

# Year in Review:

## Journal of the American Chemical Society 1988

**Number of papers:** 1957

**Most Prolific Authors:**

Paquette, L. A. (18)	Bordwell, FG (7)
Trost, B.M (12)	Bruice, T.C (7)
Whitesides, G.M. (12)	Cotton, F.A. (7)
Kobayashi (10)	Grubbs (7)
Bergman, (9)	Holmes, RR (7)
Huffman, J.C. (9)	Houk, KN (7)
Harris, TM (8)	Luszytk, J (7)
Ingold (8)	Olah, GA (7)
Meotner (8)	Rebek, J (7)
Nicolaou (8)	Rheingold, AL (7)
	Schleyer, PV (7)

**Most Cited Paper:** **1471 citations – Cramer (p 5959) – Comparative molecular field analysis (CoMFA). 1. Effect of shape on binding of steroids to carrier proteins**

**Most Cited Synthetic Organic Paper** **588 Citations – Evans – (p 3560) Directed Reduction of  $\beta$ -Hydroxy Ketones Employing Tetramethylammonium Triacetoxyborohydride**

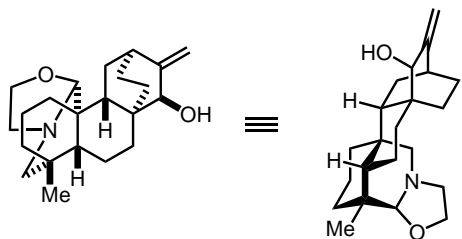
Kristy Tran  
CU Synthesis Literacy Group  
August 25, 2006

# Year in Review:

## Journal of the American Chemical Society 1988

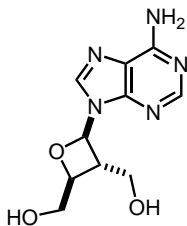
- Natural Products:** (-)-Laurenyne – 2248  
Taxol - 5917  
Zygosporin E – 4822  
(±)-Pleurotin, (±)-Dihydropleurotin – 1634  
Espramicin Series – 631, 6921, 6890  
Antibiotic X-206 – 2506  
(+)-18-Deoxynargenicin A1 – 4041  
(-)-Oxetanocin – 7217  
Tetrahydroalsoline, Cathenamine,  
Gessoschizine – 5925  
(+)-CC-1605 – 1321  
(+)-Compactin, (+)-Mevinolin – 6914  
Mesembrine – 4831  
Glycinoeclepin A – 1985  
(±)-Atisine – 6516
- Methodology:** **Me<sub>4</sub>NHB(OAc)<sub>3</sub> - Directed Reductions of b-hydroxy ketones – 588**  
**Asymmetric Diels Alder – 1238**  
**Vicinal Diol Cyclic Sulfates - 7538**  
**Asymmetric Dihydroxylation – 1968**  
**Asymmetric Hydrogenation - 629**  
Lipase catalyzed irreversible trans esterifications - 7200  
Enzymatic Baeyer-Villiger – 6892  
Arene C-H Activation/N-H Activation - 8729  
Asymmetric Hetero Diels Alder – 310  
Cyclic Conjugated Endiynes – 4866  
Diisopinocampheylchloroborane - 1539
- Physical Organic:** Transition structures of aldol reactions – 3684  
Aza Cope Rearrangements Scope and Mechanism – 4329

# Natural Product Synthesis Not Discussed



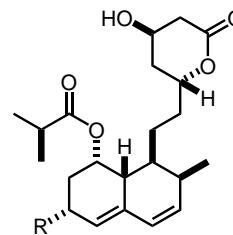
(±)-Atisine

Fukumoto - Tohoku University  
JACS 1988, 110, 1963



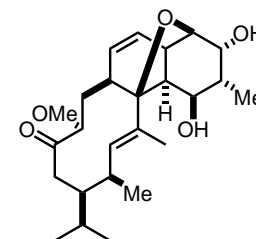
(-)-Oxetanocin

Norbeck - Abbott Labs  
JACS 1988, 110, 7217



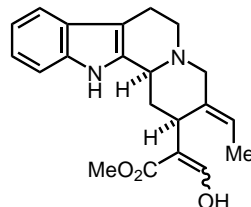
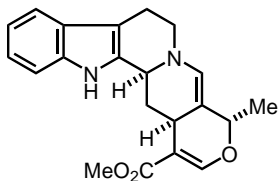
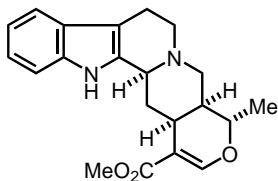
(+)-Compactin and (+)-Mevinolin

Clive - University of Alberta  
JACS 1988, 110, 6914



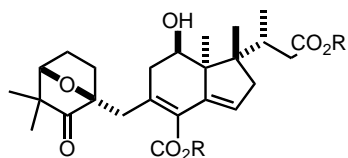
(+)-18-Deoxynargenicin A<sub>1</sub>

Kallmerten - Syracuse  
JACS 1988, 110, 7217



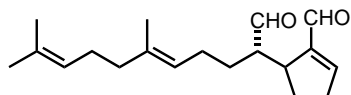
Tetrahydroalsonine, Cathenamine, and Gessoschizine

Martin - UT Austin  
JACS 1988, 110, 5925



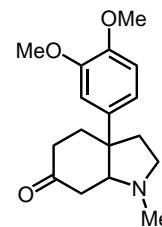
Glycinoeclepin A

Murai - Hokkaido  
JACS 1988, 110, 1985



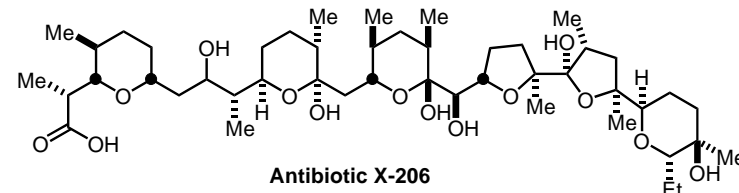
Petiodial

Trost - Stanford  
JACS, 1988, 110, 5233.



