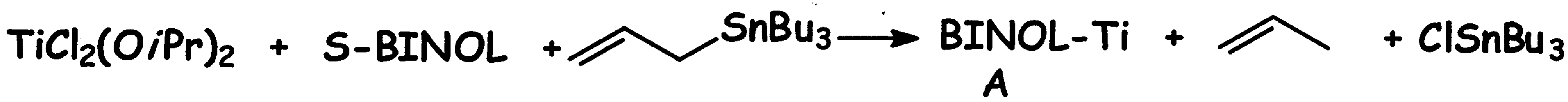


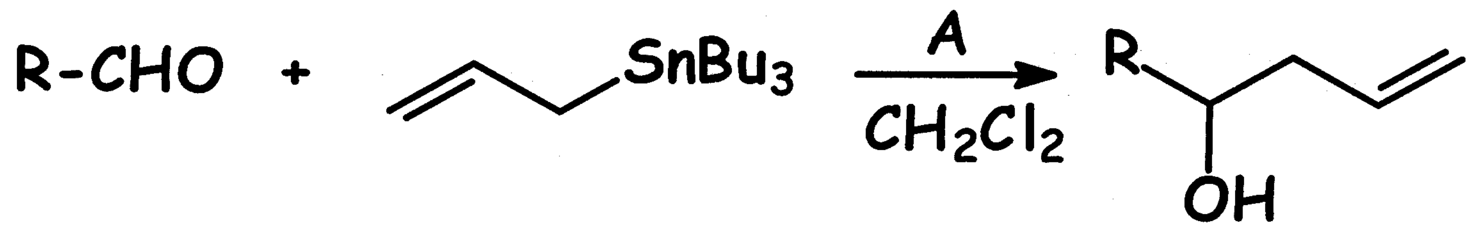
H
Cl
X
O
Ti
O
X
Cl
H
+
SnBu3
BINOL-Ti
+
Bu3SnCl
+

