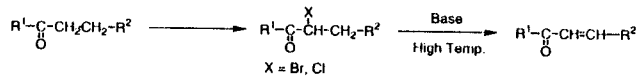
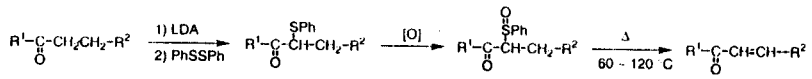
Dehydrogenation of Carbonyl Compounds

1. Halogenation and Dehydrohalogenation

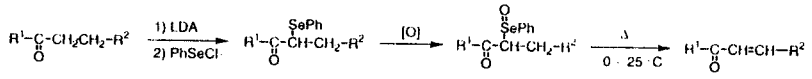


2. Sulfenylation and Elimination of Sulfoxide



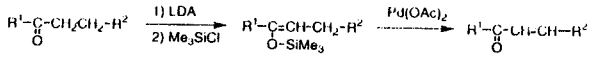
B. M. Trost et al. *J. Am. Chem. Soc.* **95**, 6840 (1973)

3. Selenylation and Elimination of Selenoxide



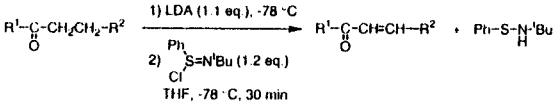
H. J. Reich et al. *J. Am. Chem. Soc.* **95**, 5813 (1973)
K. B. Sharpless et al. *J. Am. Chem. Soc.* **95**, 6173 (1973)

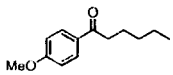
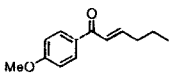
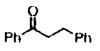
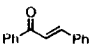
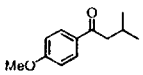
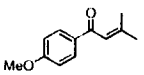
4. Trimethylsilylation and $Pd(OAc)_2$-Catalyzed Elimination



Y. Ito et al. *J. Org. Chem.* **43**, 1011 (1978)
J. Tsuji et al. *Tetrahedron Lett.* **24**, 5635 (1983)

A New and One-Pot Dehydrogenation of Ketones by Using N-tert-Butyl Phenylsulfinimidoyl Chloride

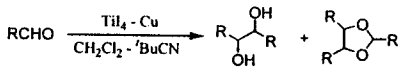


Entry	Substrate	Product	Yield (%)
1			93
2[a]			95
3			77
4			93
5			92

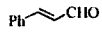
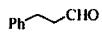
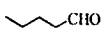
[a] 15-Crown-5 (1.1 eq.) was added.

T. Mukaiyama, J. Matsuo, and H. Kitagawa, *Chem. Lett.*, in press

Pinacol Coupling Reaction of Various Aldehydes Promoted by TiI_4 and Cu



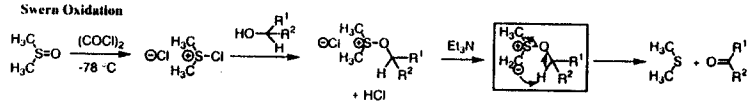
1 2

Entry	RCHO	Conditions[a]	Yield / % 1 [*dl* / *meso*][b]	2
1	PhCHO	A	94 [>99 / 1]	0
2	*p*-Cl-PhCHO	A	93 [>99 / 1]	4
3	*p*-MeO-PhCHO	A	76 [98 / 2]	9
4		A	76 [99 / 1]	8
5		B	80 [81 / 19]	11
6		B	72 [80 / 20]	8
7		B	85 [75 / 25]	0
8		B	98 [84 / 16]	0
9		B	95 [85 / 15]	0
10		C	92 [85 / 15]	0

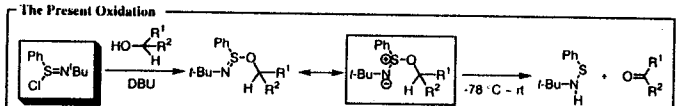
[a] See Ref. 10. Conditions A: aldehyde / TiI_4 / Cu / ^tBuCN = 0.5 / 0.5 / 1.0 / 2.0 mmol in CH_2Cl_2 (4.0 ml), -23 °C, 3 h; B: aldehyde / TiI_4 / Cu / ^tBuCN = 0.5 / 0.65 / 1.3 / 2.6 mmol in CH_2Cl_2 (4.0 ml), 0 °C, 6 h; C: aldehyde / TiI_4 / Cu / ^tBuCN = 0.5 / 0.65 / 1.3 / 2.6 mmol in CH_2Cl_2 (4.0 ml), rt, 6 h. [b] Ratios were determined by ^1H-NMR analysis of crude product mixture.

A New and Efficient Oxidation of Various Alcohols by Using N-tert-Butyl Phenylsulfinimidoyl Chloride

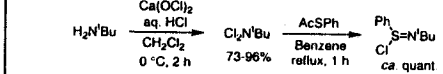
Swern Oxidation



The Present Oxidation

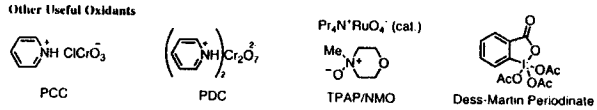


■ Preparation of *N-tert*-Butyl Phenylsulfinimidoyl Chloride

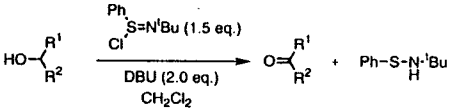


Ref.) L. N. Markovskii et al. *J. Org. Chem. USSR.* **9**, 1435 (1973)

Other Useful Oxidants



Oxidation of Various Alcohols by Using N-tert-Butyl Phenylsulfinimidoyl Chloride

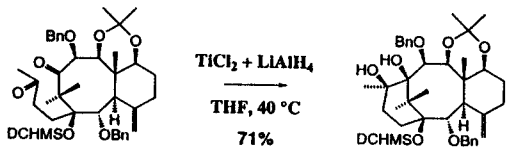


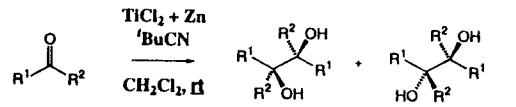
Entry	Alcohol	Conditions	Yield (%)
1		-78 °C, 30 min	98
2		0 °C, 30 min	94
3		rt, 30 min	98
4		0 °C, 1 h	92
5		-78 °C, 30 min	93
6		-78 °C, 30 min	99

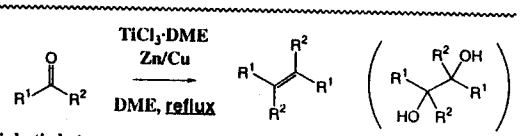
Entry	Alcohol	Conditions	Yield (%)
7		-78 °C, 30 min	94
8		rt, 30 min	91
9		rt, 30 min	quant.
10		rt, 30 min	98
11		-78 °C, 30 min	92

T. Mukaiyama, J. Matsuo, and M. Yanagisawa, *Chem. Lett.* **2000**, 1072

Pinacol Coupling Reaction Using Low-valent Titanium Reagent Generated from $TiCl_2$

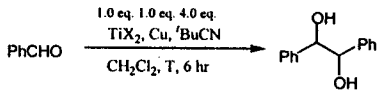






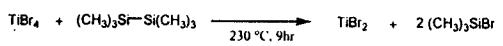
J. E. McMurry *et al.*, *J. Am. Chem. Soc.*, **96**, 4708 (1974).