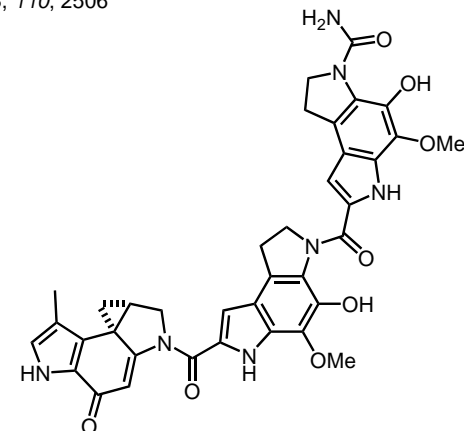
Mesembrine

Winkler - University of Chicago  
JACS 1988, 110, 4831



Antibiotic X-206

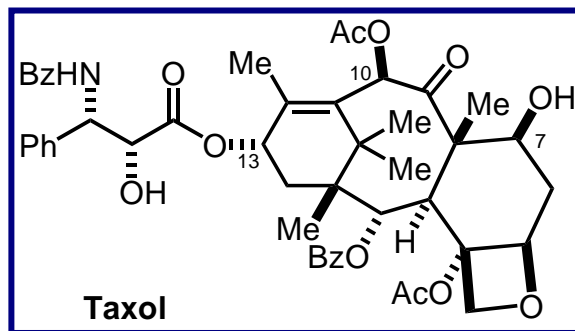
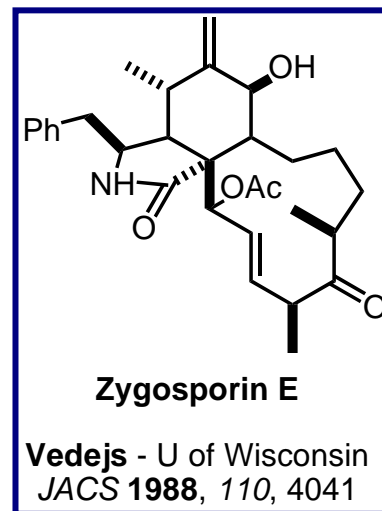
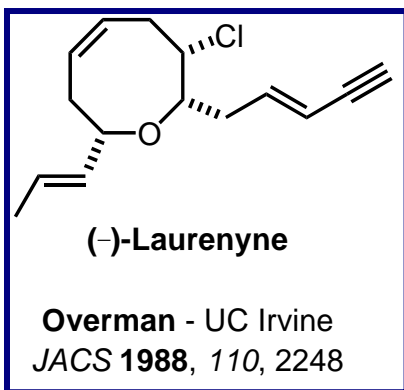
Evans - Harvard  
JACS 1988, 110, 2506



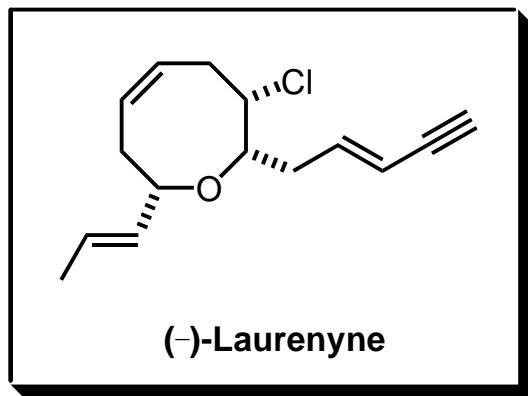
(+)-CC-1065

Boger - Purdue  
JACS 1988, 110, 1321

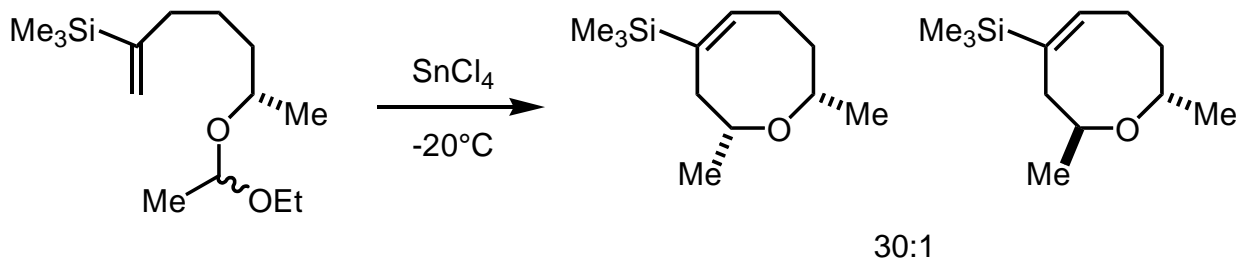
# Natural Products Discussed



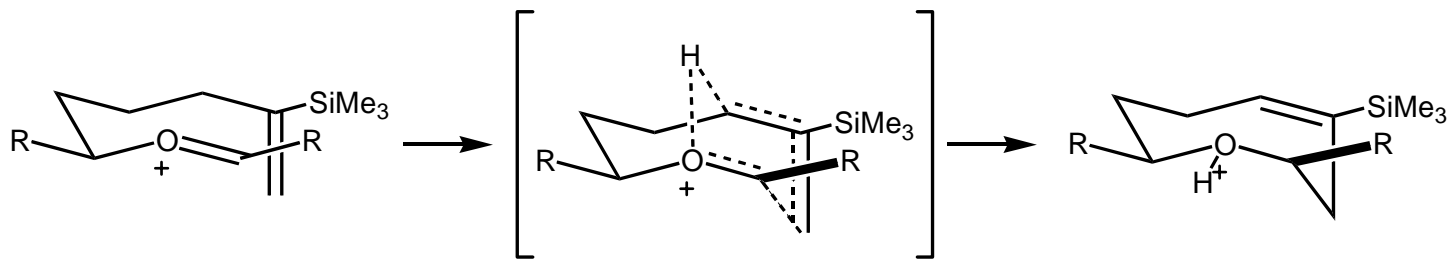
# (-)-Laurenyne



- Key step involves acetal-alkene cyclization which forms the cyclic ether D4-unsaturation and cis oriented side chains



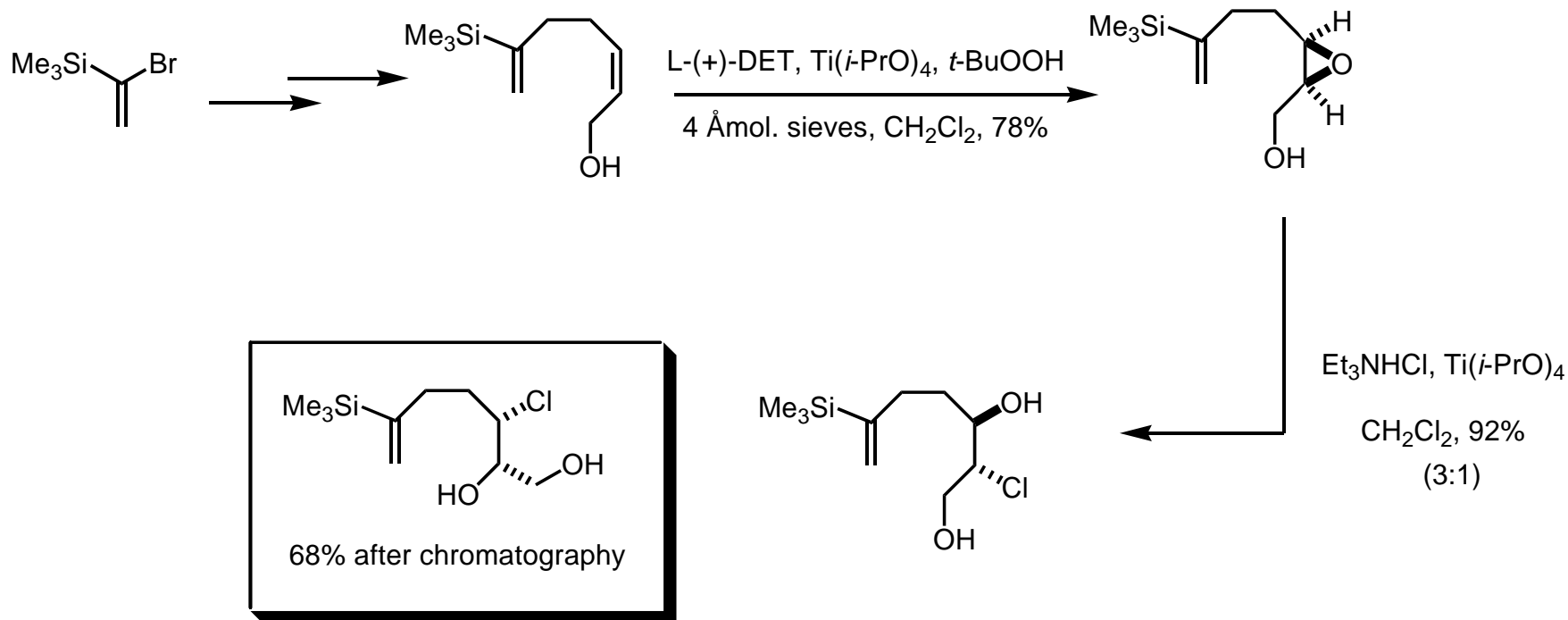
Mechanism:



Overman, L.E.; Blumenkoph, T.A.; Castaneda, A.; Thompson, A.S. *J. Am. Chem. Soc.* **1986**, *108*, 3516

Overman, L.E.; Thompson, A.S. *J. Am. Chem. Soc.* **1988**, *110*, 2248-2256

# (-)-Laurenynes

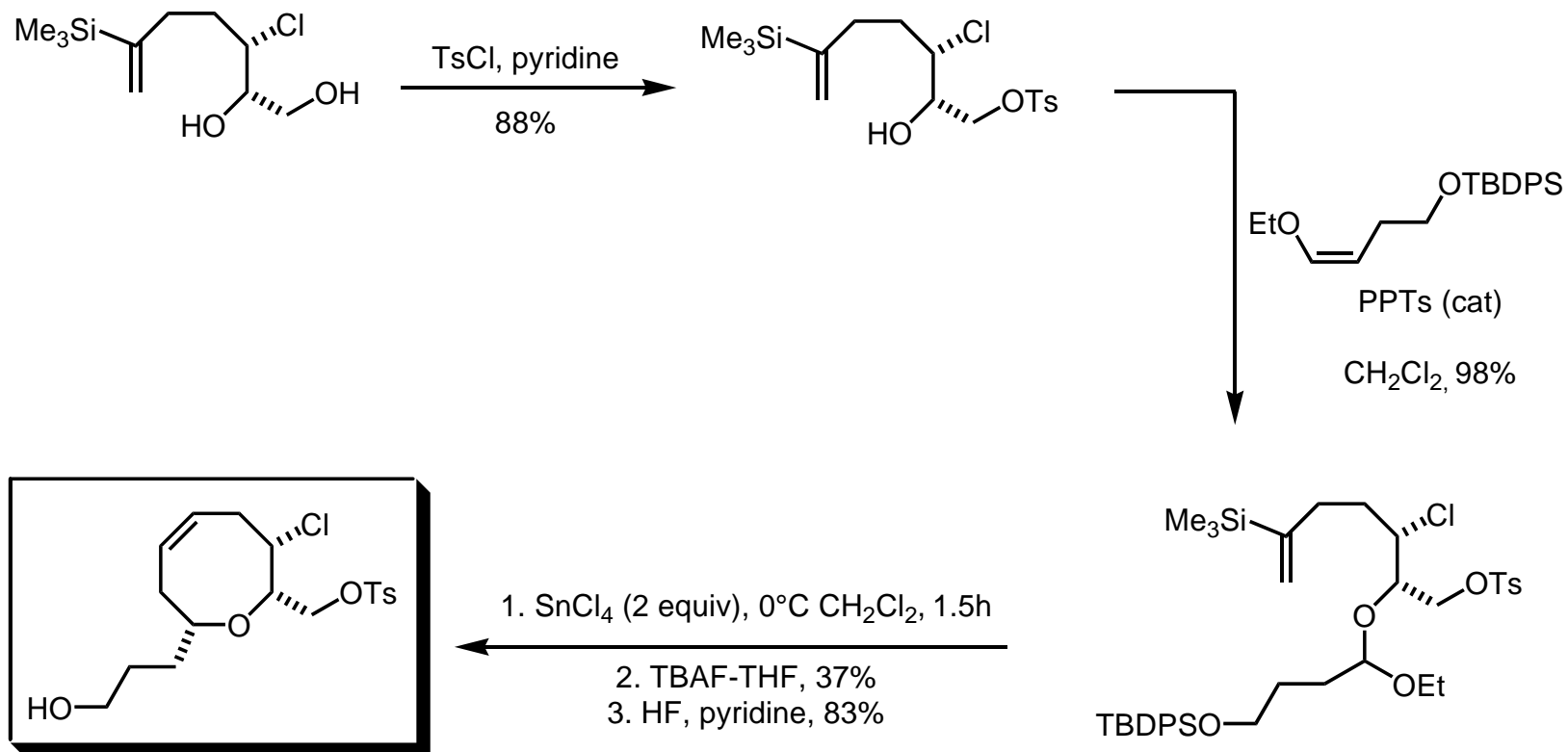


- Sharpless epoxidation unambiguously sets stereocenter.
- $\text{Et}_3\text{NHCl}$  served as a better chloride source than  $\text{NH}_4\text{Cl}$  due to better solubility in  $\text{CH}_2\text{Cl}_2$
- Diastereoselectivity typical for chloride opening of *trans* epoxides