A   X = O*i*Pr

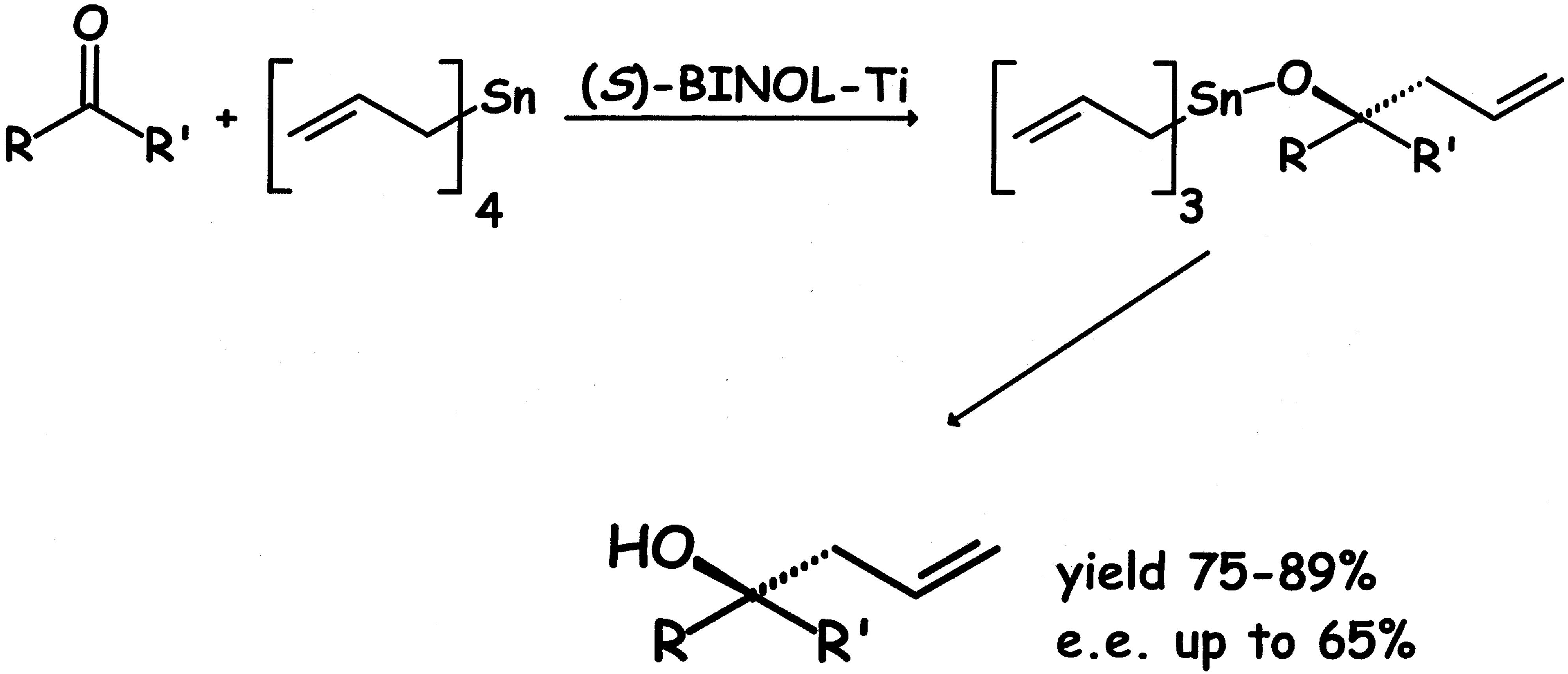


A
+
SnBu3
BINOL-Ti
+
Bu3SnCl
+

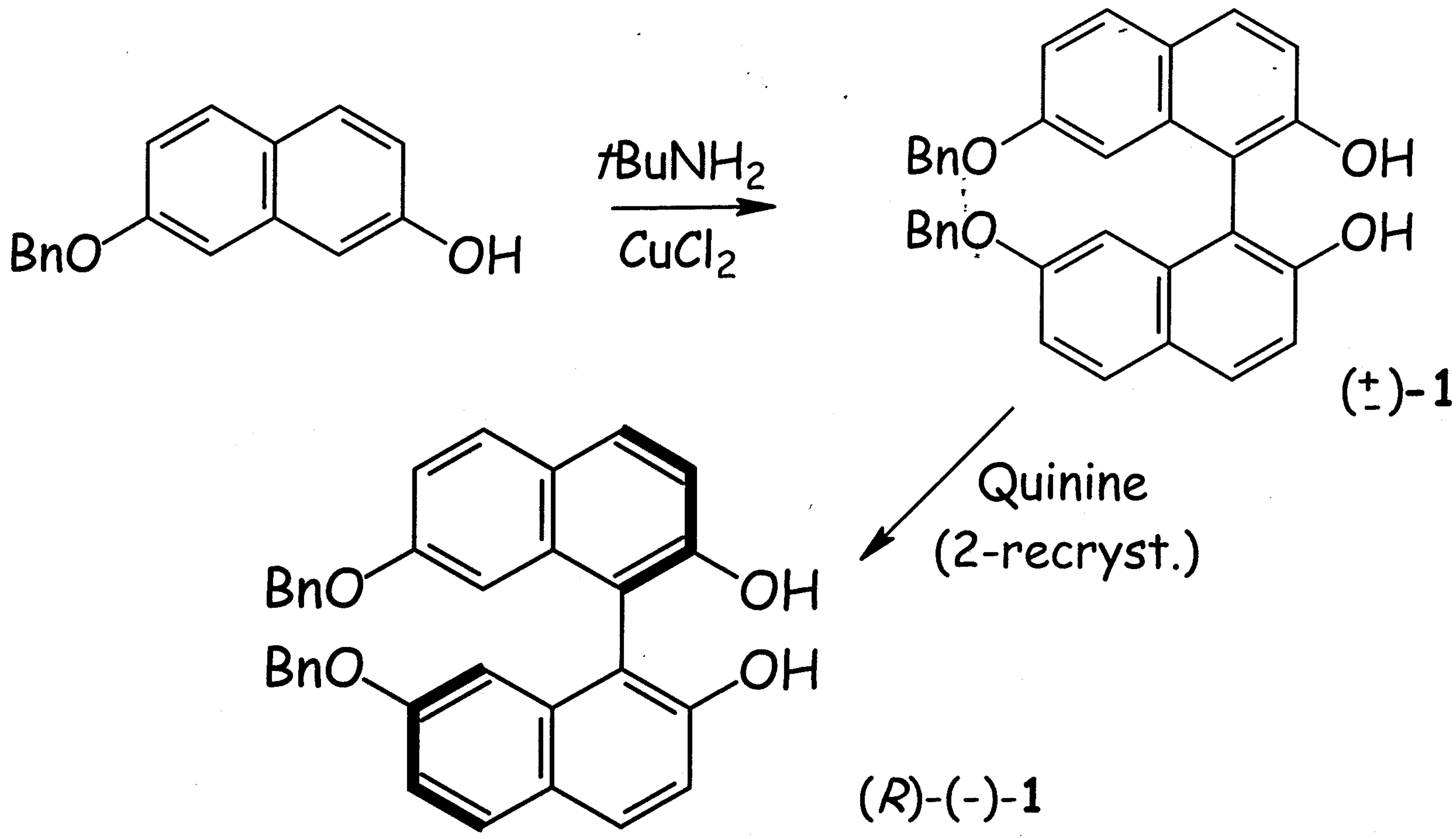


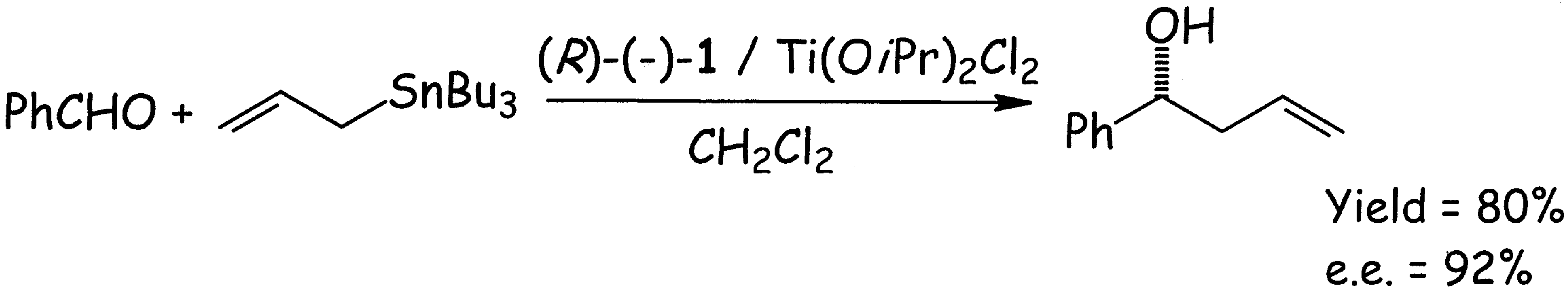


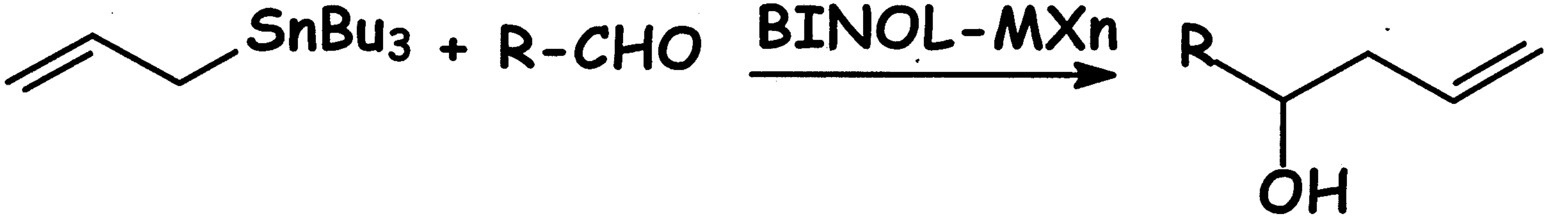
R-CHO	A %	t. (h)	Yield %	e.e. %
n-$C_7H_{15}CHO$	20	2	80	94
n-$C_7H_{15}CHO$	5	24	80	94
C_6H_5CHO	20	4	74	86
C_6H_5CHO	5	48	74	75

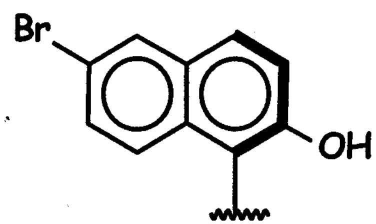
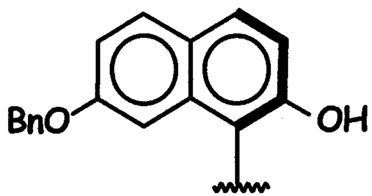
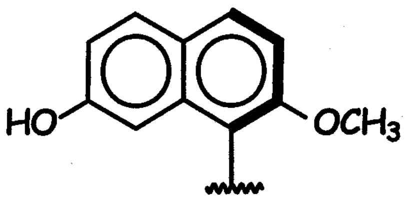


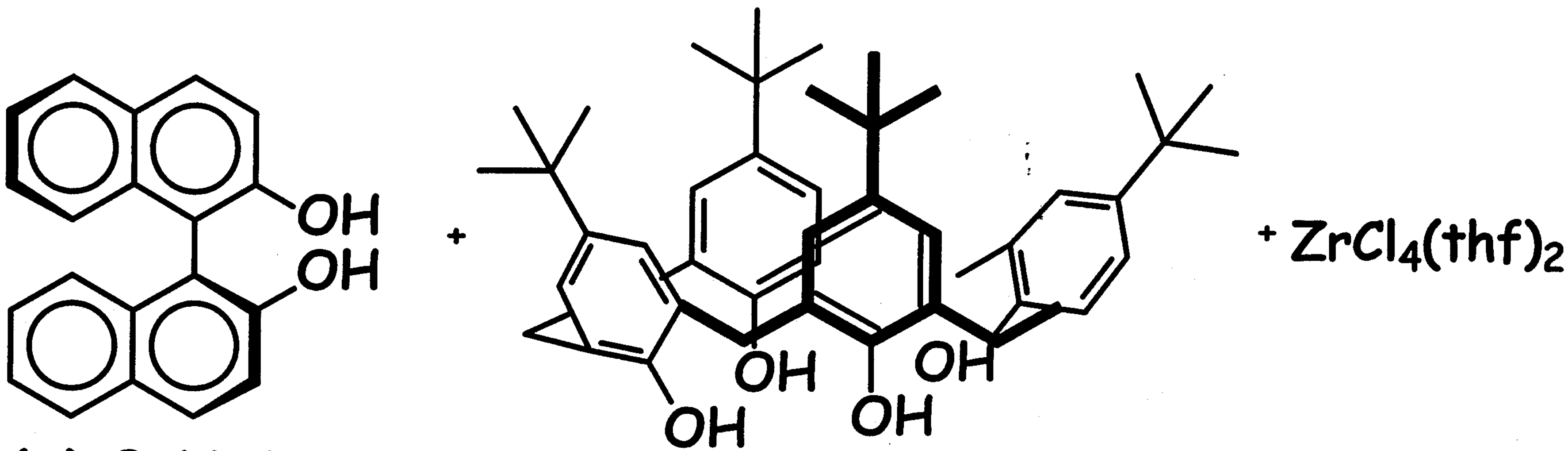
E. Tagliavini, et al.