Pinacol Coupling Using Titanium(II) Compounds and Copper

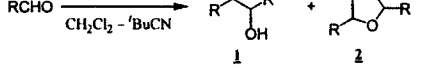


Entry	TiX_2	T / °C	Yield /%	*dl / meso*
1	$TiCl_2$	rt	79	71 / 29
2	$TiCl_2$	-23	32	90 / 10
3	$TiBr_2$	rt	90	80 / 20
4	$TiBr_2$	-23	95	96 / 4
5	$TiBr_2$	-40	80	97 / 3

Preparation of Titanium(II) Bromide



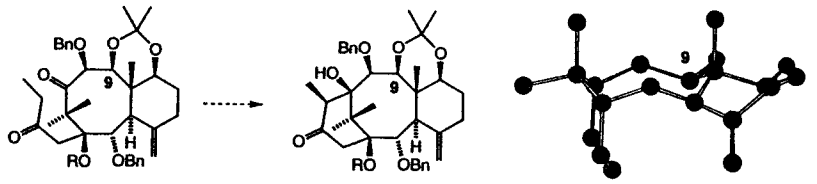
Pinacol Reaction Using Titanium(II) Bromide and Copper



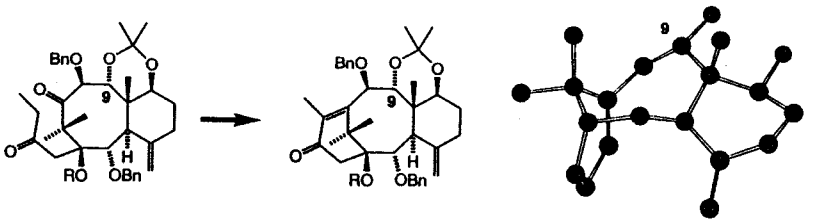
1 2

Entry	Aldehyde	Conditions [a]	Yield / %	
			1 {*dl / meso*} [b]	2
1	PhCHO	A	95 [96/4]	trace
2	*p*-Cl-PhCHO	A	97 [99/1]	0
3	*p*-MeO-PhCHO	A	74 [94/6]	13
4	Ph–CHO	A	80 [91/9]	12
5	Ph–CHO	B	82 [80/20]	7
6	–CHO	B	70 [74/26]	17
7	–CHO	B	75 [75/25]	trace
8	–CHO	B	70 [95/5]	23

a) Condition A: Ti / Cu / CHO = 1/1/1, -23 °C, 6 h; B: Ti / Cu / CHO = 1.3/1.3/1, 0 °C, 18 h. b)Ratios determined by ^{1}H-NMR analysis of crude reaction mixture.



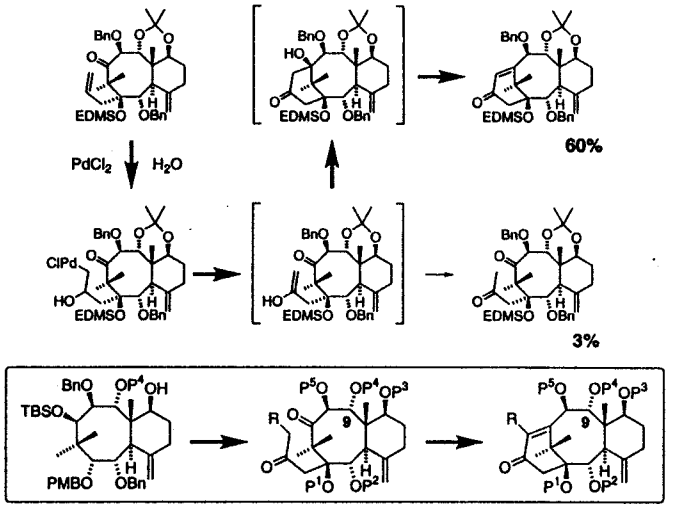
Chair-Chair



stable structure

Chair-Boat

(1999)



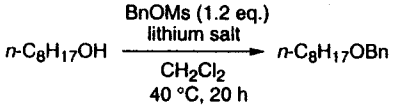
60%

3%

Aldol Product

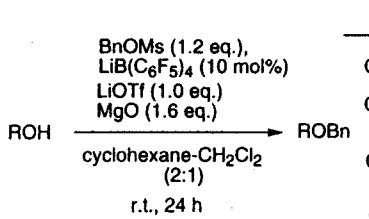
(1999)

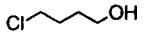
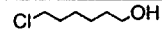
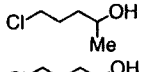
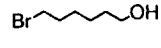
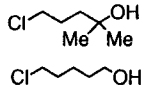
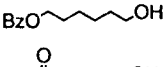
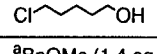
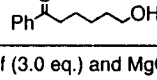
Benzylation reactions of alcohols with benzyl mesylate by using lithium salts and MgO



$LiB(C_6F_5)_4$ /mol%	MgO /eq.	LiOTf /eq.	Yield /%
10	—	—	31
10	1.6	—	54
10	1.6	1.0	79 (91[a])

[a]cyclohexane-CH_2Cl_2 (2:1), r.t., 24 h

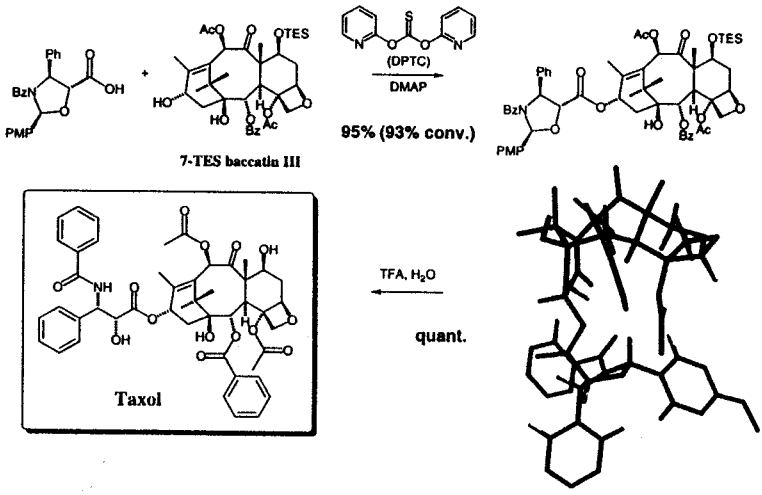


Alcohols	Yield/%	Alcohols	Yield/%
	96		quant.
	86		quant.
	71		97[a]
	90		72[a, b]

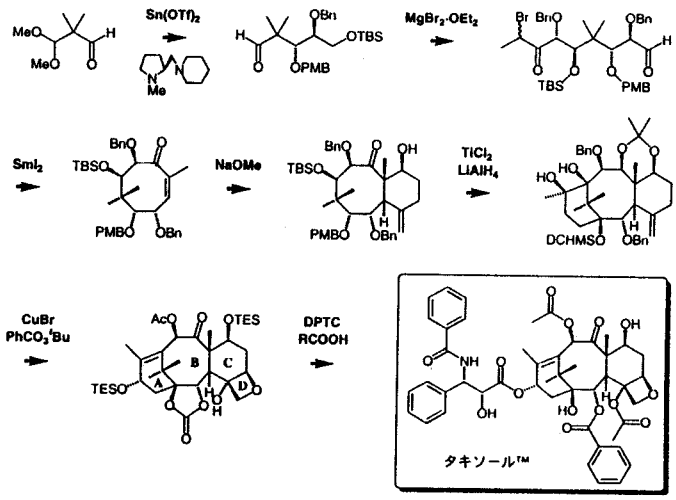
[a]BnOMs (1.4 eq.), LiOTf (3.0 eq.) and MgO (2.0 eq.) was used. [b]The reaction time was 48 h.

