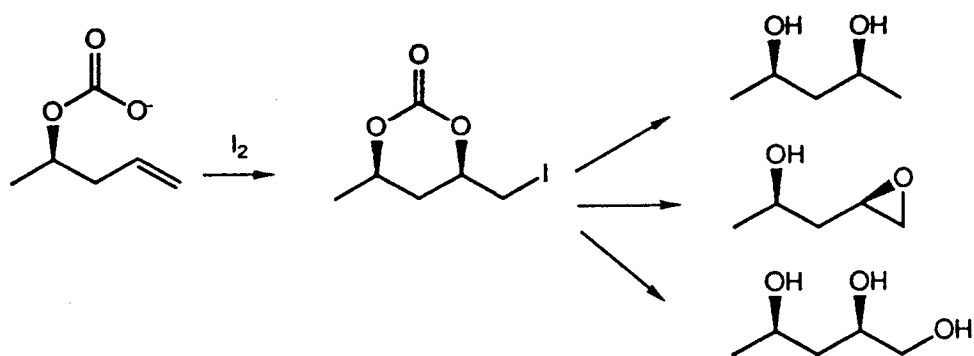
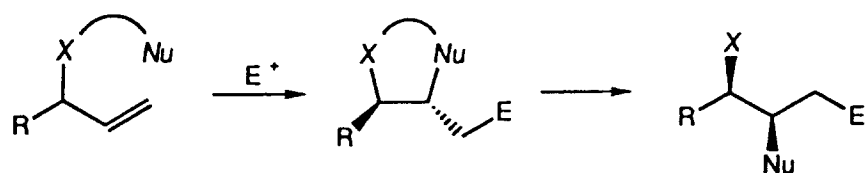
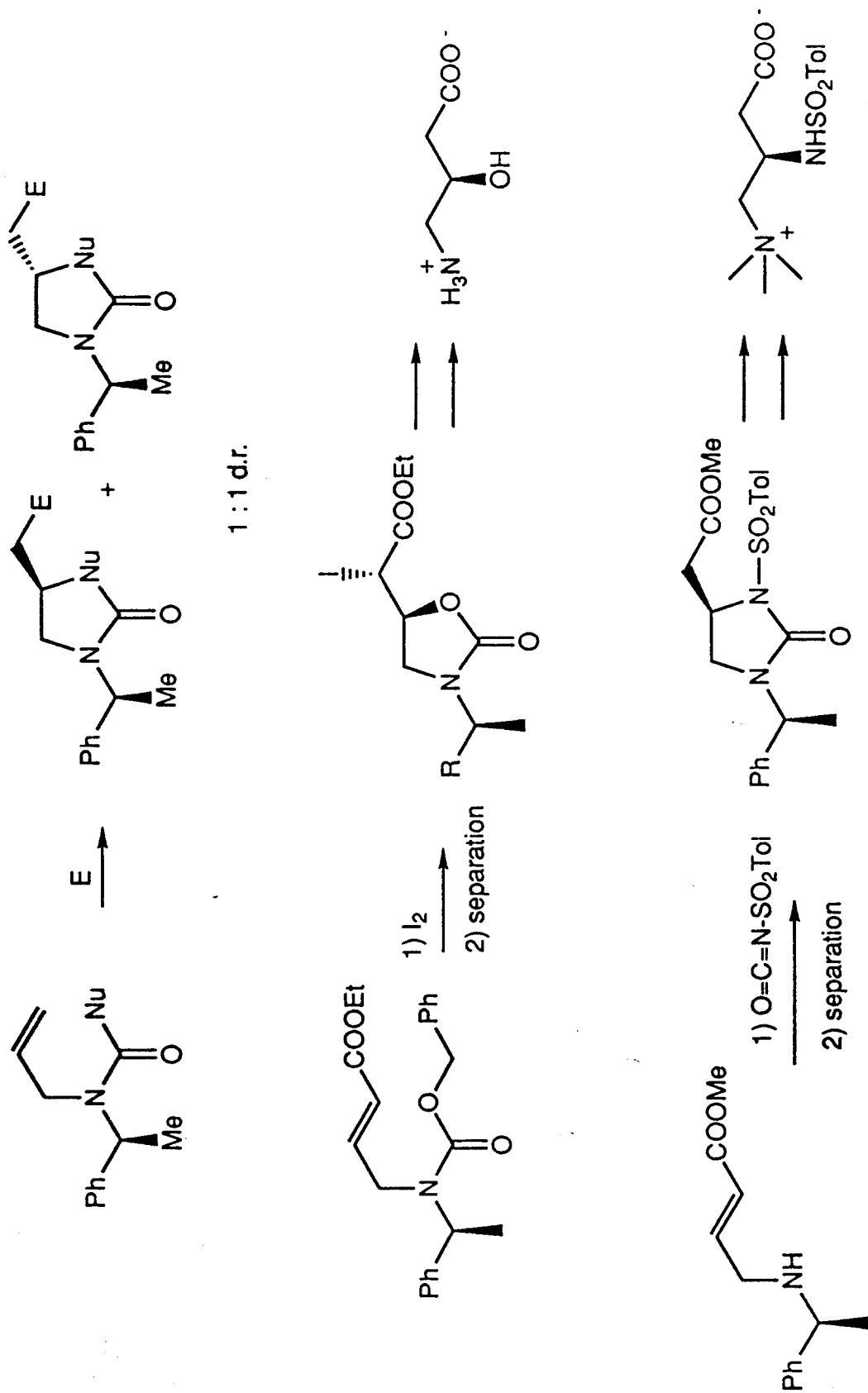
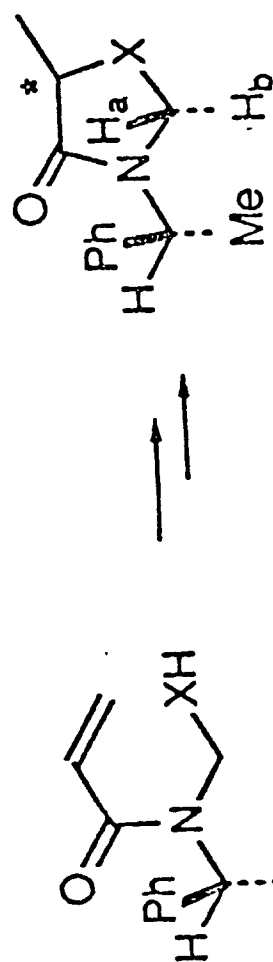
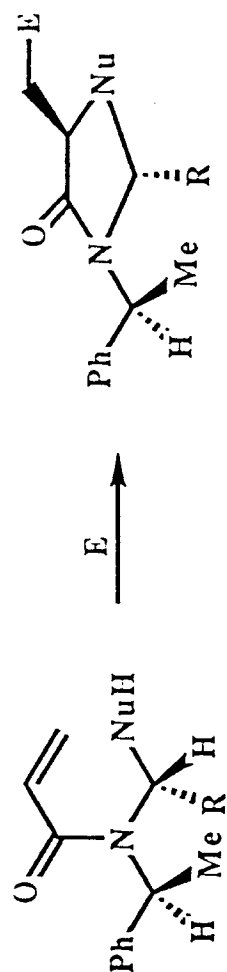
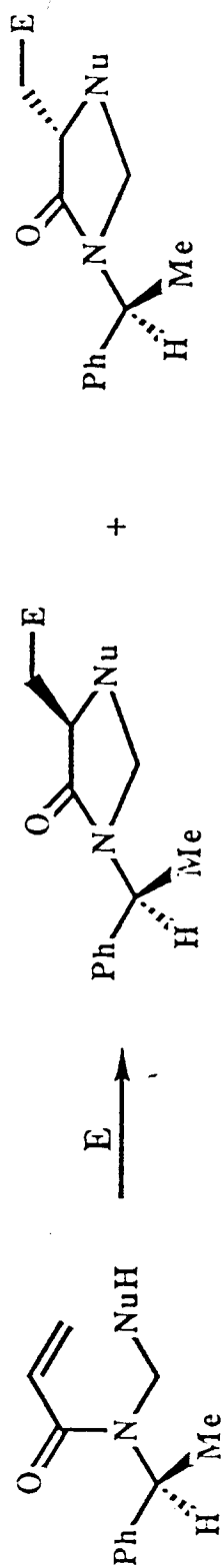
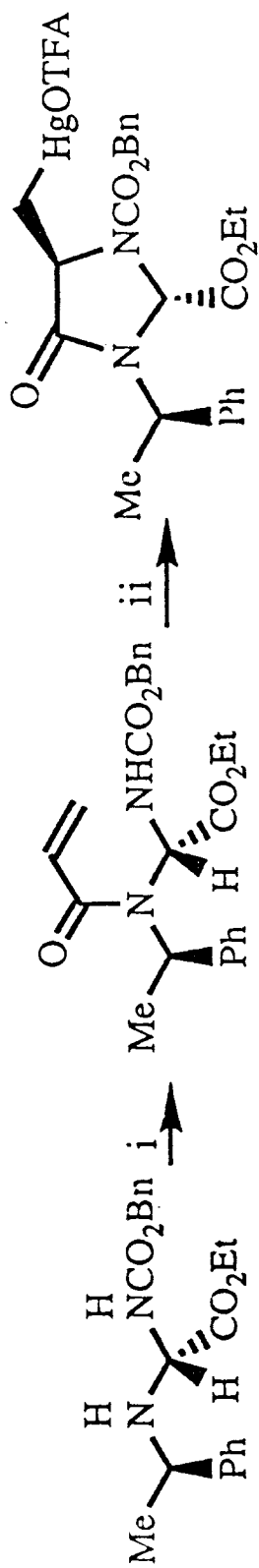