Overman, L.E.; Thompson, A.S. *J. Am. Chem. Soc.* **1988**, *110*, 2248-2256

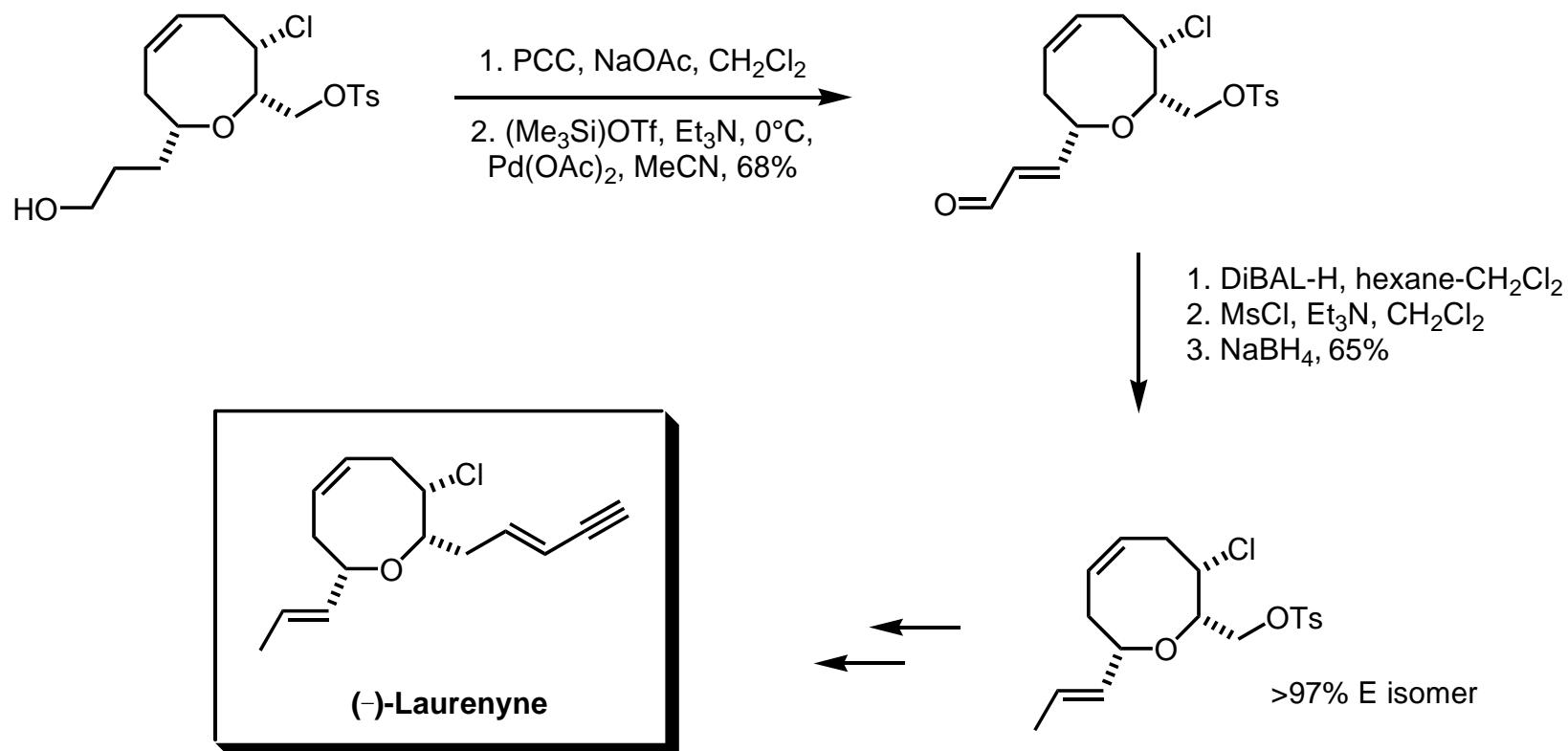
Caron, M.; Sharpless, K.B. *J. Org. Chem.* **1985**, *50*, 1557.

# (-)-Laurenyne



- **Limitations of acetal-alkene cyclization:** Side chain cannot have an unsaturation nor a  $\beta$  or  $\gamma$  heteroatom.

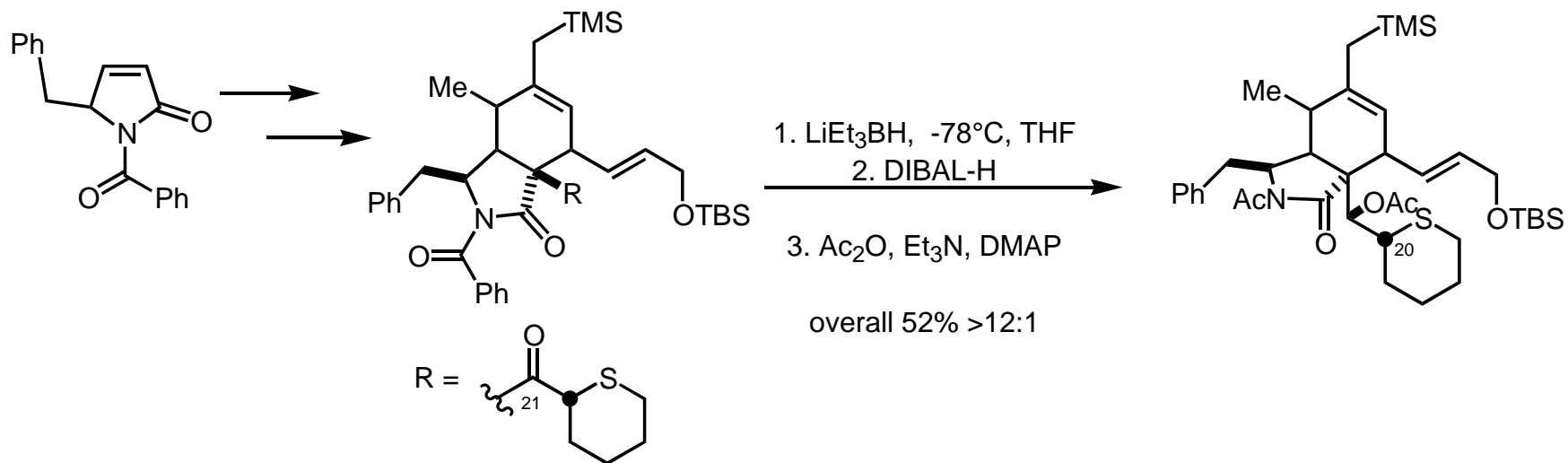
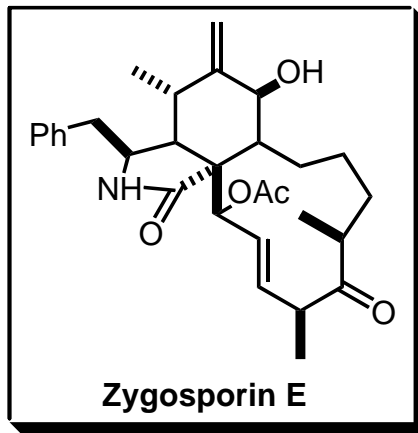
# (-)-Laurenyne



- Unambiguous synthesis of 2*S*, 7*S*, 8*S* isomer.
- Rotation was found to opposite to that of the natural product was positive. Absolute configuration of natural product, (+)-Laurenyne, needed to be revised to the 2*R*, 7*R*, 8*R* isomer