Completion of the Total Synthesis of Taxol

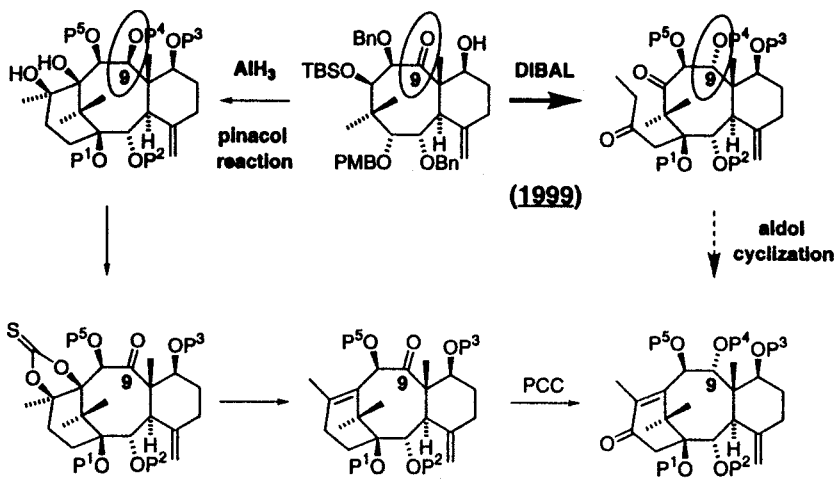
※ target-oriented *new* reaction chemistry



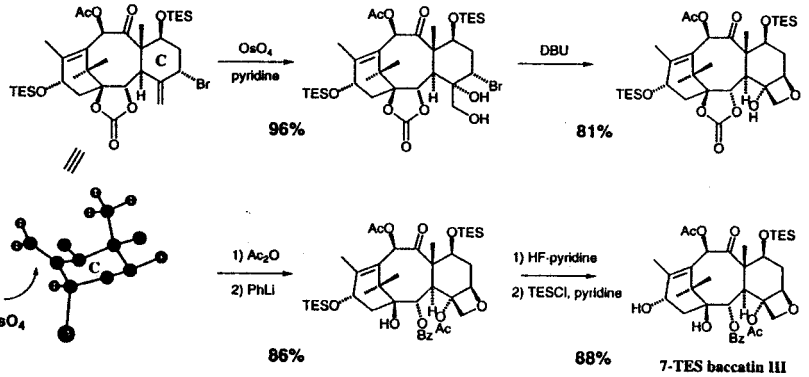
Asymmetric Total Synthesis of Antitumor Agent Taxol (1992-1997)



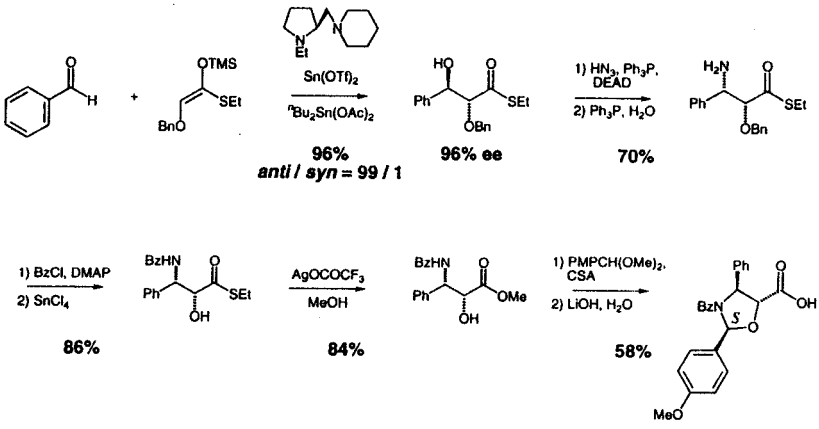
Synthesis of 9-Epitaxoids by A ring Formation



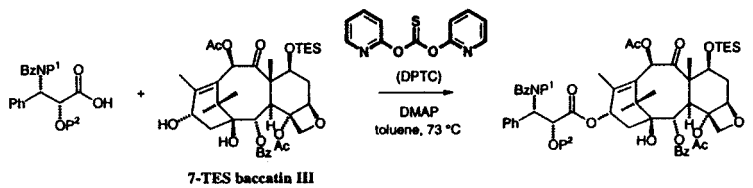
Synthesis of ABCD Ring System (Route II-d)