BnO
OH
tBuNH2
CuCl2
BnO
BnO
OH
OH
(±)-1
Quinine
(2-recryst.)
BnO
BnO
OH
OH
(R)-(-)-1


PhCHO +
SnBu3
(R)-(-)-1 / Ti(OiPr)2Cl2
CH2Cl2
OH
Ph
Yield = 80%
e.e. = 92%

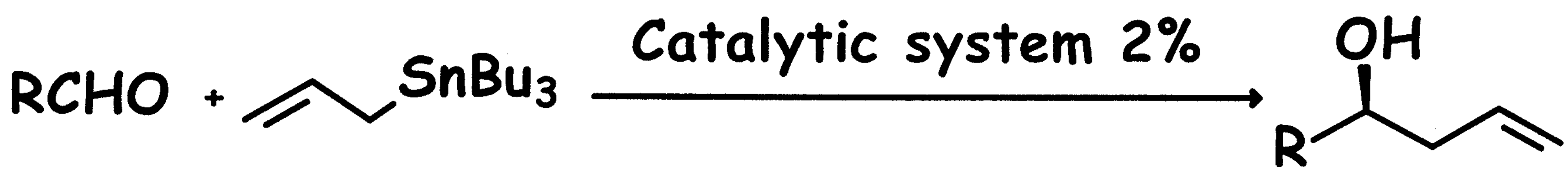


	MXn	R-	Yield (%)	e.e. (%)
	$TiCl_2(O\textit{i}Pr)_2$	nC_7H_{15}	60	72
	$Zr(O\textit{i}Pr)_4$	"	70	73
	$TiCl_2(O\textit{i}Pr)_2$	C_6H_5	80	92
	$Zr(O\textit{i}Pr)_4$	nC_7H_{15}	90	77
	$TiCl_2(O\textit{i}Pr)_2$	nC_7H_{15}	14	-



(S)-BINOL

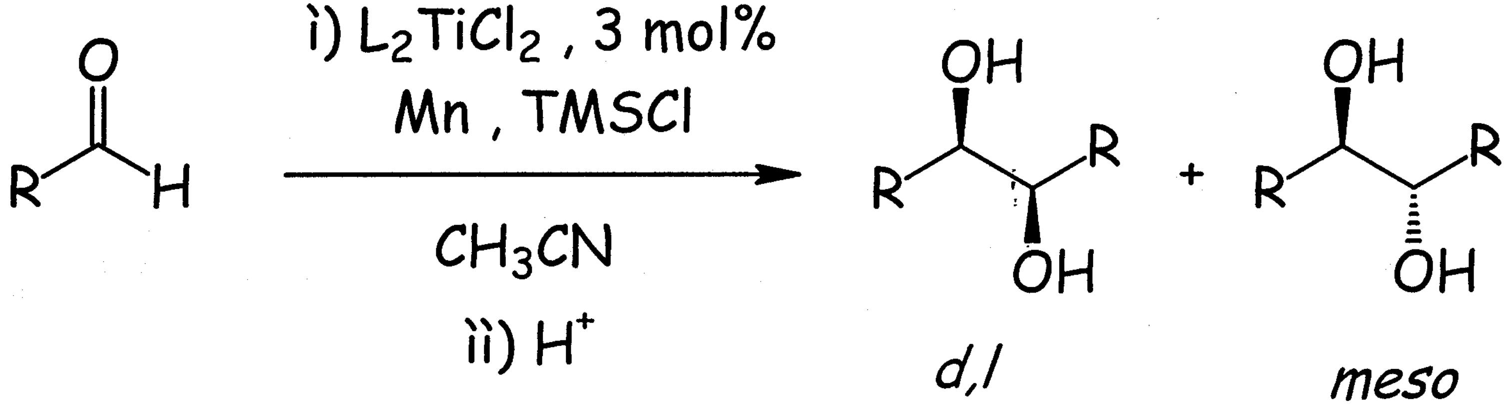
Catalytic system



Enantioselective allylation with Zr-BINOL complex activated by 4-*tert*-butylcalix[n]arenes

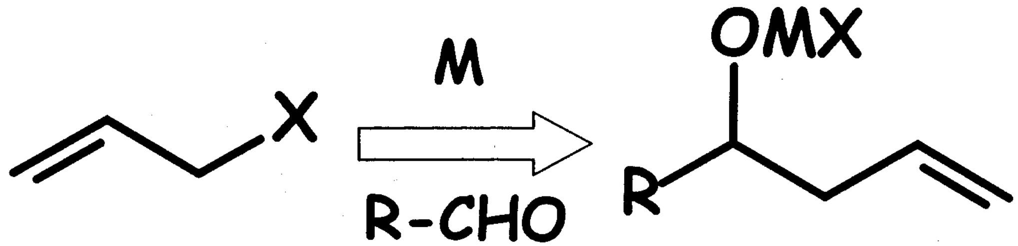
$ZrCl_4(thf)_2$ %	Calix[n]Arene	%	RCHO	Yield %	e.e. %
10	Calix[4]Arene	10	n-C_7H_{15}CHO	68	93
5	"	5	n-C_7H_{15}CHO	65	96
2	"	1	n-C_7H_{15}CHO	40	92
2	"	0.5	n-C_7H_{15}CHO	57	95
10	"	10	c-C_6H_{11}CHO	52	90
6	"	6	PhCHO	78	78
5	"	5	PhCHO	85	85
10	"	10	PhCH=CHCHO	38	77
4	Calix[6]Arene	3	PhCH=CHCHO	43	62
4	Calix[8]Arene	3	PhCH=CHCHO	30	70

Diastereoselective pinacol coupling of aldehydes catalyzed by titanium-Schiff bases complexes

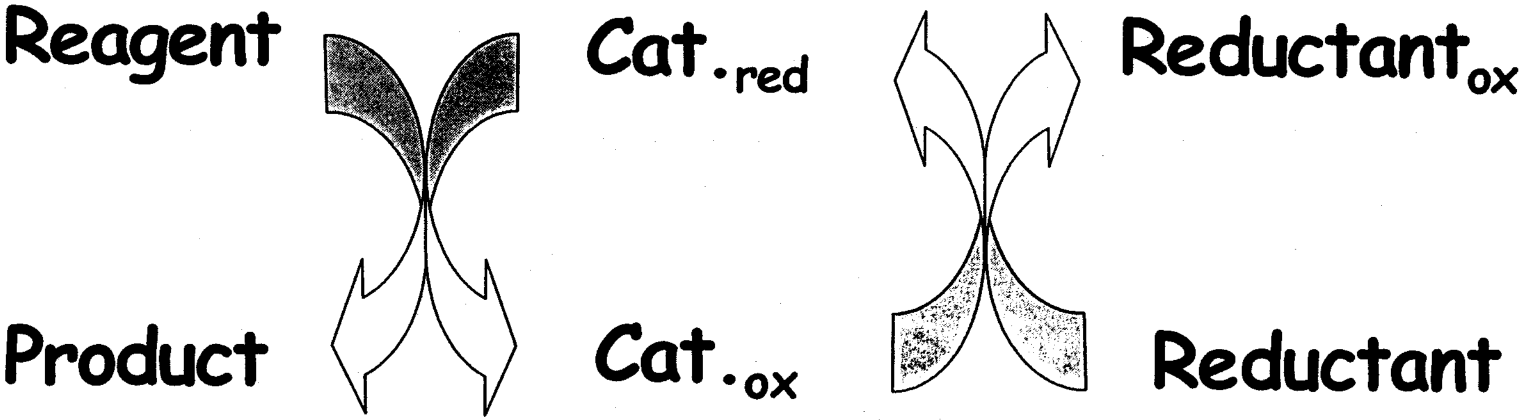


Ligand	RCHO	Yield(%)	*d,l* : *meso*
1	PhCHO	**75**	**99 : 1**
2	PhCHO	**80**	**97 : 3**
5	PhCHO	43	95 : 5
2	2-ThienylCHO	70	88 : 12
1	4-MeO-C_6H_4CHO	**65**	**92 : 8**
1	4-BrC_6H_4CHO	**83**	**95 : 5**
2	4-AcOC_6H_4CHO	**81**	**91 : 9**