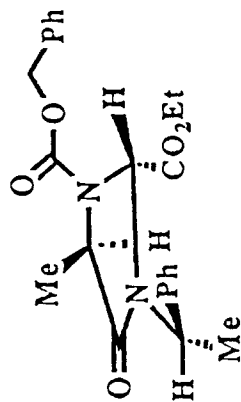
X = O, NR





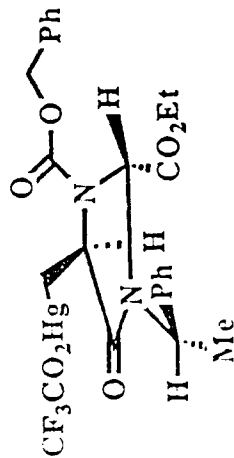
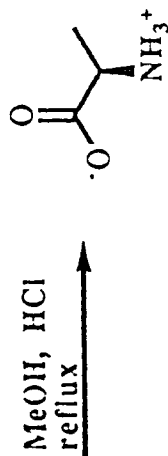
(S,R)

(S,R)

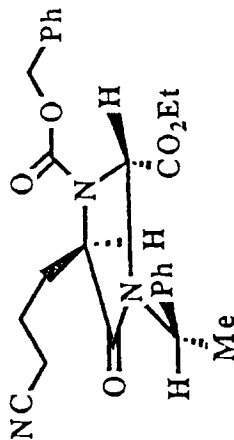


(2R,5R,1'S)

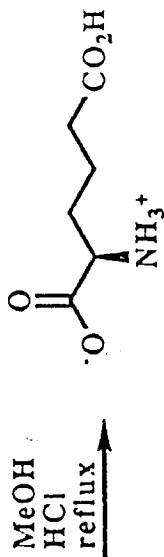
D-(-)-Alanina



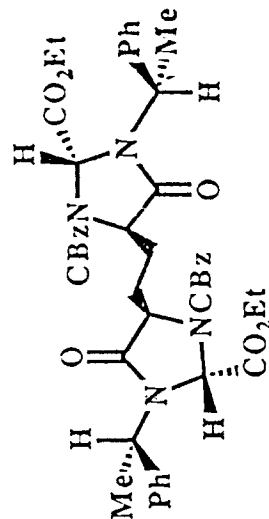
(2R,5R,1'S)



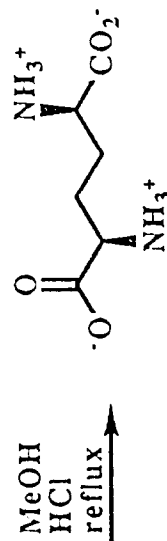
(2R,5R,1'S)



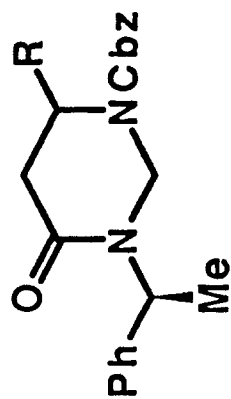
acido (D)-2-aminoadipico



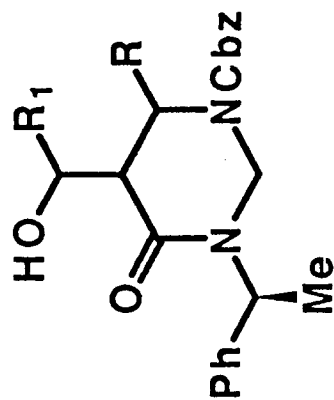
(2R,5R,1'S,2''R,5''R,1'''S)