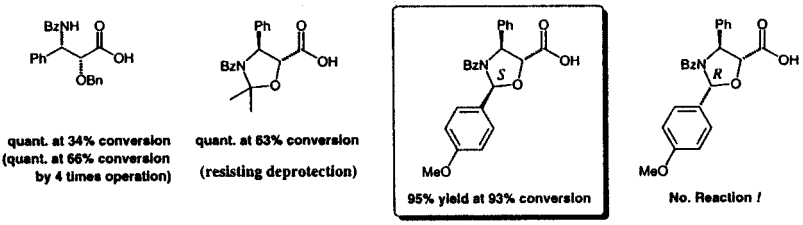


Enantioselective Synthesis of Side Chain of Taxol

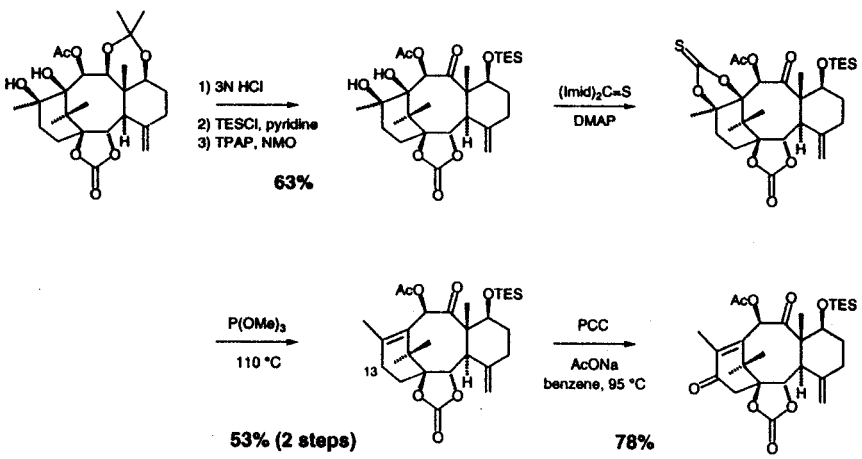


Dehydration Condensation between Side Chains and 7-TES Baccatin III

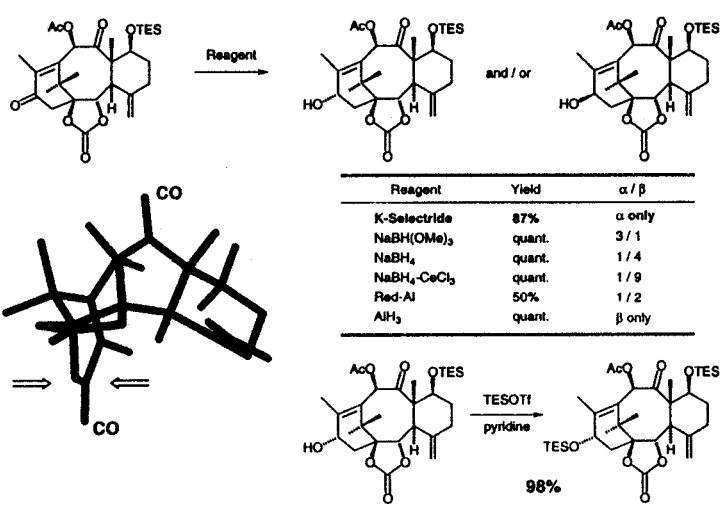




Synthesis of ABC Ring System (Route II-d)

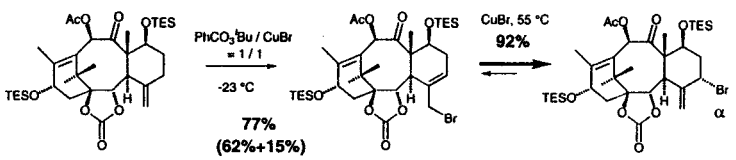


Synthesis of ABC Ring System (Route II-d)

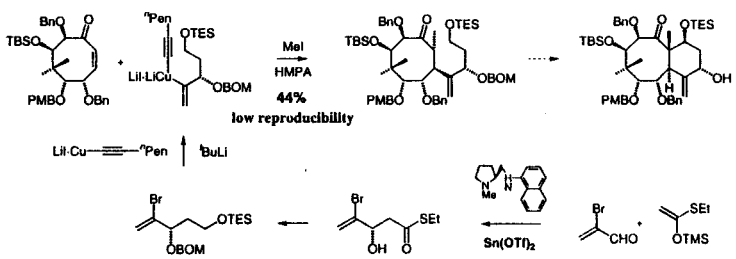


Reagent	Yield	α / β
K-Selectride	87%	α only
$NaBH(OMe)_3$	quant.	3 / 1
$NaBH_4$	quant.	1 / 4
$NaBH_4$-$CeCl_3$	quant.	1 / 9
Red-Al	50%	1 / 2
AlH_3	quant.	β only

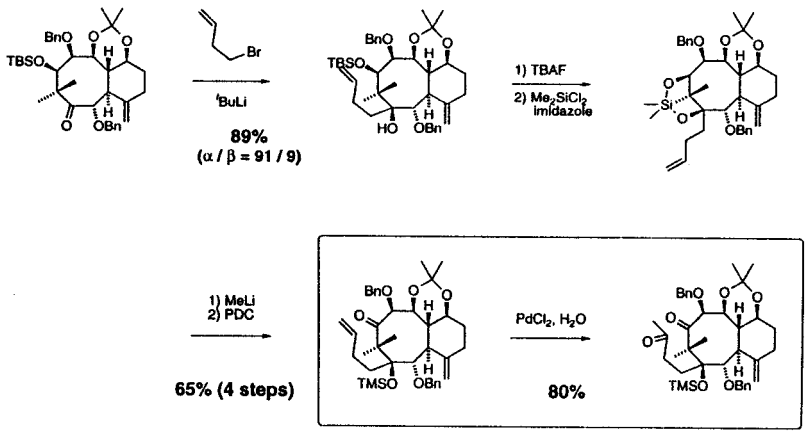
Synthesis of ABCD Ring System (Route II-d)



Chem. Lett., **1996**, 223.

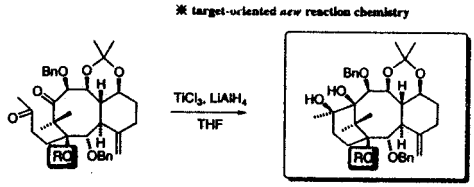


Synthesis of ABC Ring System (Route II-d) (H)

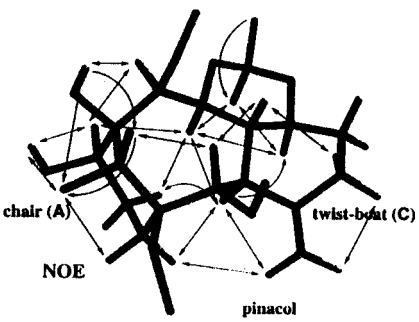


Synthesis of ABC Ring System (Route II-d) (H)

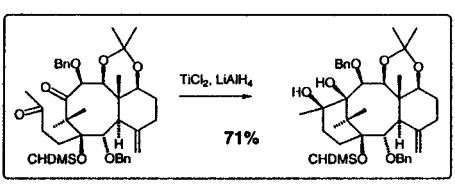
※ target-oriented *new* reaction chemistry

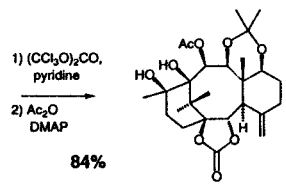


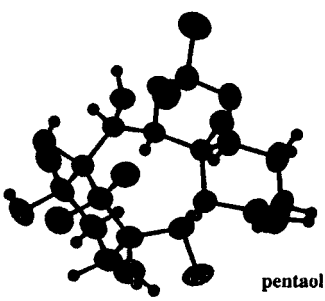
Entry	OR	Yield / %
1	$-O-SiMe_3$	5
2	$-O-Si-$ 	40
3	$-O-Si-$ 	64
4	$-O-Si-$ 	73



Synthesis of ABC Ring System (Route II-d) (Me)