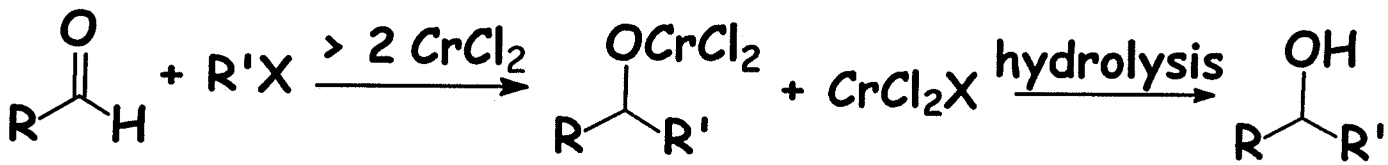
Barbier Reaction

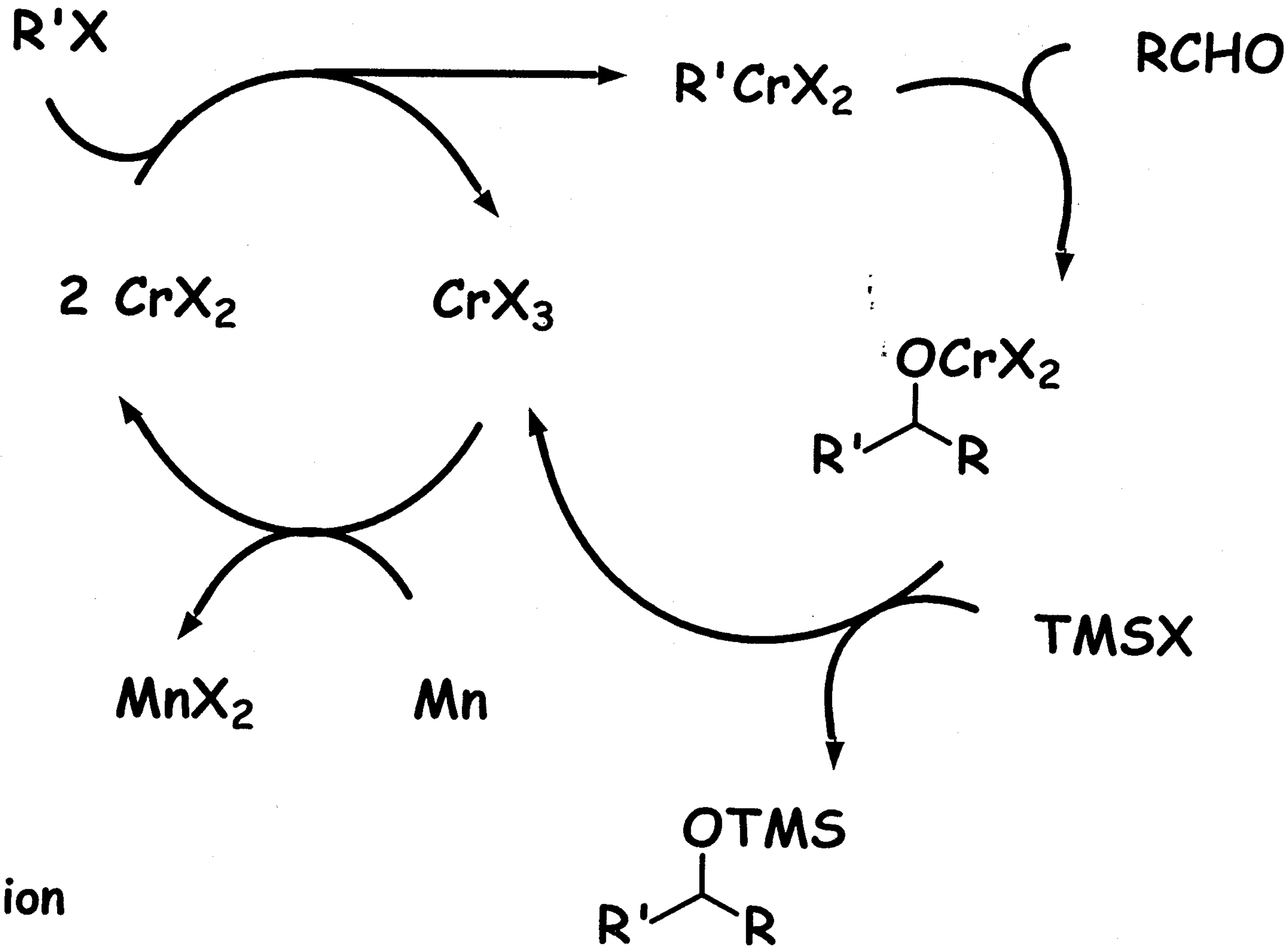


Catalytic Redox Processes

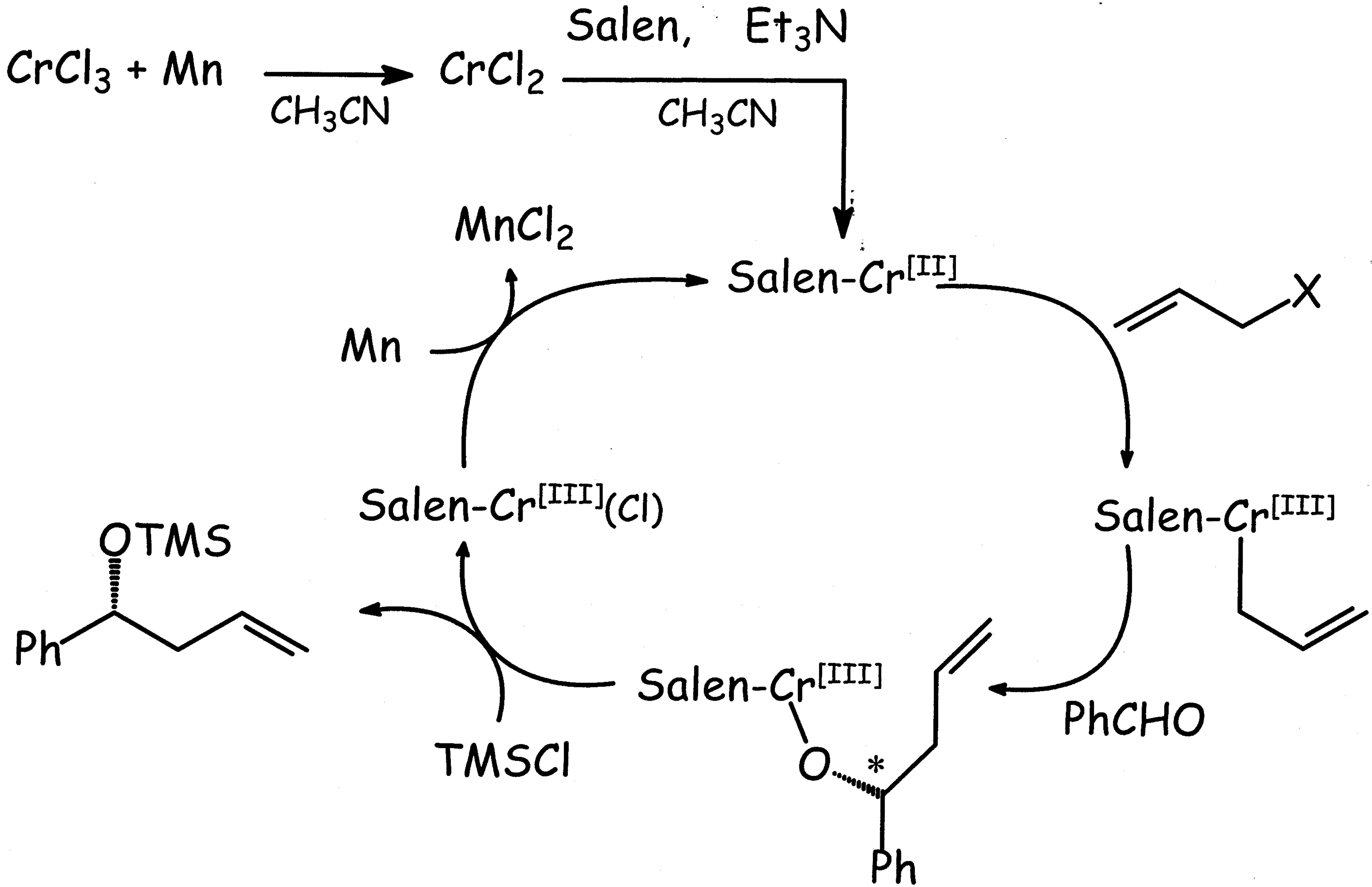


Nozaky-Hiyama-Kishi Reaction

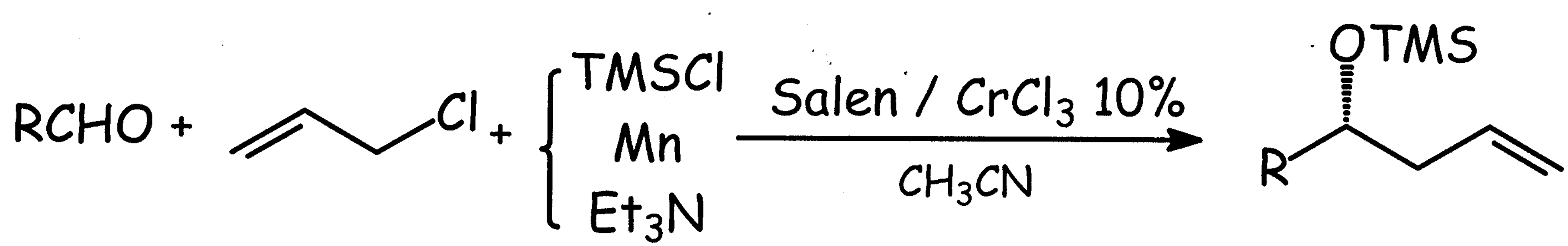


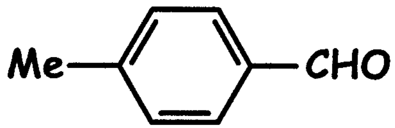
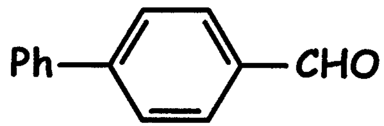
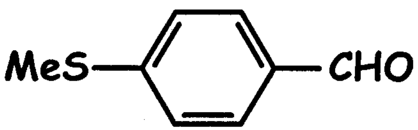