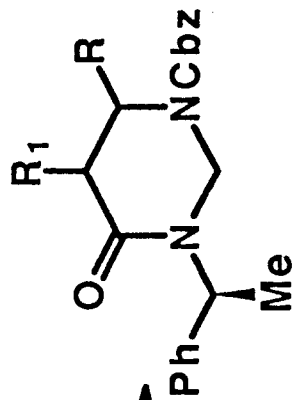
acido (R,R)-2,5-diammino-esandioico



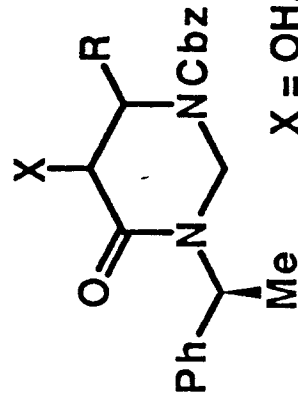
1.B:
2. R₁CHO



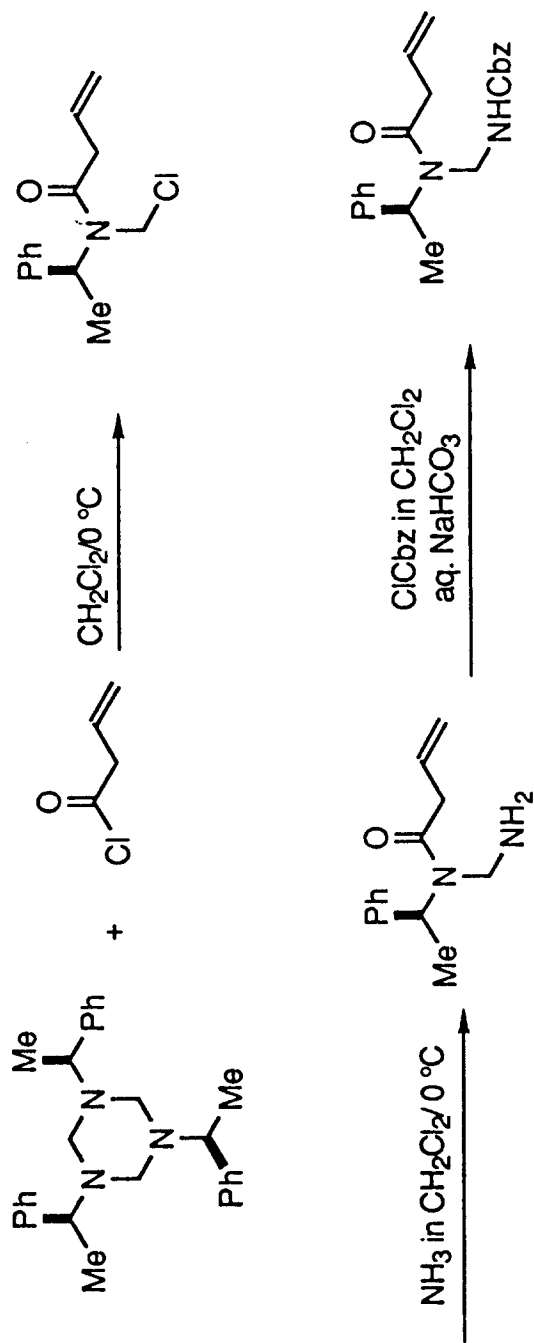
1.B:
2. R₁X

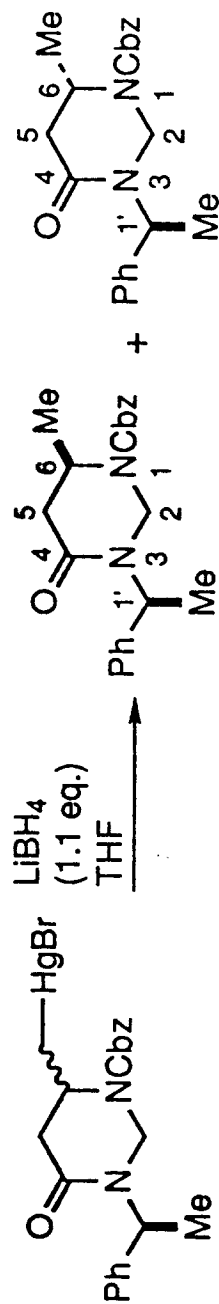


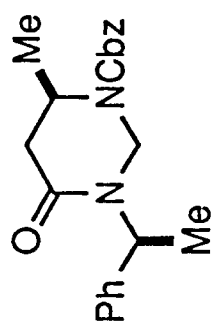
1.B:
2. L-X



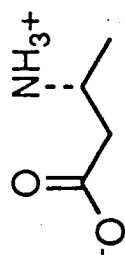
X = OH, Br, Cl



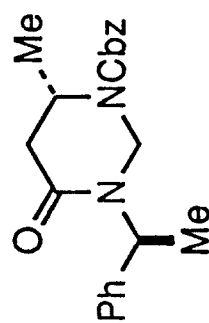




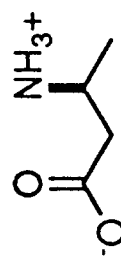
(1'S,6R)



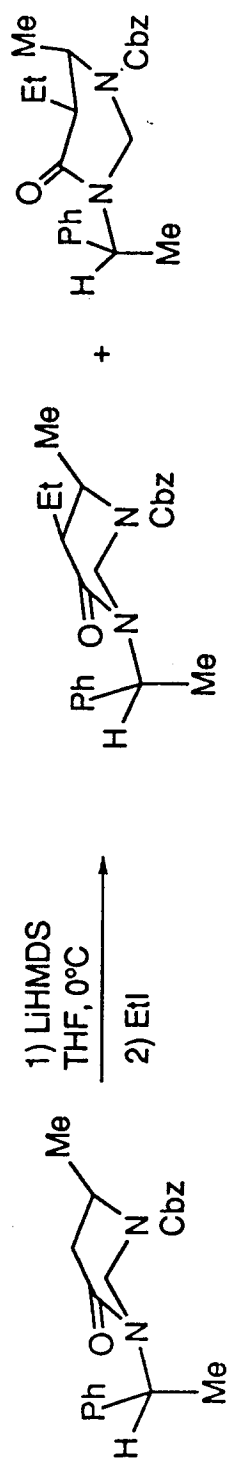
(R)-(-)