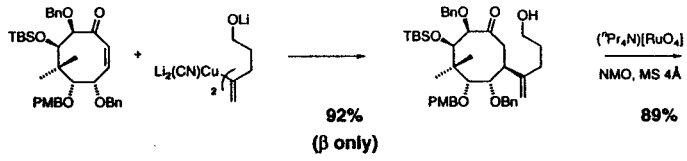


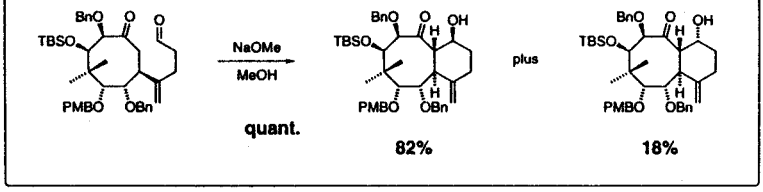


pentaol

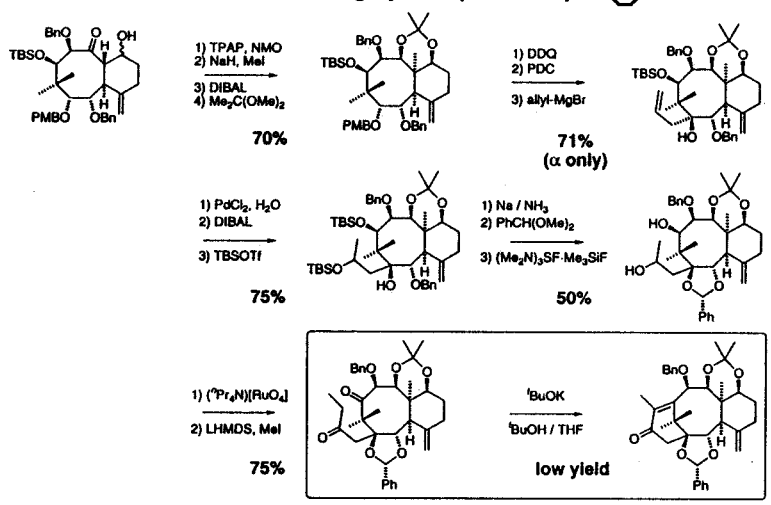
X-ray Analysis

Synthesis of BC Ring System (Route II-b)



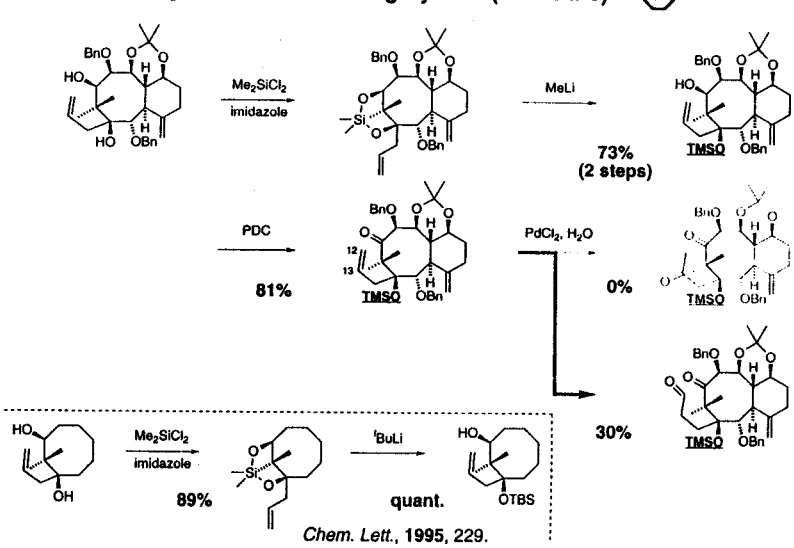


Synthesis of ABC Ring System (Route II-b)



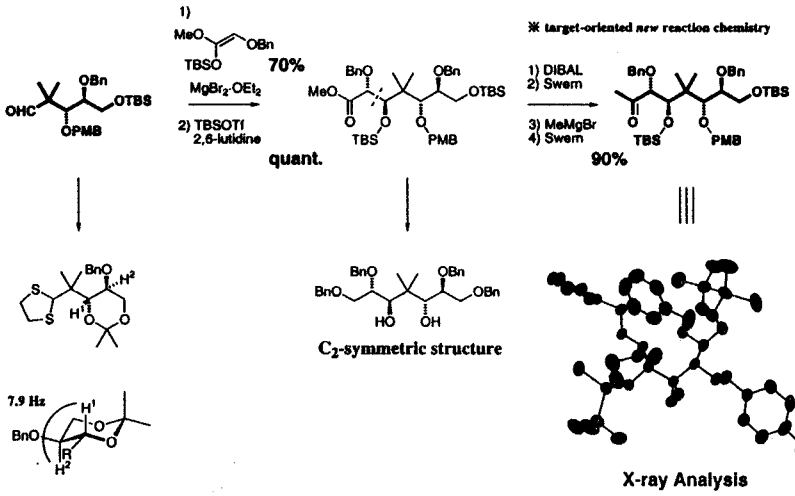
(1996, April)

Synthesis of ABC Ring System (Route II-c)

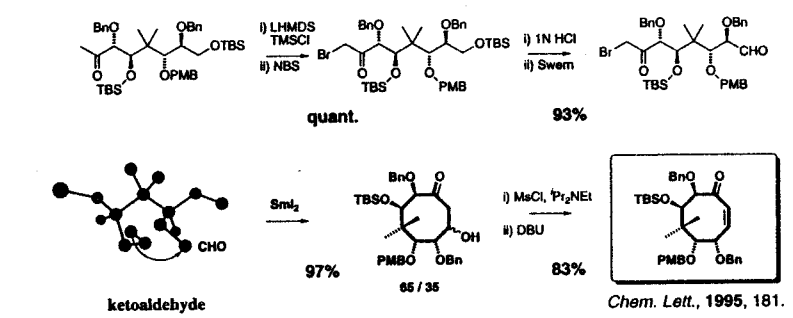


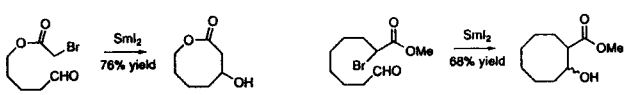
Chem. Lett., 1995, 229.

Synthesis of the Optically Active Polyoxy Unit



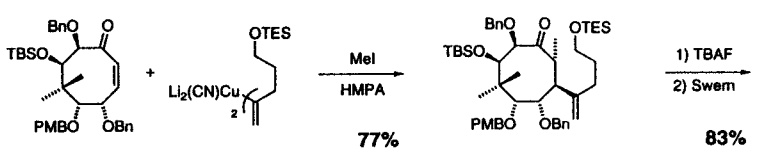
Synthesis of the 8-Membered Ring Compound Using SmI_2

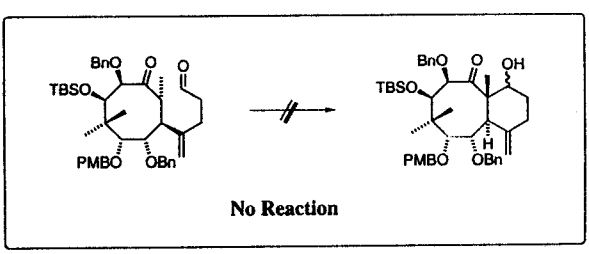




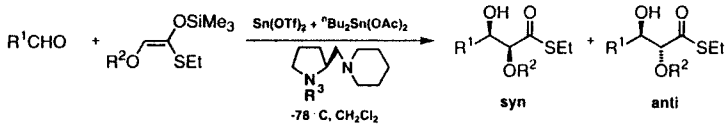
J. Inanaga and M. Yamaguchi, *Tetrahedron Lett.*, **27**, 3889 (1986)
J. Inanaga and M. Yamaguchi, *Tetrahedron Lett.*, **32**, 6371 (1991)