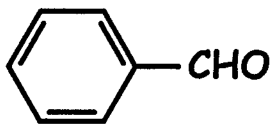
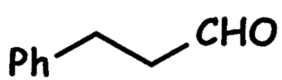
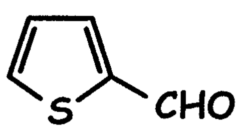


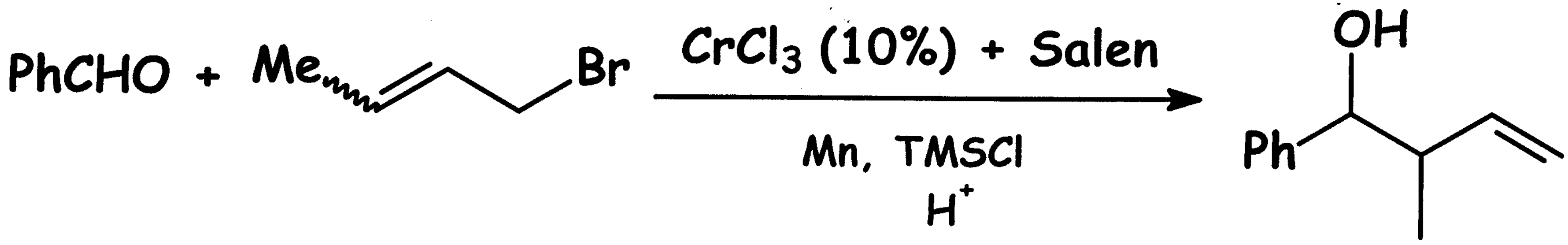
Fürstner
Catalytic version

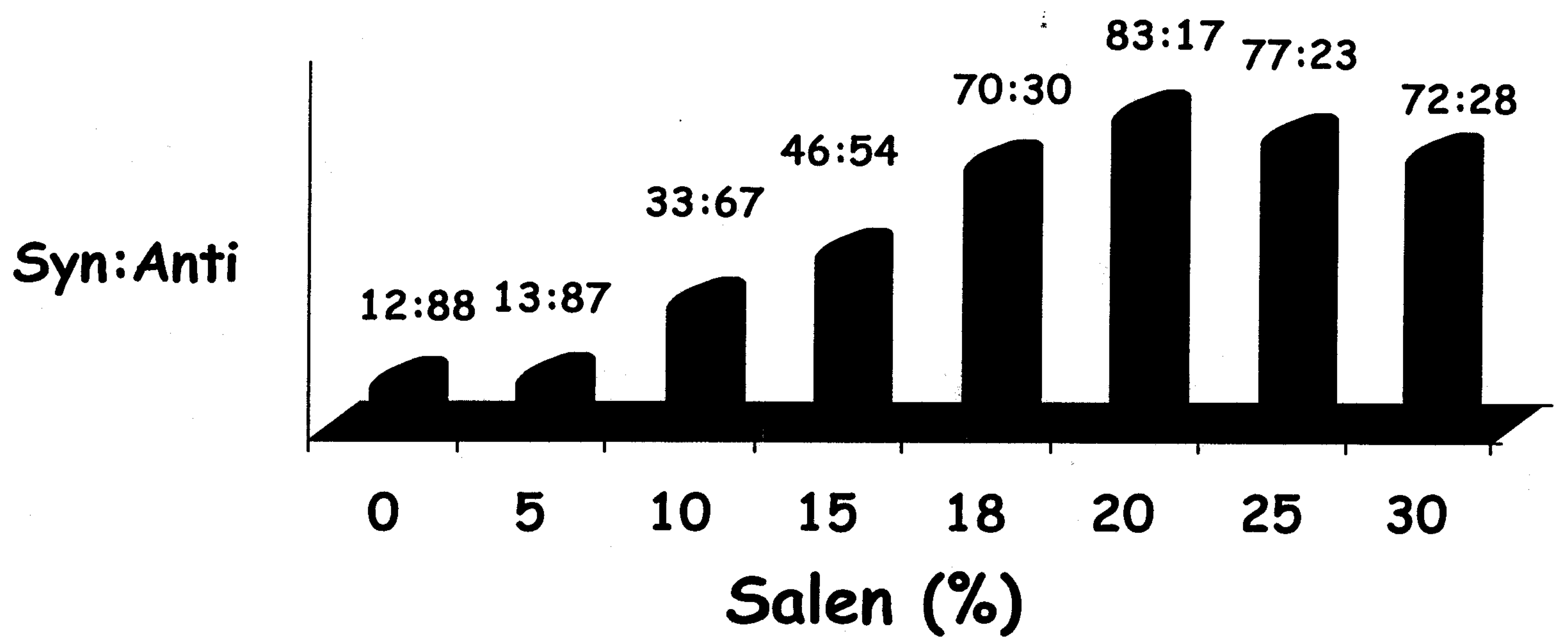


CrCl3 + Mn
CH3CN
CrCl2
Salen, Et3N
CH3CN
MnCl2
Salen-Cr[II]
Mn
X
Salen-Cr[III](Cl)
Salen-Cr[III]
OTMS
Ph
Salen-Cr[III]
O
*
Ph
PhCHO
TMSCl