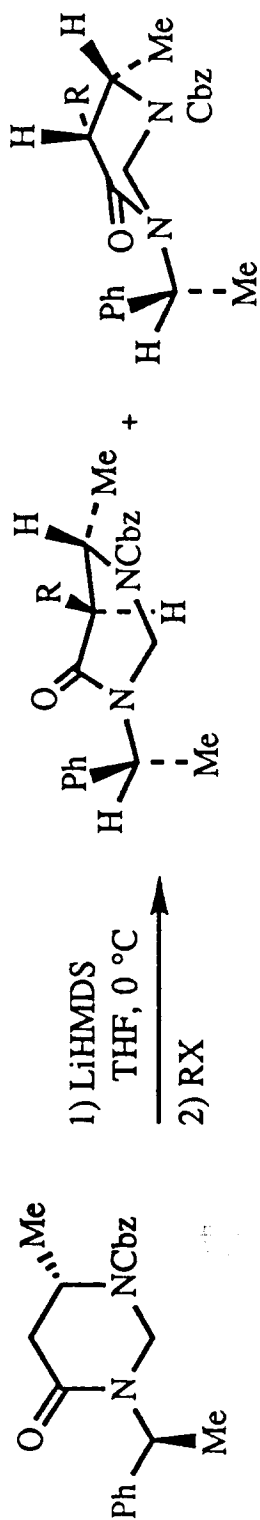
(1'S,6S)



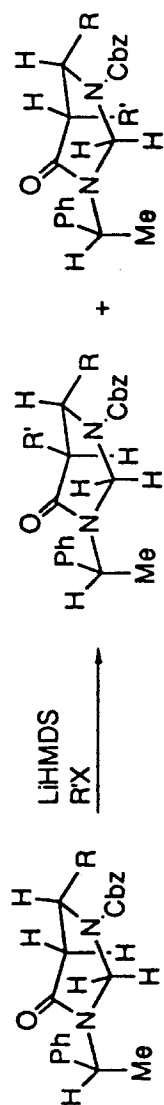
(S)-(+)



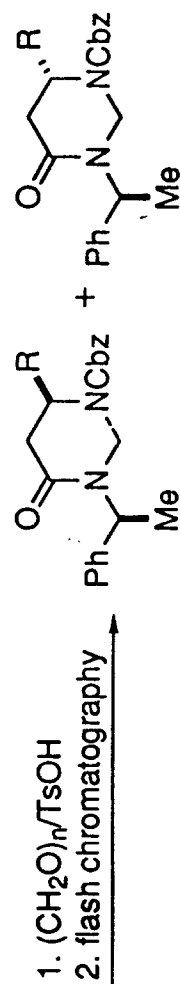
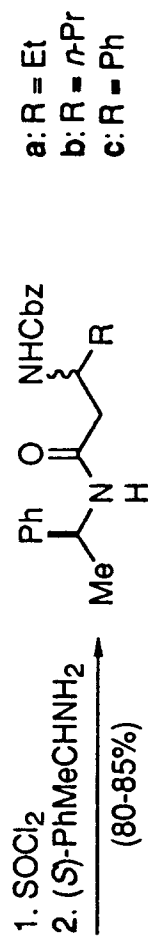
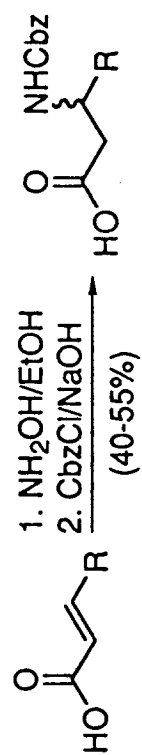
Reaction temp. °C	Reaction time h	eq. LiHMDS	Yield %	Dialkylated %	Trans/cis ratio
0	2	0.9	84	-	87 : 13
0	2	1.1	78	11	96 : 4
-20	1	1	53	2	91 : 9
-20	4	1	89	3	91 : 9
-78 - r. t.	14	1	86	10	94 : 6

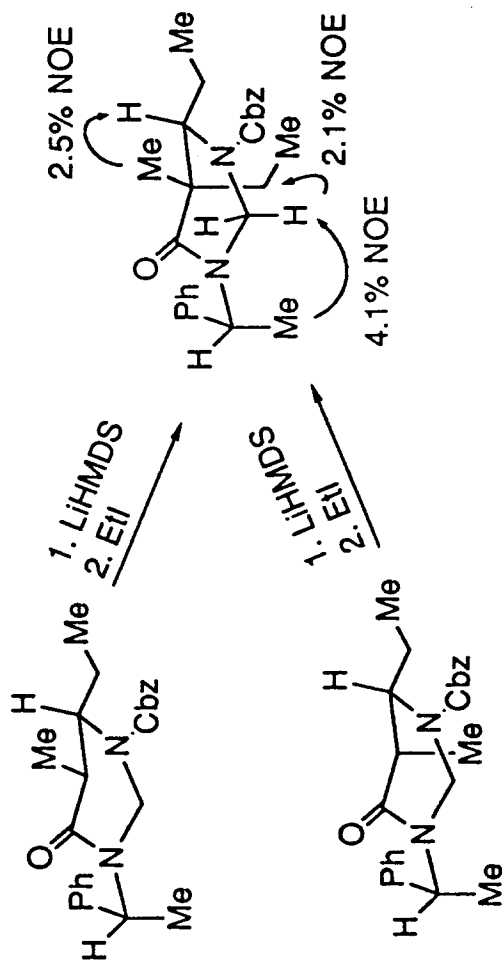


Reaction temp. °C	Reaction time h	equiv. LiHMDS	Alkylating agent	Yield %	Dialkylated %	Trans/cis ratio
0	21	0.8	EtI	77	-	85 : 15
0	2	1.1	EtI	92	8	94 : 6
-78 - r.t.	4	1	EtI	87	6	94 : 6
-78 - r.t.	14	1	EtI	89	10	97 : 3
0	50	1	i-Bul	56	-	87 : 13
0	5	1	BnBr	90	-	93 : 7