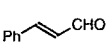
Synthesis of BC Ring System (Route II-a) (H)





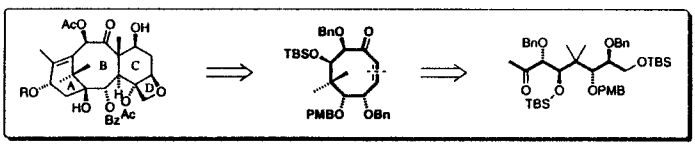
Synthesis of Optically Active 1,2-Diol Units



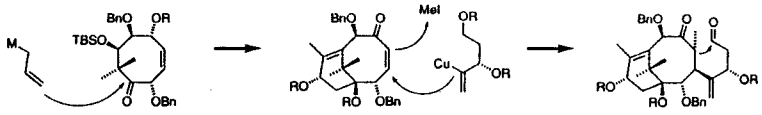
Entry	R^1CHO	R^2O	R^3	Yield / %	syn : anti	ee / % (config)
1	PhCHO	BnO	Et	83	1 : 99	96 (anti)
2		$^tBuMe_2SiO$	^nPr	79	85 : 15	92 (syn)
3		BnO	Et	83	2 : 98	96 (anti)
4		$^tBuMe_2SiO$	^nPr	76	94 : 6	93 (syn)
5	EtCHO	BnO	Et	72	2 : 98	97 (anti)
6		$^tBuMe_2SiO$	^nPr	46	92 : 8	82 (syn)
7		BnO	Et	85	2 : 98	97 (anti)
8		$^tBuMe_2SiO$	^nPr	75	97 : 3	94 (syn)
9		BnO	Et	88	2 : 98	98 (anti)
10		$^tBuMe_2SiO$	^nPr	76	90 : 10	92 (syn)

(1990-1992)

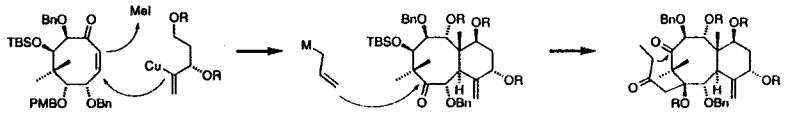
Retrosynthesis of Taxol



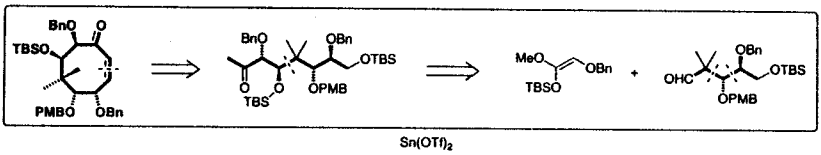
B to AB to ABC Ring Route (Route I)

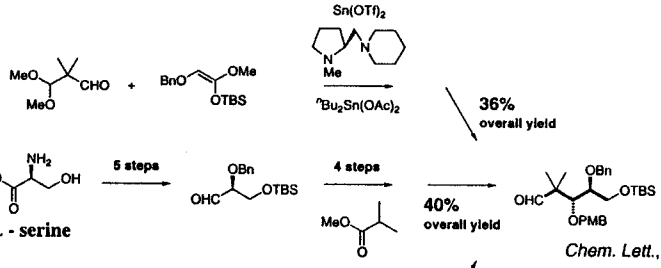


B to BC to ABC Ring Route (Route II)

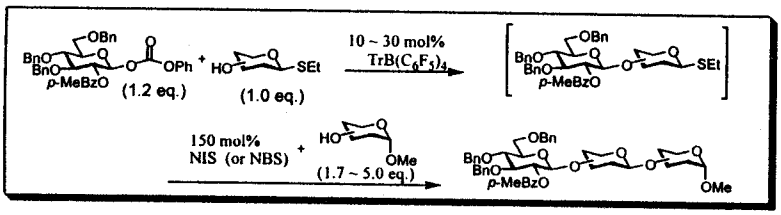


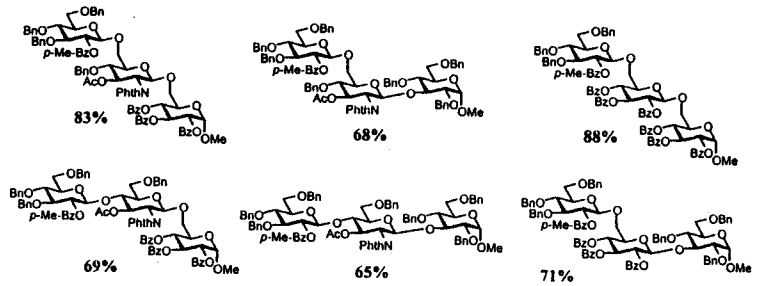
Retrosynthesis of Optically Active 8-Membered Ring Compound



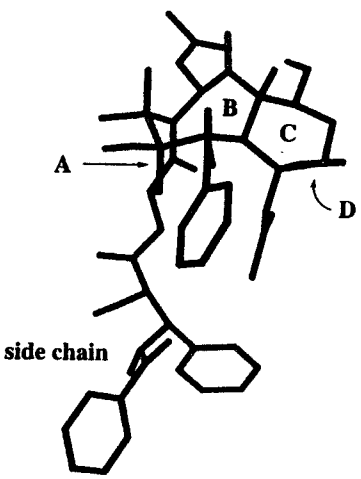


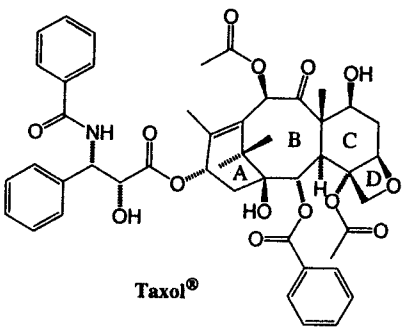
One-Pot Synthesis of Trisaccharides





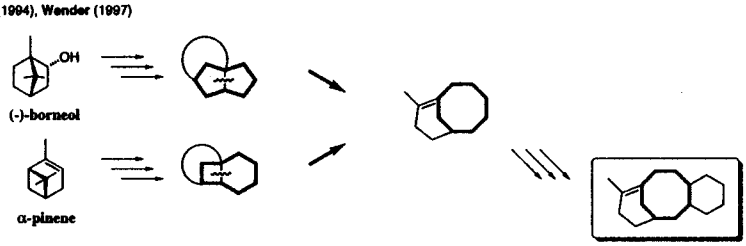
Asymmetric Total Synthesis of Antitumor Agent Taxol (1992-1997)



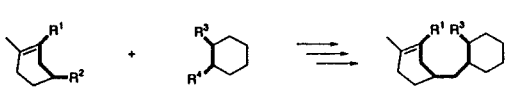


(isolated in 1971)