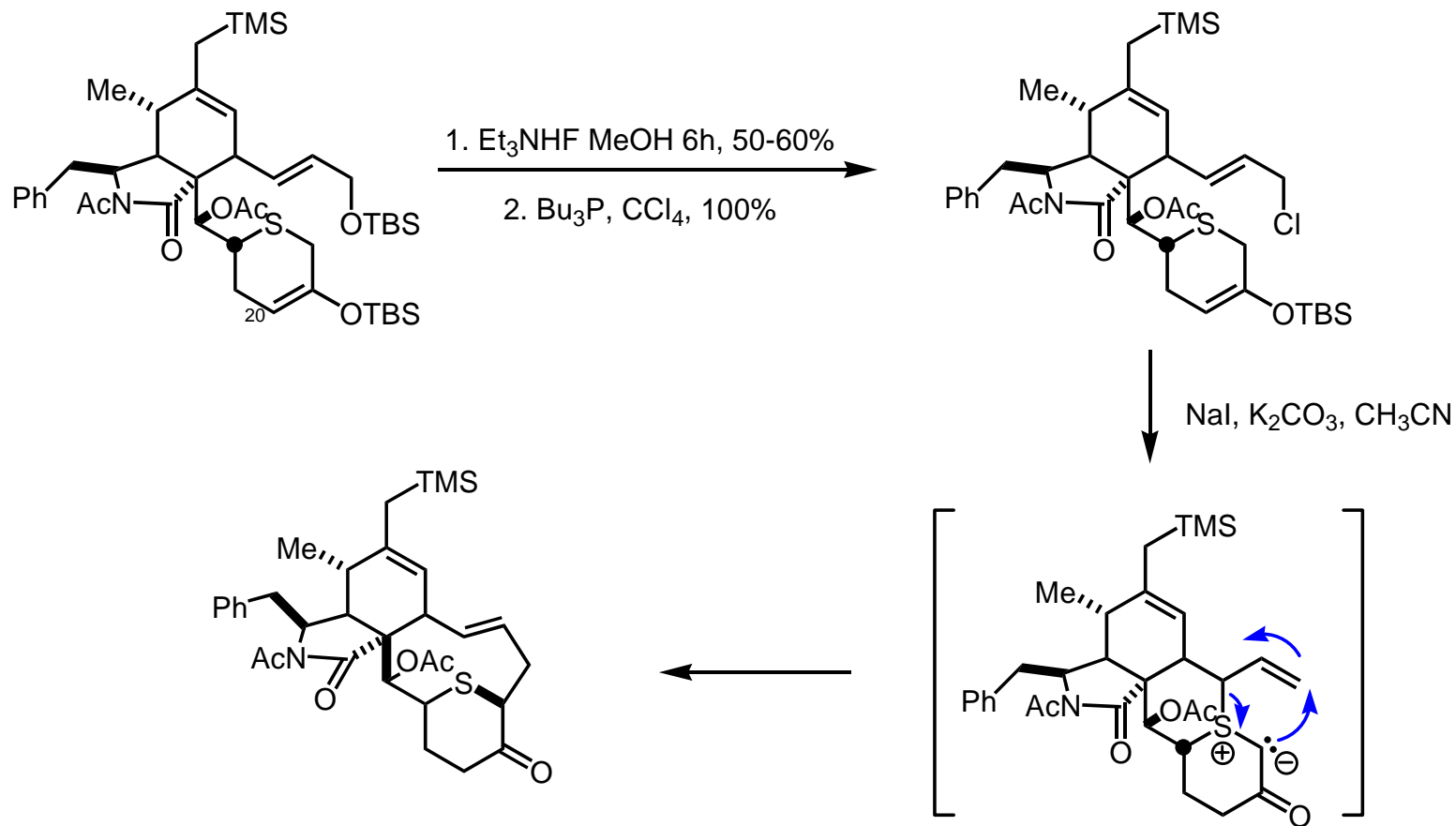
# Zygosporin E

## A Sulfur Mediated Total Synthesis of Zygosporin E – Vedejs - 4822



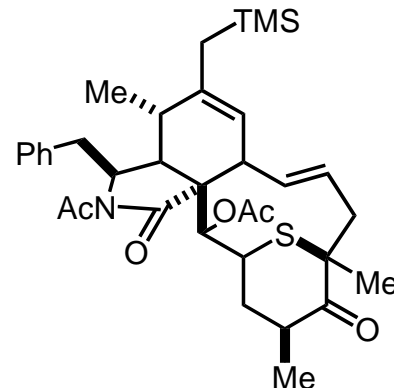
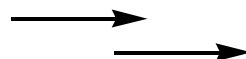
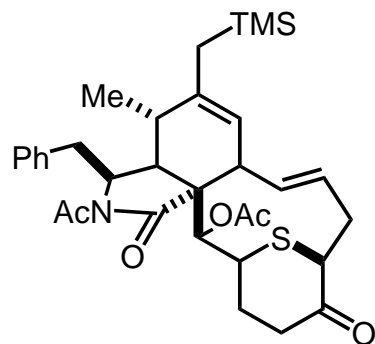
- Selective reduction at C21 required debenzoylation of amide.

# Zygosporin E: Sulfur Ylide Cyclizations



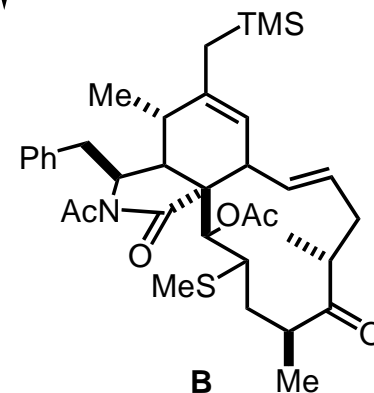
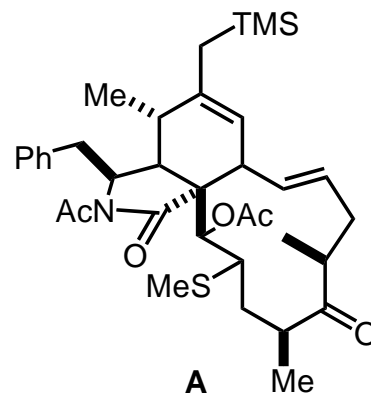
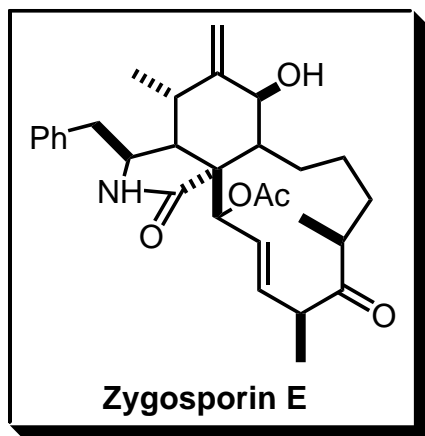
**Key Step!**

# Zygosporin E: Reductive Desulfenylation



1. MeO BF<sub>4</sub> then Rieke Zinc DME  
THF, HOAc, rt

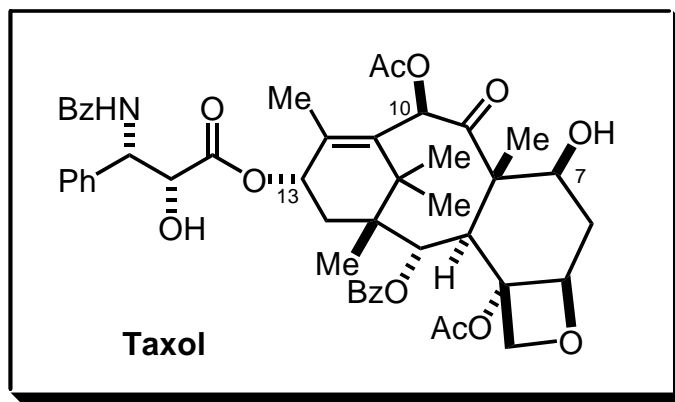
2. K<sub>2</sub>CO<sub>3</sub>, MeOH 87%  
**A: B** 1 : 2.6



**A** yields natural Zygosporin E  
**B** yields unnatural epi Zygosporin E

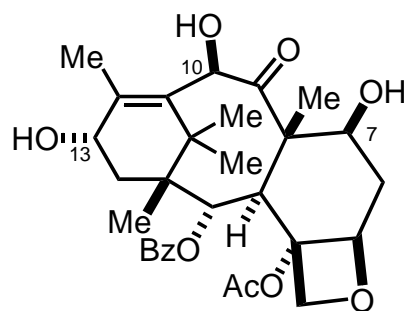
# Practical Approach to Taxol

A Highly Efficient, Practical Approach to Taxol - Greene, Guerette-Voegelein - 5917 (389 Citations)



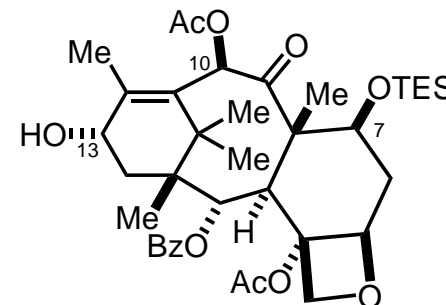
- Taxol, a potent cancer chemotherapeutic agent. Isolated from the bark of Yew, very slow growing evergreens. Isolation of Taxol for cancer treatment would be “fatal to the source”.