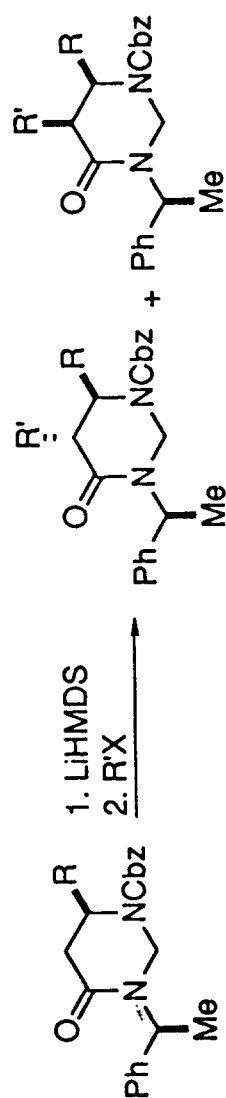


R	R'	Time	Alkylating agent	Yield %	Trans/cis ratio	Dialkylated %
		h	(eq.)			
Et	Me	2	Me ₂ SO ₄ (2)	66	80:20	3
Et	Me	3	Me ₂ SO ₄ (2)	80	82:18	7
n-Pr	Me	2	Me ₂ SO ₄ (2)	86	77:23	/
Ph	Me	2	Me ₂ SO ₄ (2)	50	92:8	/

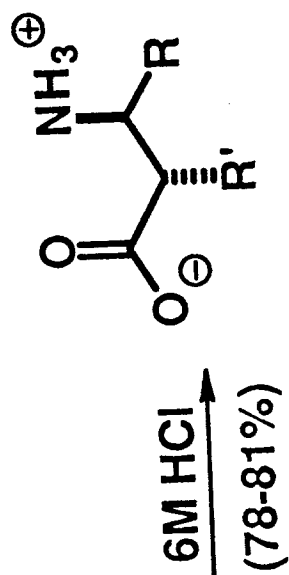
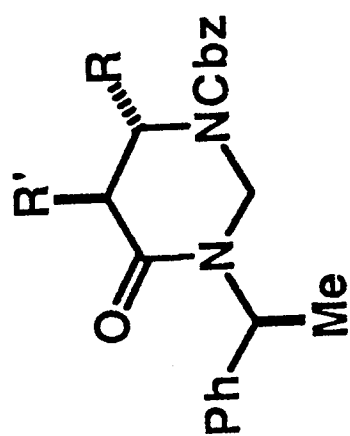




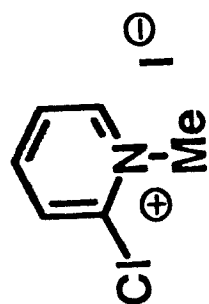
Starting material	Temp. °C	Time h	Diastereomeric		Yield %
			ratio		
5,6 trans	0	1	96 : 4		5
5,6 trans	rt	72	90 : 10		47
5,6 cis	0	1	91 : 9		99



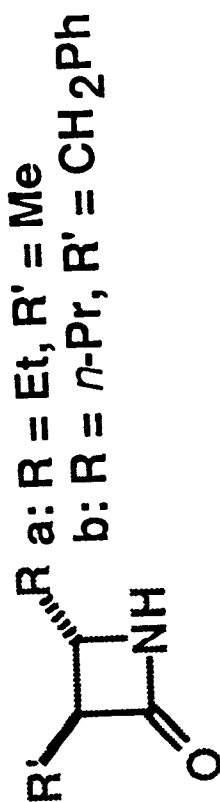
R	R'	Alkylating agent (1.5 eq.)	Yield (%)	Trans/cis ratio
Et	Et	EtI	78	96:4
<i>n</i> -Pr	Et	EtI	90	>99
<i>n</i> -Pr	CH ₂ Ph	PhCH ₂ Br	85	>99
Ph	Et	EtI	96	>99
Et	CH ₂ Ph	PhCH ₂ Br	95	>99
<i>n</i> -Pr	Et	EtI	92	>99
<i>n</i> -Pr	CH ₂ Ph	PhCH ₂ Br	88	>99
Ph	Et	EtI	80	>99



6M HCl
(78-81%)

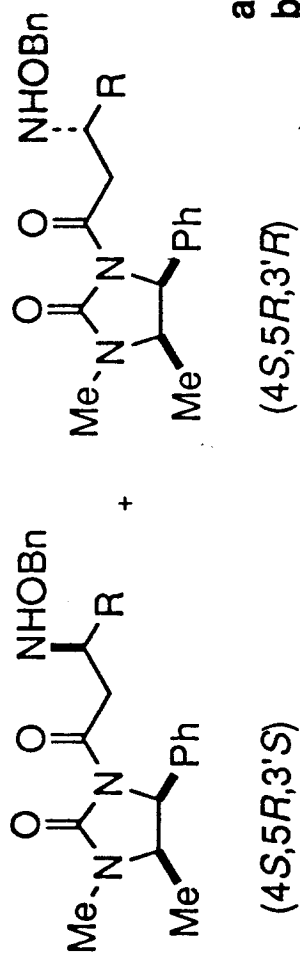
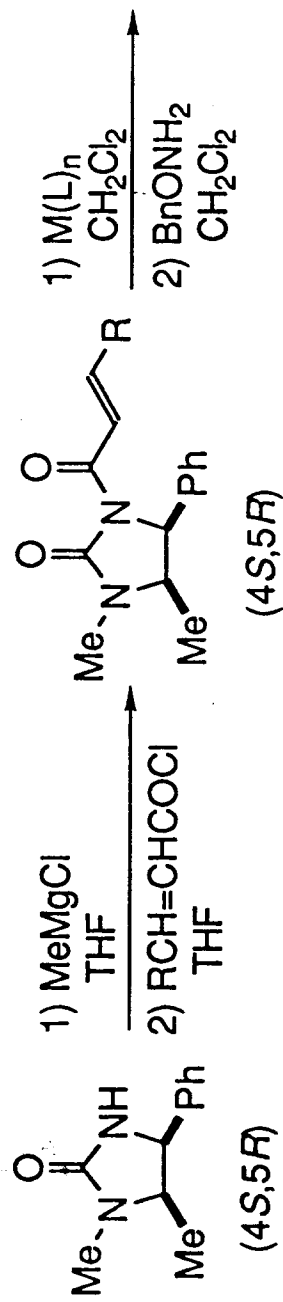


Et₃N/CH₃CN
(81-85%)