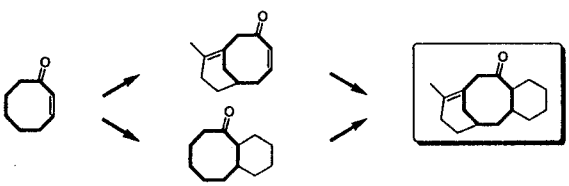
Holton (1994), Wender (1997)



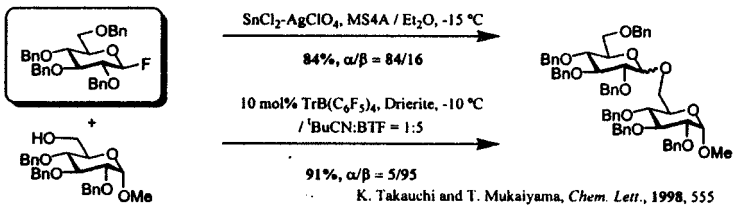
Nicolaou (1994), Danishefsky (1995), Kuwajima (1998)



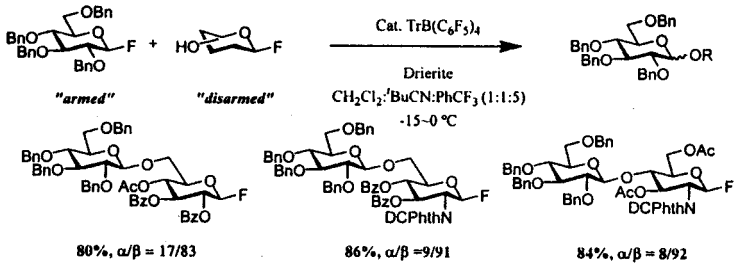
Mukaiyama (1997)



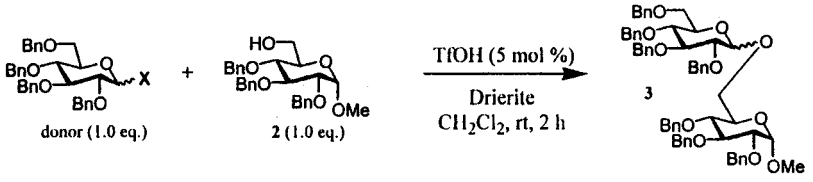
$TrB(C_6F_5)_4$ catalyzed glycosylation with glycosyl fluoride



K. Takauchi and T. Mukaiyama, *Chem. Lett.*, **1998**, 555



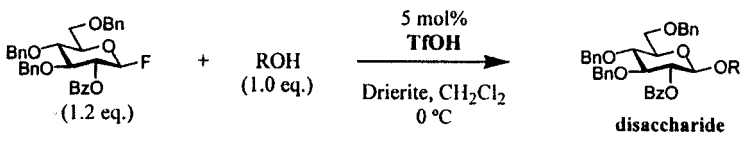
TfOH catalyzed glycosylation using various glycosyl donors.

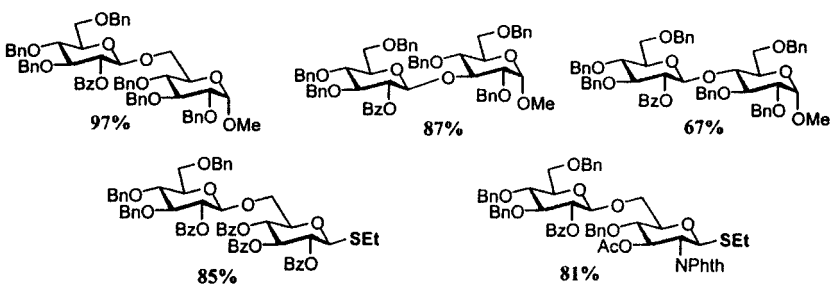


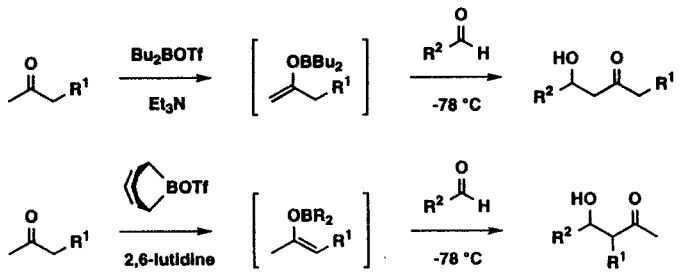
Entry	X	Yield /%	α/β[a]	Entry	X	Yield /%	α/β[a]
1	Br (α)	9	45/55	5	OH (mix)	51	73/27
2	Cl (α)	6	52/48	6	OAc (α)	75	68/32
3	**F (α)**	**87**	66/34	7	OCOOPh (β)	61	72/28
4	**F (β)**	**83**	67/33	8	**SEt (β)**	**0**	—

[a]Ratios were determined by HPLC analysis.

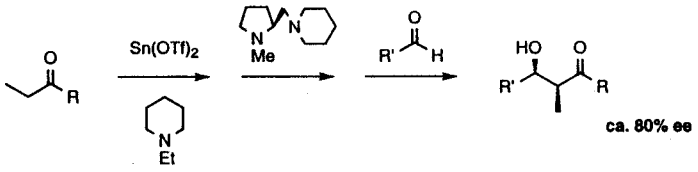
TfOH catalyzed β-selective glycosylation with various glycosyl acceptors



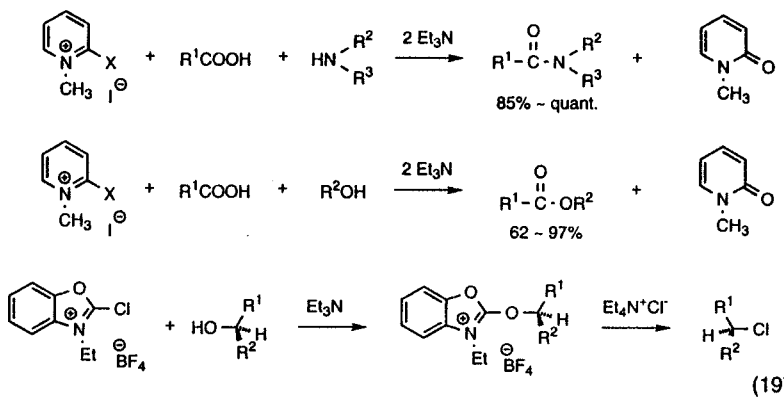




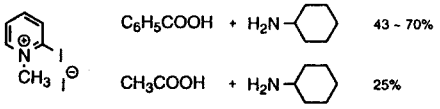
(1976)



(1982)