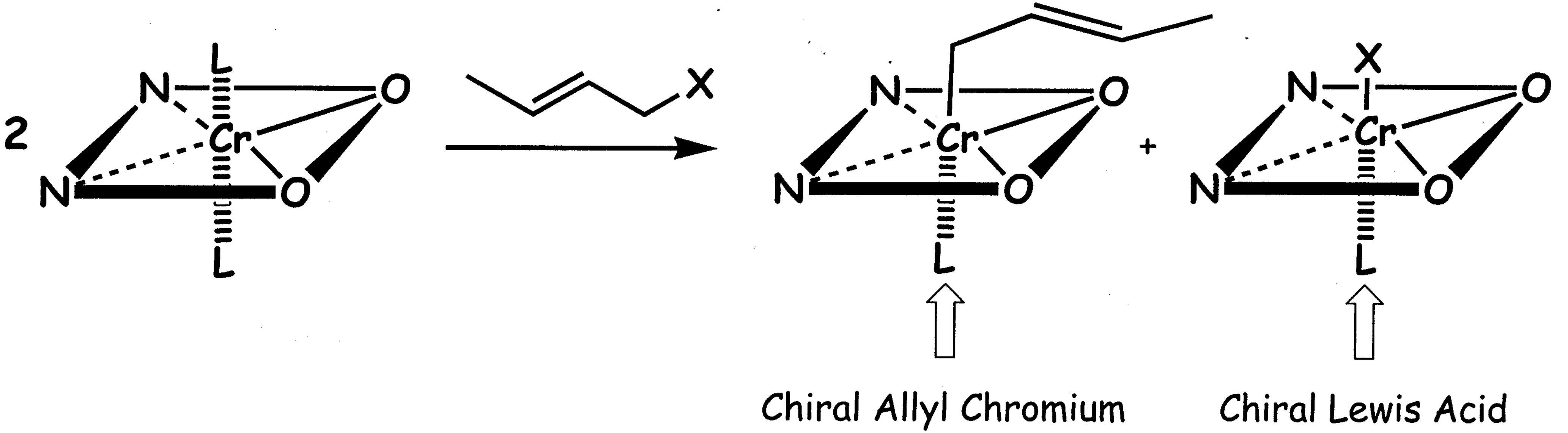
RCHO	Yield (%)	e.e. (%)	Config.
	67	78	*R*
	54	82	*R*
	46	78	*R*
	42	89	*R*
	45	77	*S*
	40	65	*R*


PhCHO + Me Br
CrCl3 (10%) + Salen
Mn, TMSCl
H+
OH
Ph

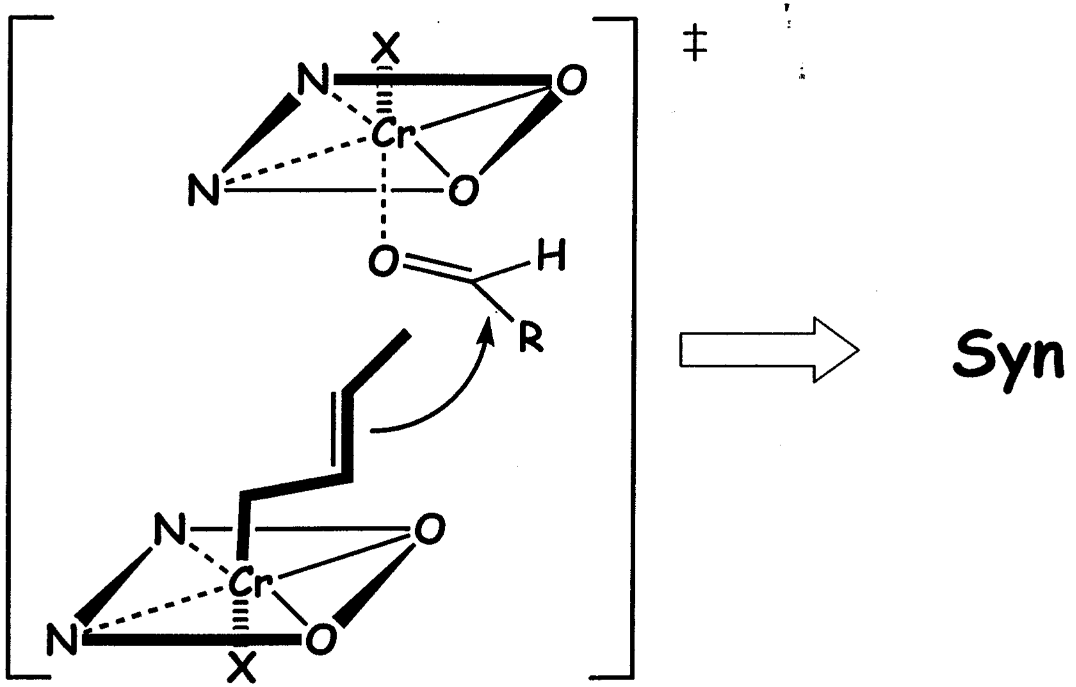

Syn:Anti
12:88
13:87
33:67
46:54
70:30
83:17
77:23
72:28
0
5
10
15
18
20
25
30
Salen (%)