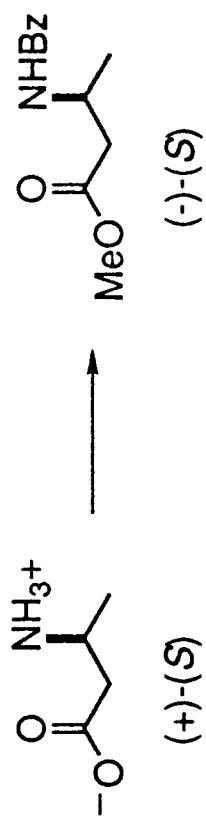
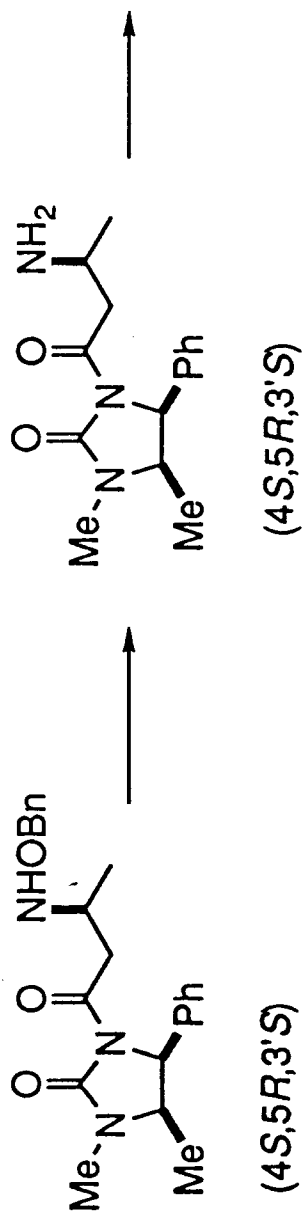


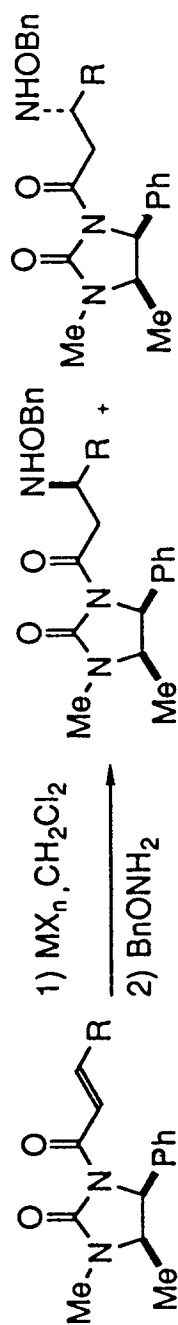
R a: R = Et, R' = Me

b: R = *n*-Pr, R' = CH₂Ph

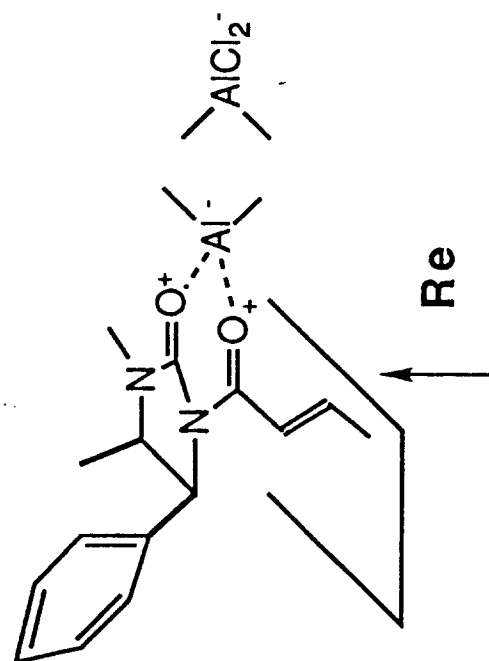
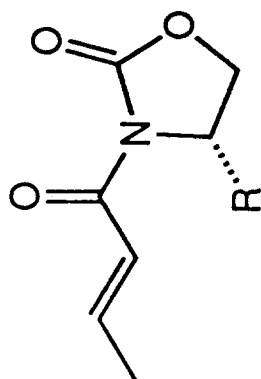
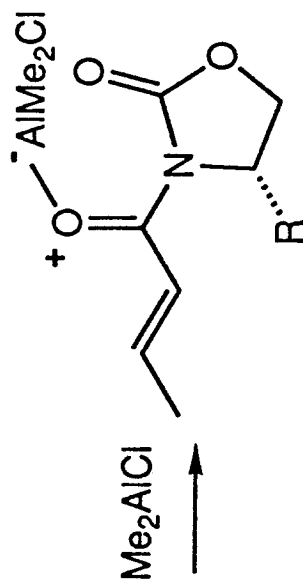
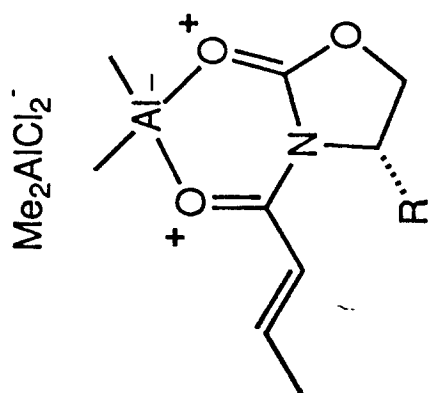