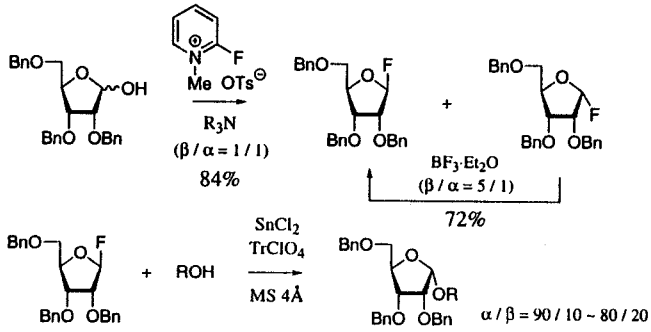


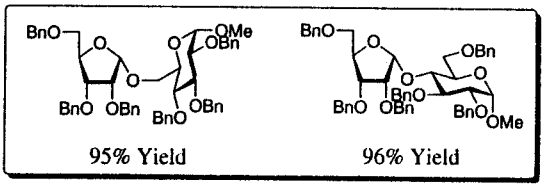
(1975)



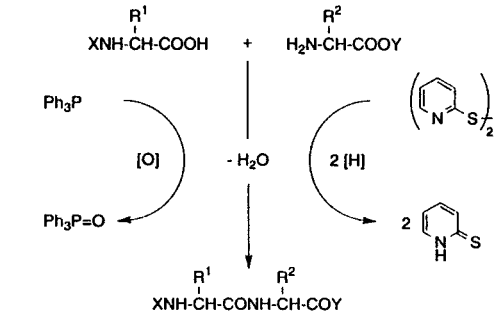
J. K. Sutherland and D. A. Widdowson, *J. Chem. Soc.*, **1964**, 4650.

1-Fluorosugar from 1-Hydroxysugar

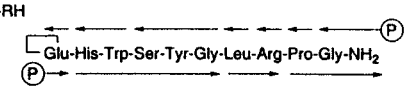




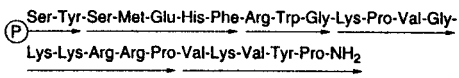
(1983)



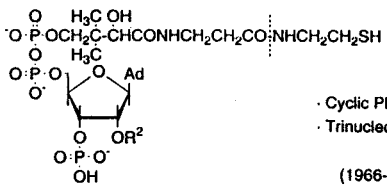
· LH-RH



· ACTH (1-24)

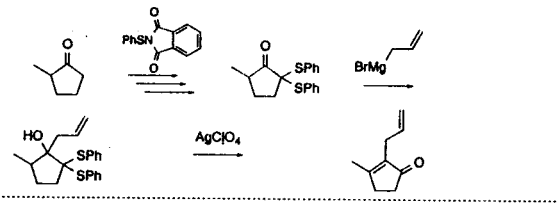


· Coenzyme A



· Cyclic Phosphate
· Trinucleotide

(1966-1973)

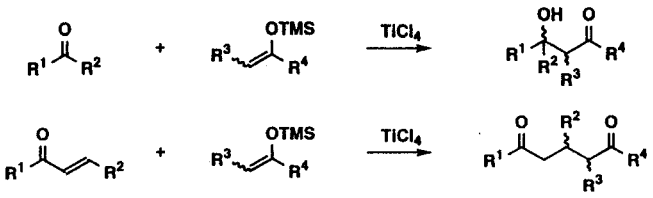


MX_n : $SnCl_4$, $AlCl_3$, $ZnCl_2$, $TiCl_4$, $SbCl_5$, $FeCl_3$, etc.

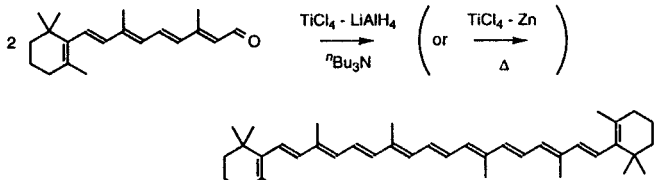
(1972)

$TiCl_4$ ⟶ Functional Groups Interconversion

Low-valent Titanium Species ⟶ Pinacol Coupling



(1974)



β-Carotene 90%

(1976)

Research on fundamental subject

New and unique seeds will come out by exploring the unknown, that is, the **unexpected** phenomena disclose the unnoticed interesting topics.

0 → 1 ***new* reaction chemistry**

Research on targeted subject

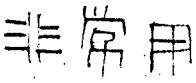
By setting a right strategy, it will be completed *via* feedback between repeated experiments and discussions even though the **unpredictable** phenomena are quite often observed during the course.

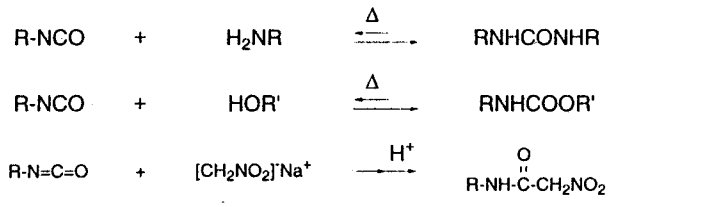
1 → 1 0 **i) targeted reaction chemistry;** ***e.g. asymmetric synthesis*** **ii) total synthesis of complex molecule**

Research on target-oriented *new* reaction chemistry

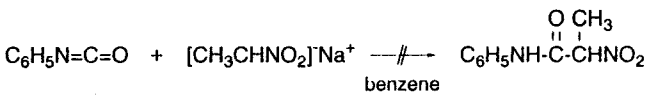
Accumulated knowledge and susceptibility **Associated with** targeted subject

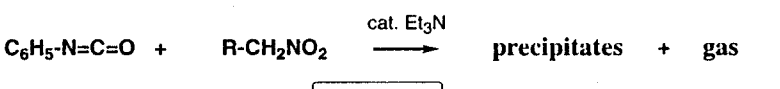
n → 8 **target-oriented *new* reaction chemistry**

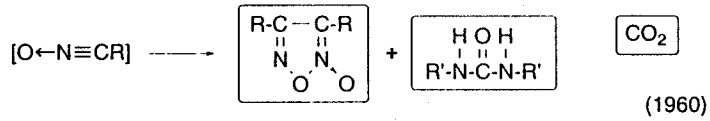




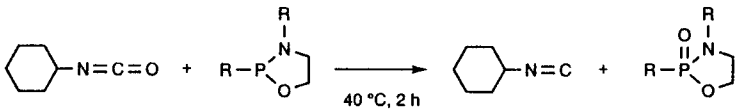
A. Michael, *Ber*, **38**, 22, 39, 46 (1905)
W. Steinkopt and H. M. Daege, *ibid.*, **44**, 497 (1911)



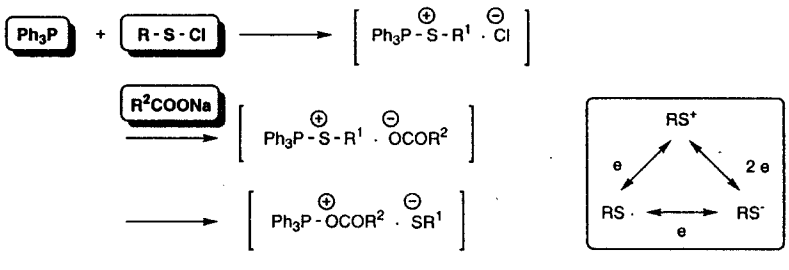




(1960)



(1965)



(1967)