Readily isolable from the leaves of the Yew tree



10-Deacetyl baccatin III

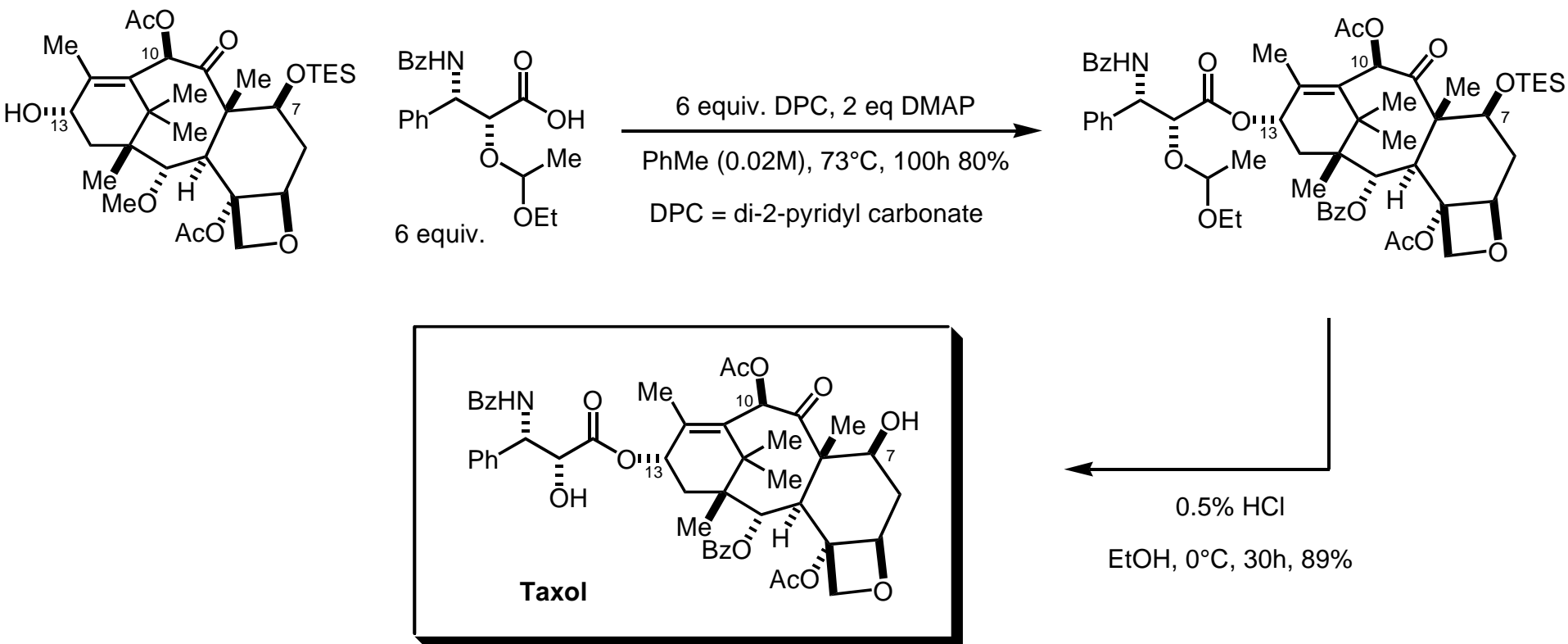
1. TES-Cl, pyridine 84-86%  
2. MeCOCl, pyridine 84%



- Drawbacks: Tetraol sensitive to acidic and basic conditions. Differentiation of hydroxyls C7 and C10. Selective esterification of C13

# Practical Approach to Taxol

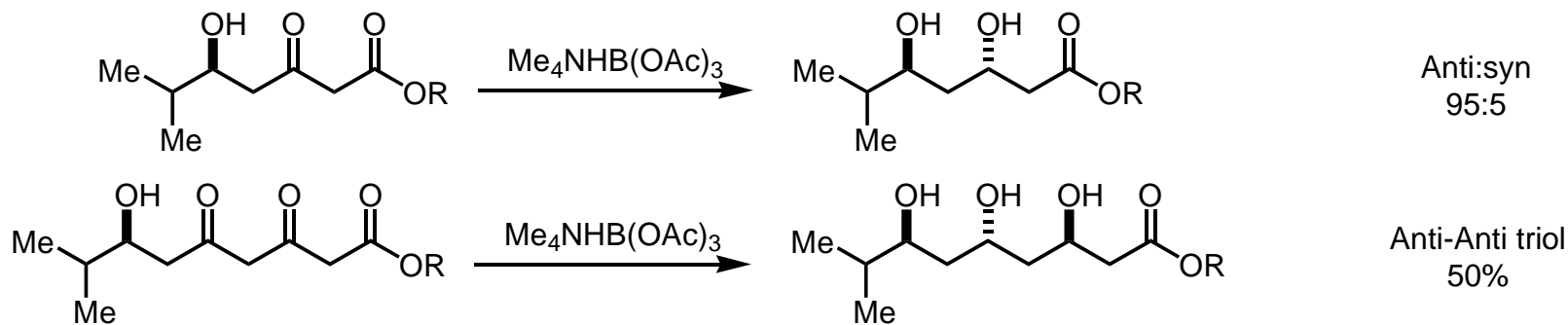
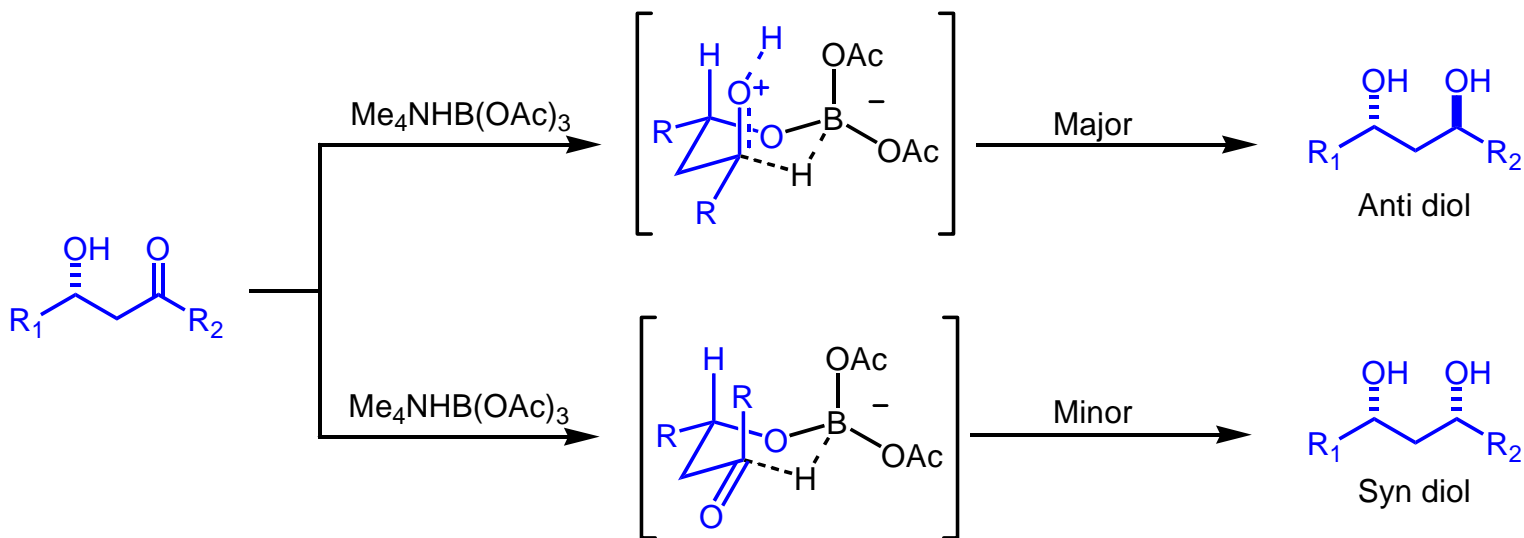
A Highly Efficient, Practical Approach to Taxol - Greene, Guerette-Voegelein - 5917 (389 Citations)