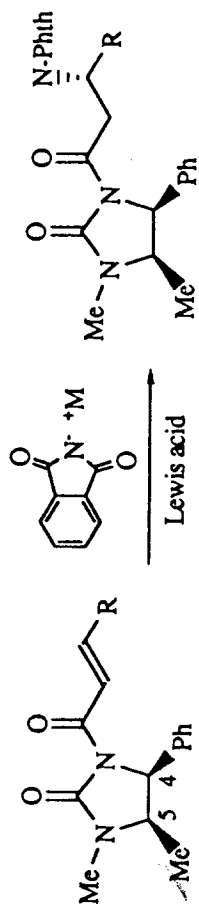
a : R = CH₃
 b : R = n-C₃H₇



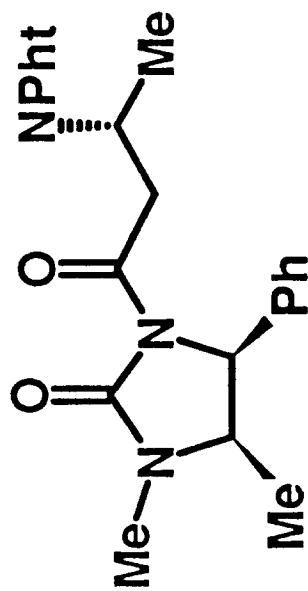


R	MX	yield %	diastereomeric ratio	
			4/5	
CH_3	ZnCl_2 (1 eq.)	92	55 : 45	
CH_3	TiCl_4 (1 eq.)	80	80 : 20	
C_3H_7	TiCl_4 (1 eq.)	90	77 : 23	
C_3H_7	$\text{TiCl}_2(\text{O}-i\text{Pr})_2$ (1 eq.)	38	50 : 50	
CH_3	$\text{AlCl}(\text{Me})_2$ (1 eq.)	65	26 : 74	
CH_3	$\text{AlCl}(\text{Me})_2$ (1.4 eq.)	65	19 : 81	
CH_3	$\text{AlCl}(\text{Me})_2$ (2 eq.)	70	20 : 80	
C_3H_7	$\text{AlCl}(\text{Me})_2$ (1.4 eq.)	81	13 : 87	
C_3H_7	$\text{AlCl}(\text{Me})_2$ (2 eq.)	83	11 : 89	





Lewis acid eq.	Nucleophile eq.	Solvent	Temp. °C	Time h	Diastereomeric ratio	Yield %
-	Phth-Li (1)	THF	0 - π	70	-	-
AlMe ₂ Cl (1.2)	Phth-Li (2)	CH ₂ Cl ₂ /THF	-78 - π	24	70 : 30	60
AlMe ₂ Cl (1.2)	Phth-DBU (1.5)	CH ₂ Cl ₂	-78 - π	72	83 : 17	90
	Phth-MgCl (2)	THF	0 - π	24	95 : 5	30
	Phth-MgCl (5)	THF	0 - π	24	95 : 5	90

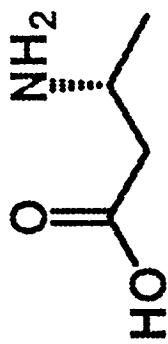


(4*S*,5*R*,3'*R*)

1) LiOH (4.8 eq)
H₂O₂ (12 eq)
THF/H₂O

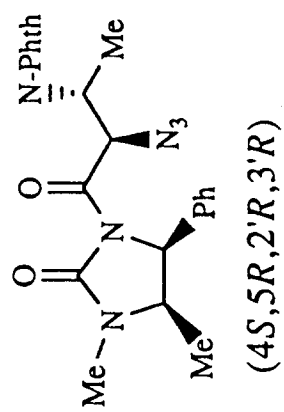
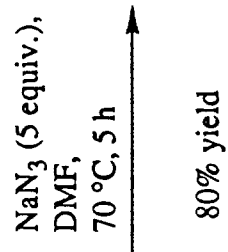
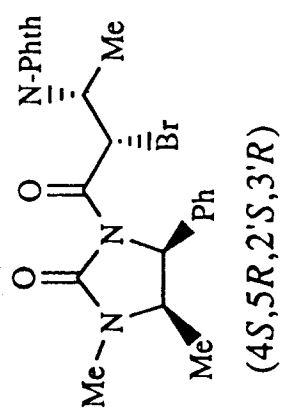


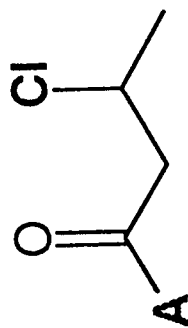
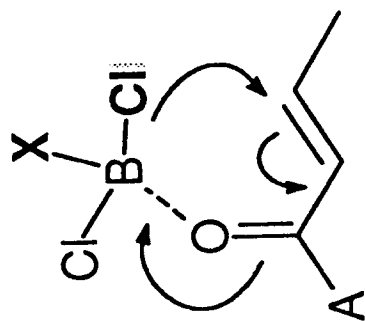
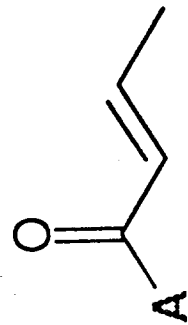
2) ion exchange resin
1.5M NH₄OH



(*R*)-(-)

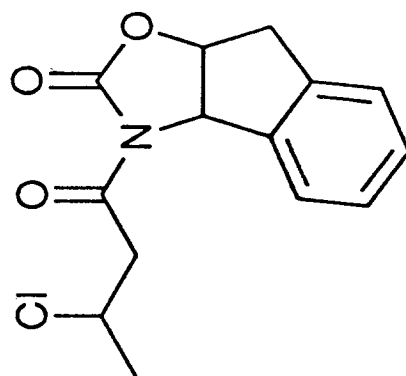
[α]_D = -39.0 (c 0.7, H₂O)