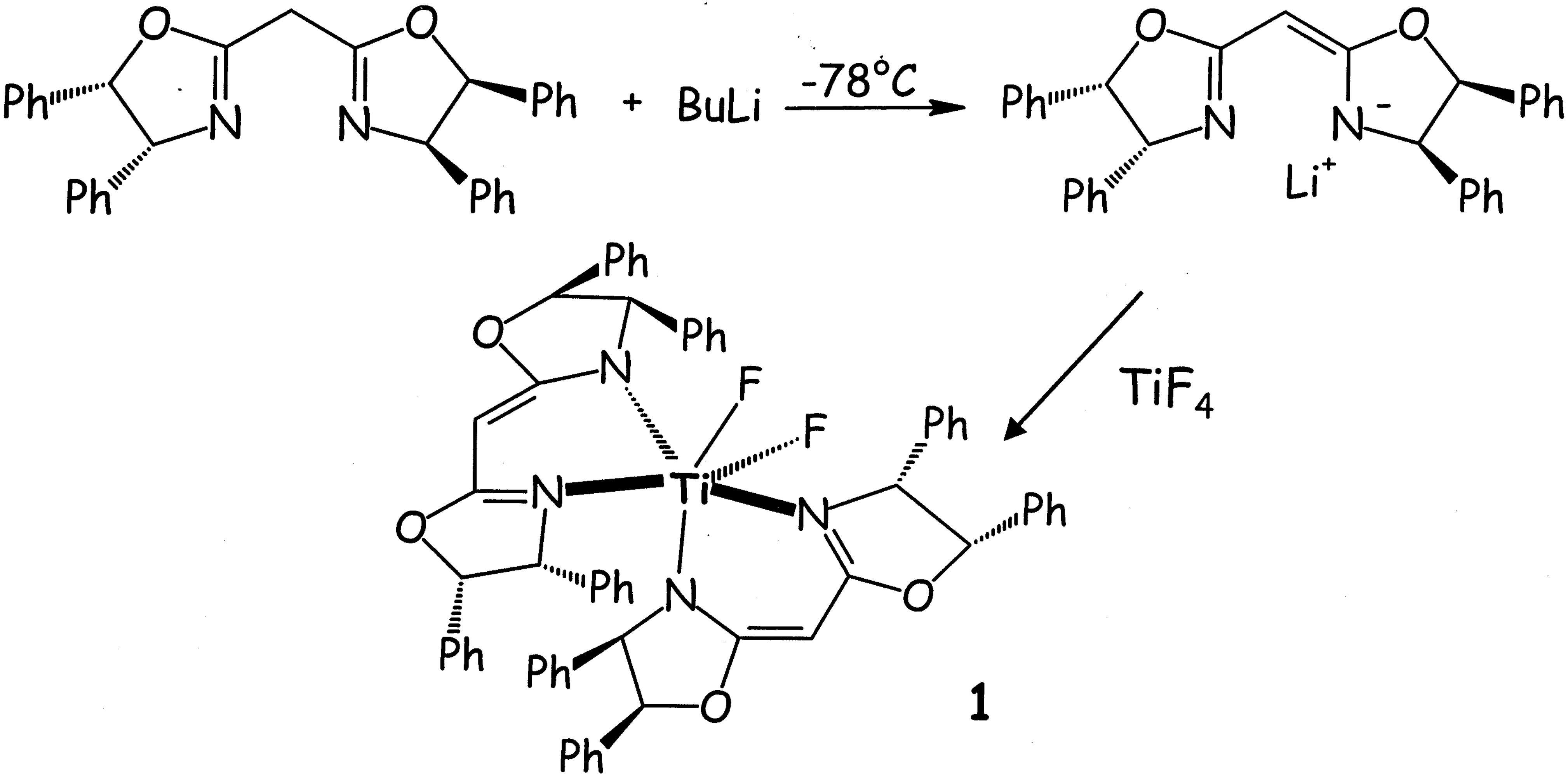
Catalyst 10% ($CrCl_3$/Salen ; 1/2)

RCHO	Yield (%)	*Anti*:*Syn*	e.e.$_{Anti}$ (%)	e.e.$_{Syn}$ (%)
PhCHO	56	17:83	36	90
p-CH_3PhCHO	48	26:74	24	85
p-PhPhCHO	47	29:71	16	84
p-FPhCHO	53	23:77	27	90
p-ClPhCHO	46	31:69	24	82
p-BrPhCHO	43	30:70	19	81

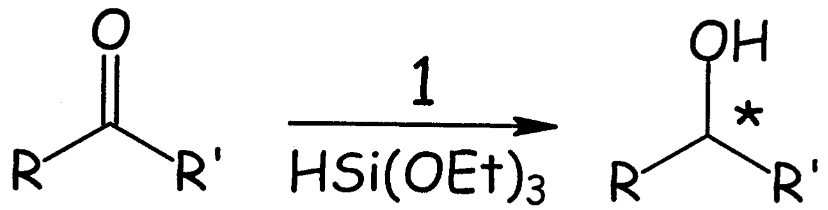


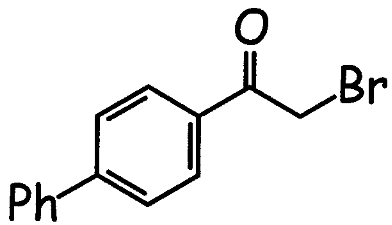
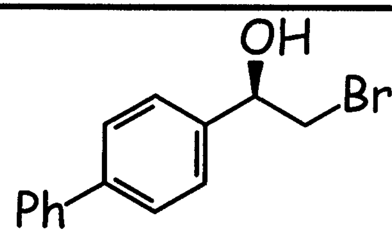
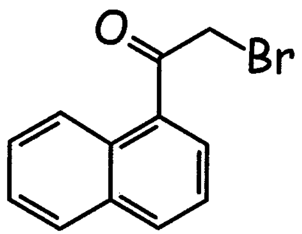
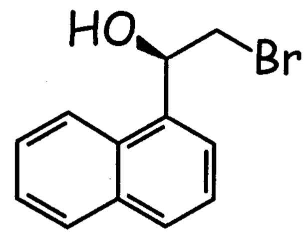
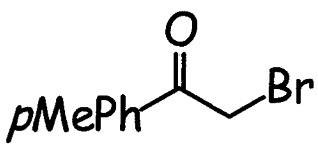
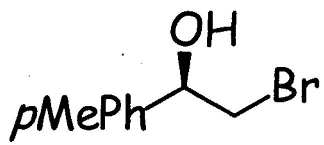
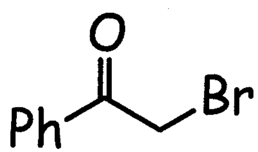
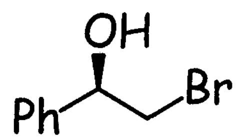
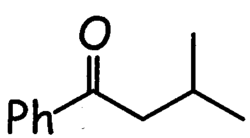
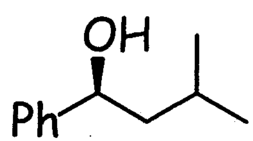
Intermolecular Mechanism