- Acylation of C13 hydroxyl was difficult.
- Very hindered since it is placed in the concave side of the molecule

# Me<sub>4</sub>NHB(OAc)<sub>3</sub> – Reductions of β-hydroxy ketones

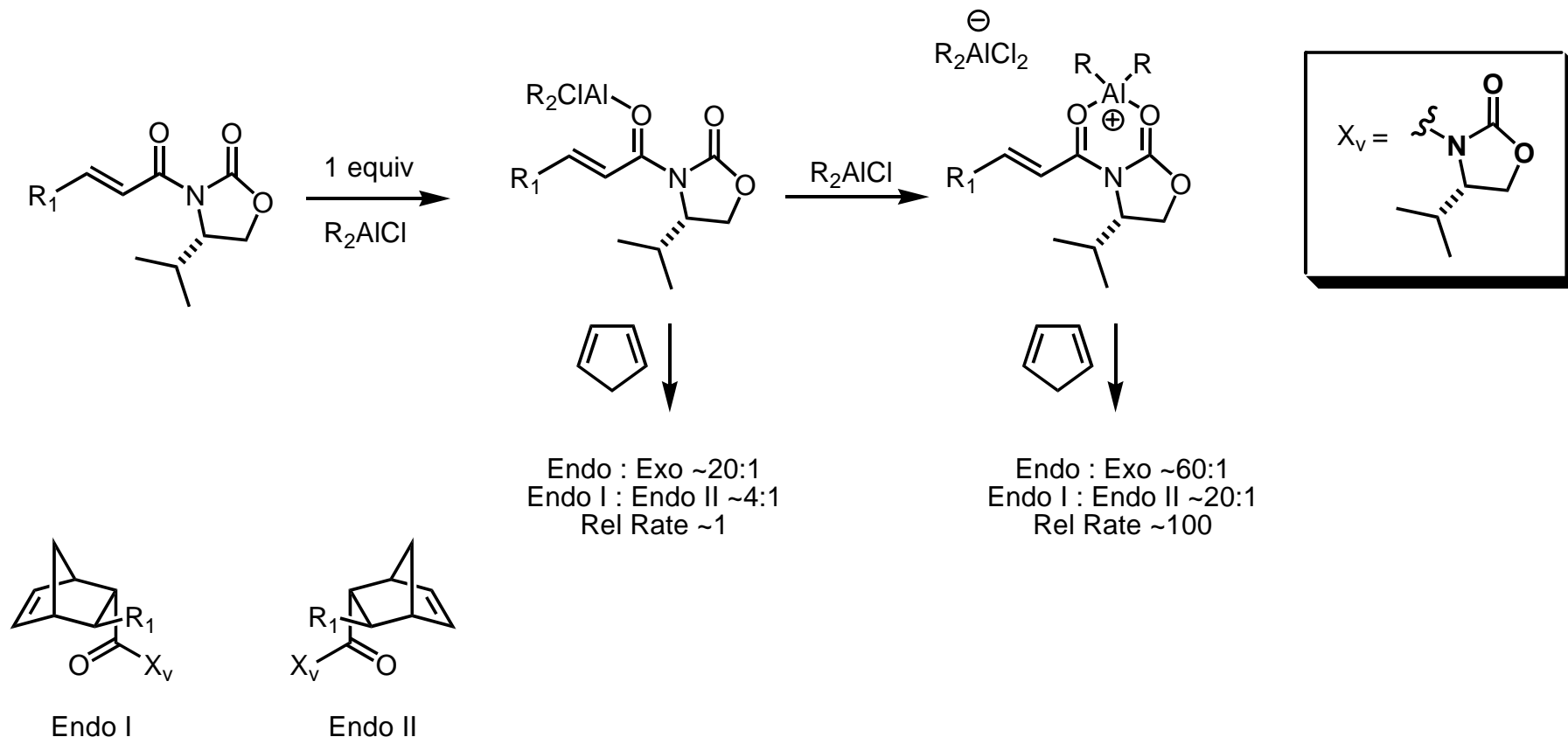
Directed Reduction of β-Hydroxy Ketones Employing Tetramethylammonium Triacetoxyborohydride - Evans - 3560 (588 Citations)



- No significant effect by α-Alkyl substitution.
- Intramolecular hydride delivery with no reduction in the absence of hydroxyl group
- Stereopropagation

# Asymmetric Diels Alder

## Asymmetric Diels Alder Cycloaddition Reactions with Chiral $\alpha,\beta$ -Unsaturated N-Acyloxazolidinones - Evans - 1238 (547 Citations)