A = chiral auxiliary

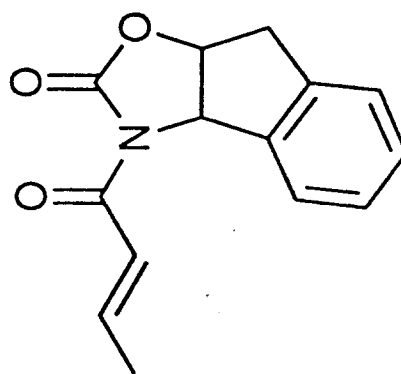
X = OiPr, Cl



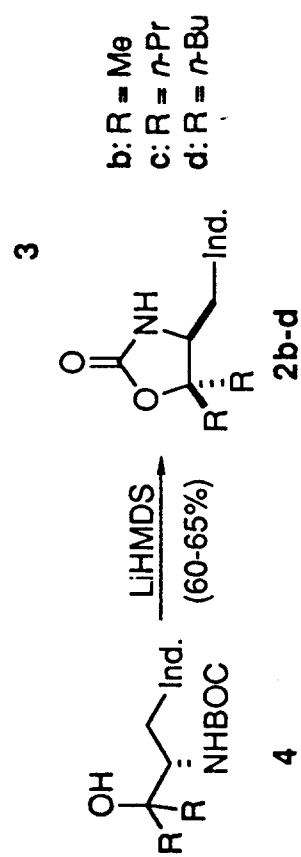
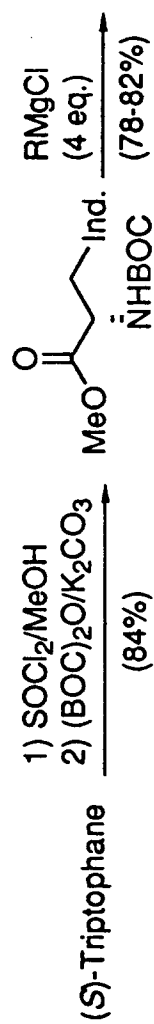
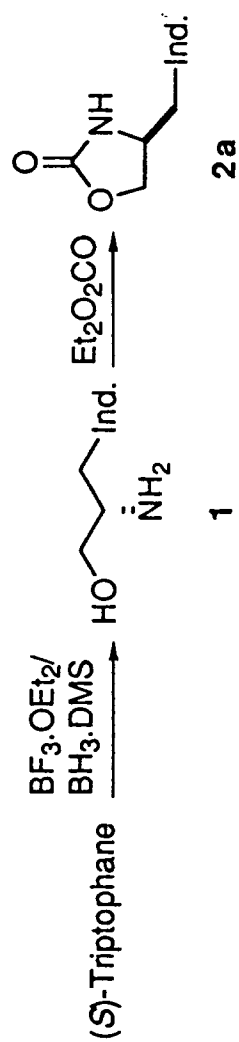
$\text{BCl}_2(\text{OiPr})$

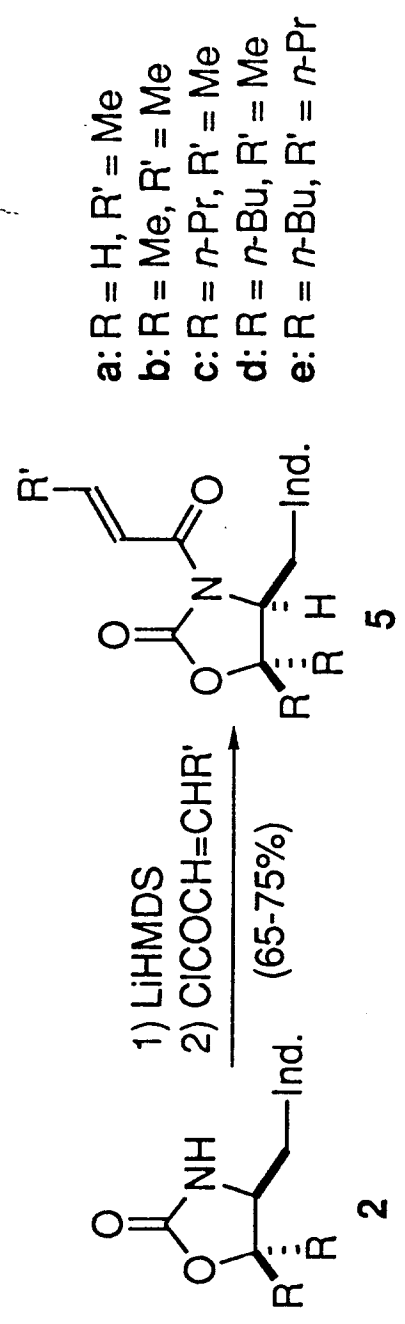


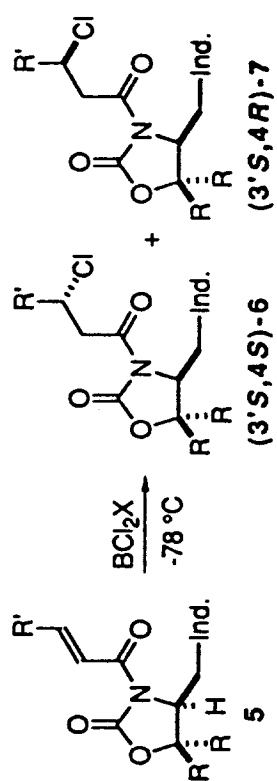
d.r. = 90:10



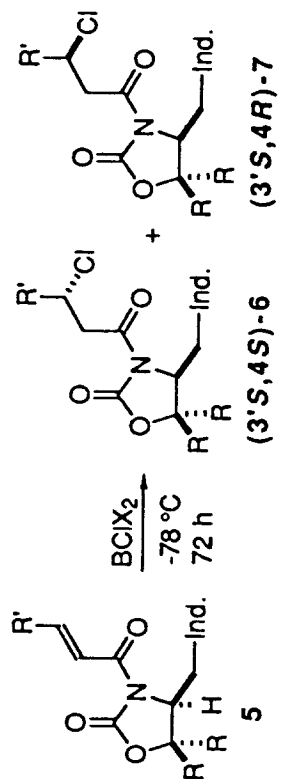
± cis







R	R'	Lewis acid 3 eq.	Reaction time h	Yield %	d.r. 6/7
H	Me	BCl ₂ O- <i>i</i> Pr	7	30	50:50
Me	Me	BCl ₂ O- <i>i</i> Pr	7	98	75:25
<i>n</i> -Pr	Me	BCl ₂ O- <i>i</i> Pr	3	80	83:17
<i>n</i> -Bu	Me	BCl ₂ O- <i>i</i> Pr	7	90	86:14
<i>n</i> -Bu	Me	BCl ₂ OMe	17	98	92:8
<i>n</i> -Bu	Me	BCl ₂ OPh	18	50	45:55
<i>n</i> -Bu	<i>n</i> -Pr	BCl ₂ O- <i>i</i> Pr	6	80	>99:1
<i>n</i> -Bu	<i>n</i> -Pr	BCl ₂ OMe	6	80	>99:1



R	R'	Lewis acid eq.	Yield %	d.r. 6/7
H	Me	BCl(O- <i>i</i> Pr) ₂ (3)	15	50 : 50
Me	Me	BCl(O- <i>i</i> Pr) ₂ (3)	50	27 : 73
<i>n</i> -Pr	Me	BCl(O- <i>i</i> Pr) ₂ (3)	30	25 : 75
<i>n</i> -Pr	Me	BCl(O- <i>i</i> Pr) ₂ (10)	40	33 : 67
<i>n</i> -Bu	Me	BCl(O- <i>i</i> Pr) ₂ (3)	60	20 : 80
<i>n</i> -Bu	Me	BCl(OMe) ₂ (3)	60	40 : 60
<i>n</i> -Bu	<i>n</i> -Pr	BCl(O- <i>i</i> Pr) ₂ (3)	38	46 : 54
<i>n</i> -Bu	<i>n</i> -Pr	BCl(OMe) ₂ (3)	27	43 : 57