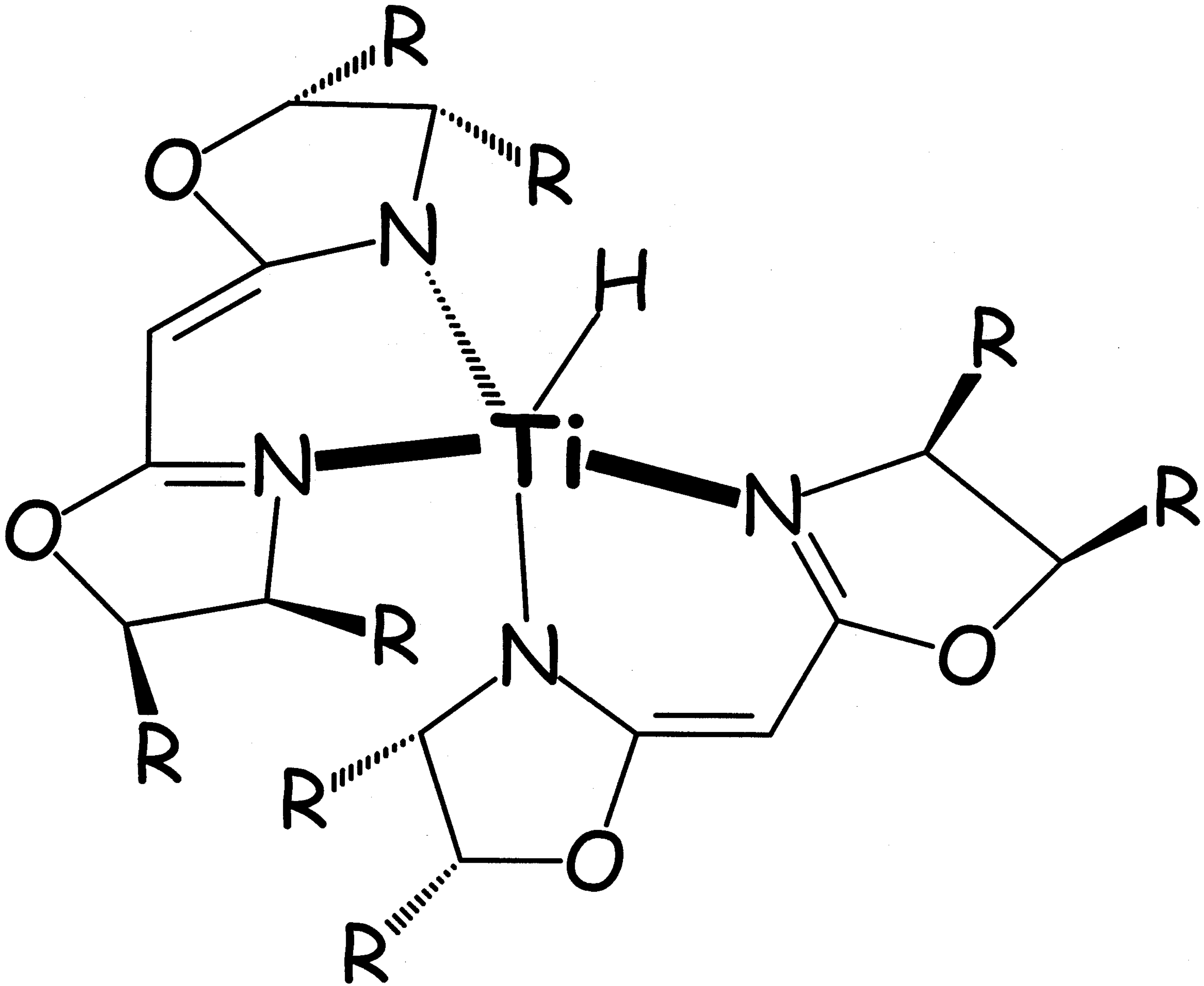

Ph
Ph
Ph
Ph
BuLi
-78°C
Ph
Ph
Li+
Ph
Ph
TiF4
F
F
Ti
Ph
Ph
Ph
Ph
Ph
Ph
Ph
Ph

1

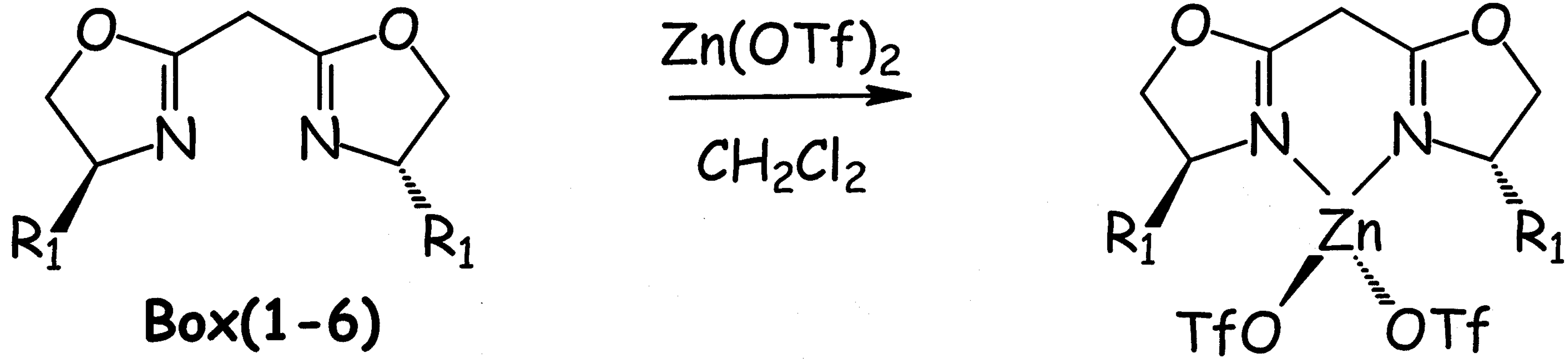

R
R'
1
HSi(OEt)3
OH
*
R
R'

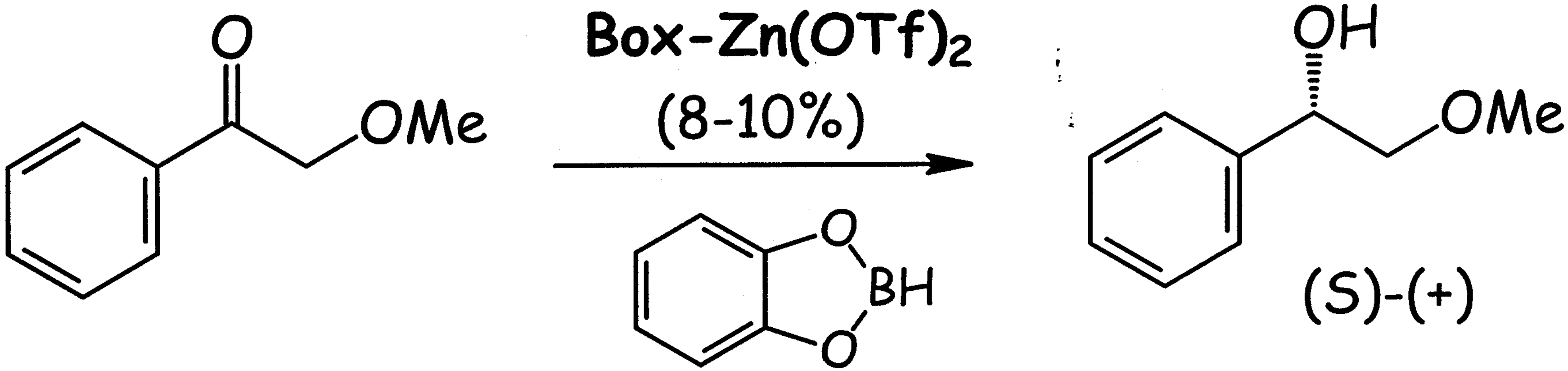
Ketone	Alcohol	Yield (%)	e.e. (%)
		54	78
		64	84
		61	83
		60	84
		61	85

Ligand 2; TiF_4; $(EtO)_3SiH$

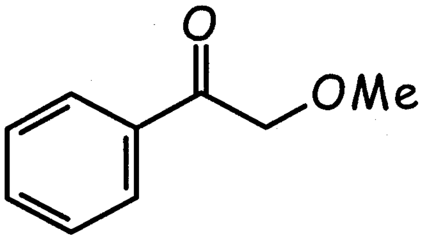
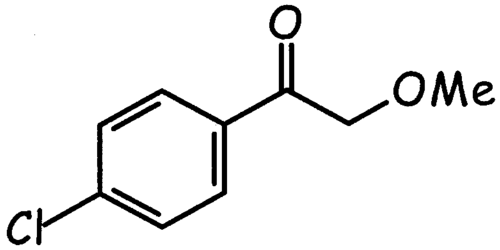
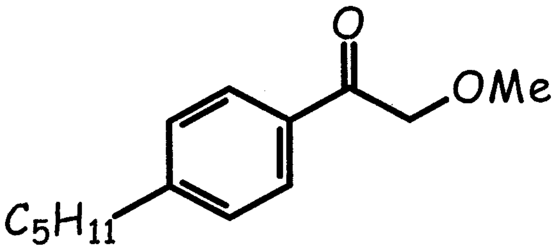


R
R
O
N
H
N
Ti
N
R
R
O
R
R
N
O
R
R
O


O
N
R1
Box(1-6)
Zn(OTf)2
CH2Cl2
Zn
TfO
OTf


O
OMe
Box-Zn(OTf)2
(8-10%)
BH
OH
(S)-(+)

Enantioselective reduction of α-methoxy-ketones promoted by the BOX-$Zn(OTf)_2$ catalyst

Ketone	Yield (%)	e.e. (%)
	78	82
	69	81
	78	67

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