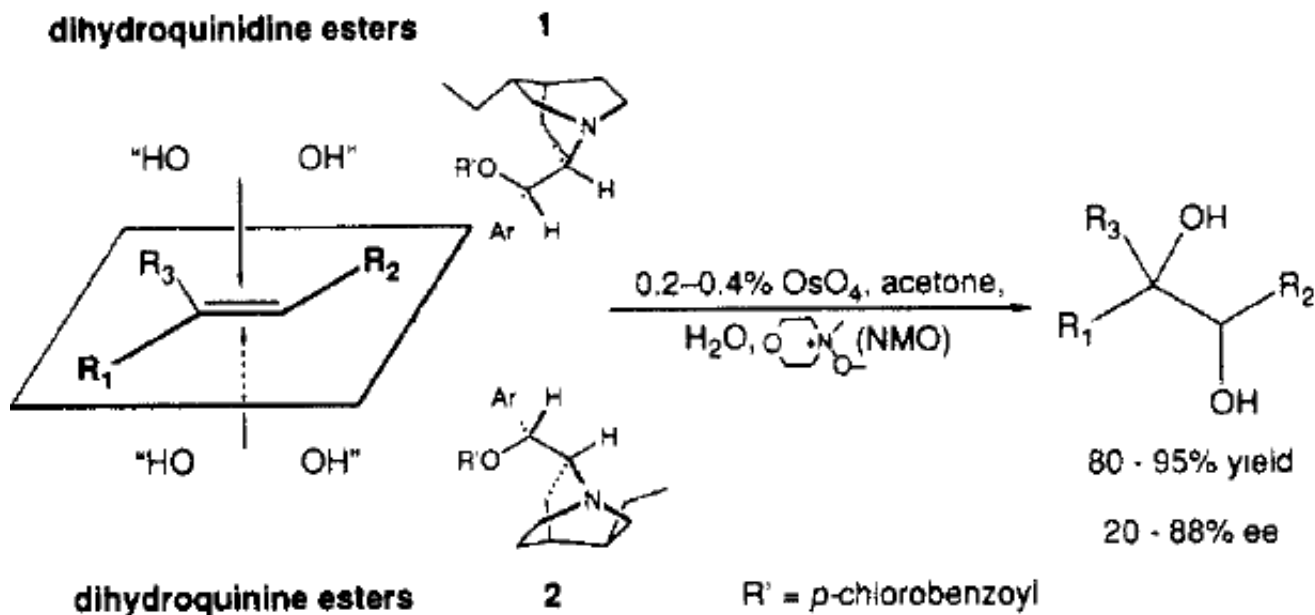


- *s-cis* conformer is favored. Poor diastereoselectivity results unless bidentate chelation is achieved between Lewis acid and both carbonyl groups.
- Dramatic rate increase with >1 equiv of Lewis acid
- Typical reaction conditions: 1.4 mol equiv.  $R_2AlCl$ , xs cyclopentadiene,  $-100^\circ C$ , 2-5 min
- Intramolecular variants also discussed



# Asymmetric Dihydroxylation

Asymmetric Dihydroxylation via Ligand- Accelerated Catalysis - Sharpless - 1968 (430 Citations)

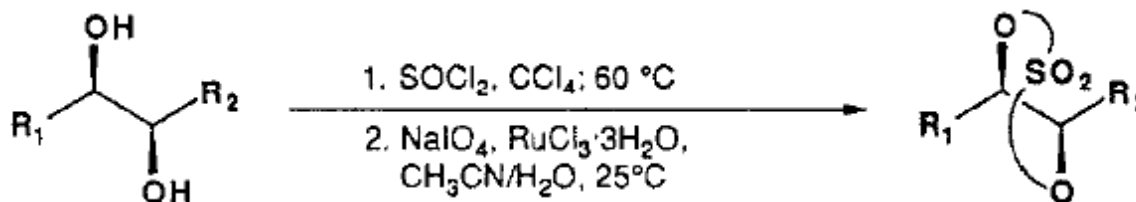


- Tertiary amines known to accelerate dihydroxylation of olefins with OsO<sub>4</sub>
- No directing functional group required
- Very little osmium is required; as little as 1:50000 osmium:substrate
- Uses readily available and recoverable cinchona alkaloids
- Insensitive to air and water.

# Vicinal Diol Cyclic Sulfates

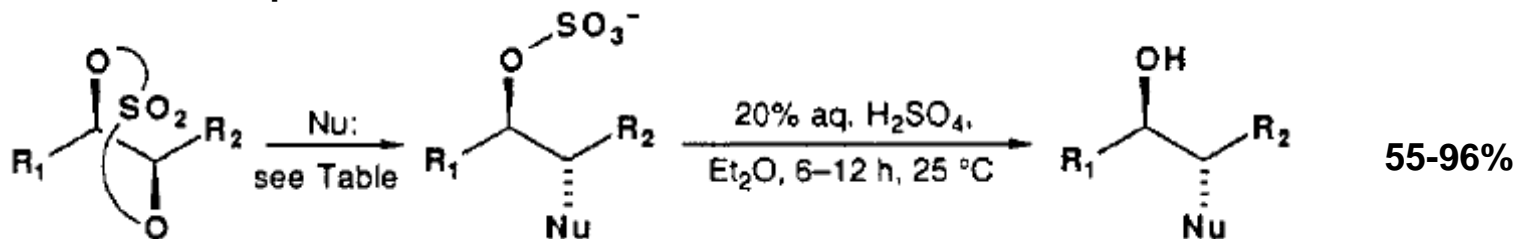
Vicinal Diol Cyclic Sulfates – Like epoxides only more reactive - Sharpless - 7538 (392 Citations)

## Synthesis of Cyclic Sulfates



- Cyclic sulfates previously very impractical to synthesize
- Highly active catalytic  $\text{RuO}_4$  system developed. Typical reaction times: 1.5 hours 1:1500 catalyst loading
- Pure cyclic sulfates obtained after extraction and filtration through pad of silica gel.

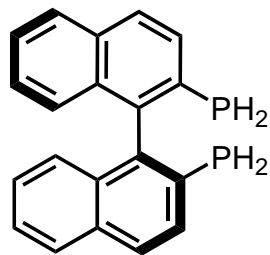
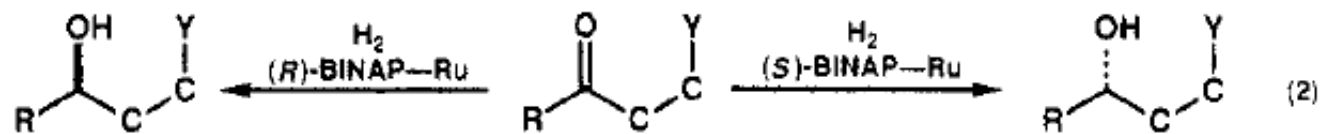
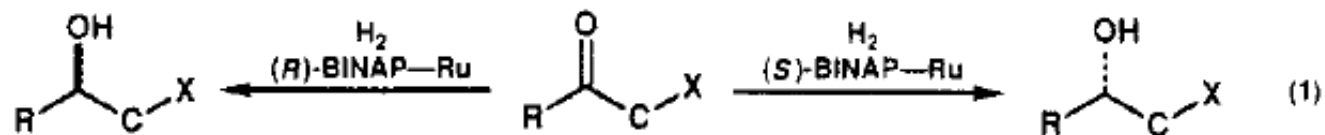
## Cyclic Sulfates as Electrophiles



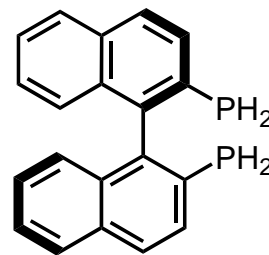
- Variety of nucleophiles tested:  $\text{H}^-$ ,  $\text{F}^-$ ,  $\text{N}_3^-$ ,  $\text{PhCO}_3^-$ ,  $\text{NO}_3^-$ ,  $\text{SCN}^-$ ,  $\text{PhCH}_2^-$

# Asymmetric Hydrogenation

## Homogeneous Asymmetric Hydrogenation of Functionalized Ketones - Noyori - 629 (326 Citations)



(S)-BINAP



(R)-BINAP

- Often exhibits excellent yields and excellent enantioselectivities (92 to >99%)
- Simultaneous coordination of carbonyl oxygen to X or Y (heteroatom)