Pericyclic Rxns

Cyclic TS w/ bond formation & breaking occurring at same time.

5 types
- electrocyclic
- cycloadditions
- sigmatropic rearrangements
- Cheletropic
- sigmatropic shifts

Electrocyclic Rxns (Opening/Closing)

Examples

favored by ring strain

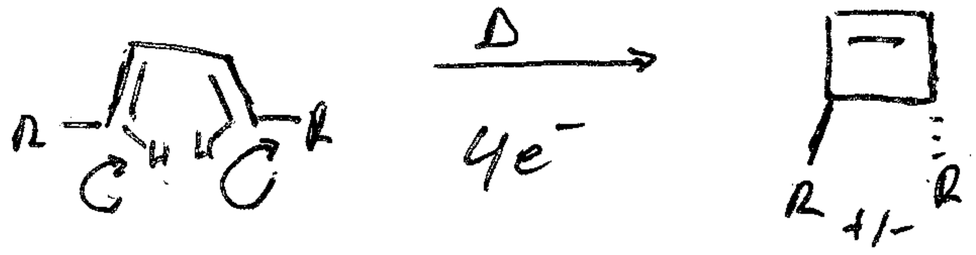
σ ~98
π ~75

3π bonds

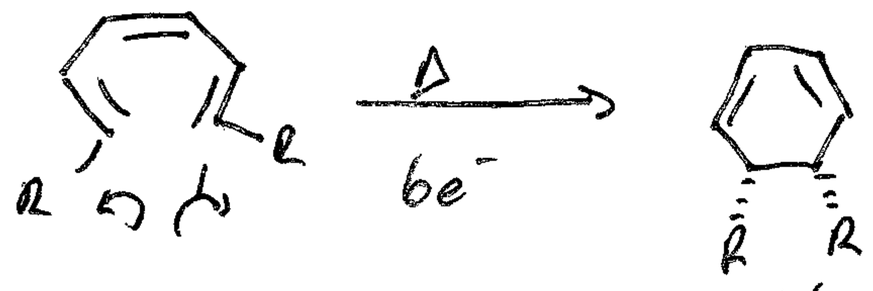
2π/1σ

π vs σ

Diastereoselectivity

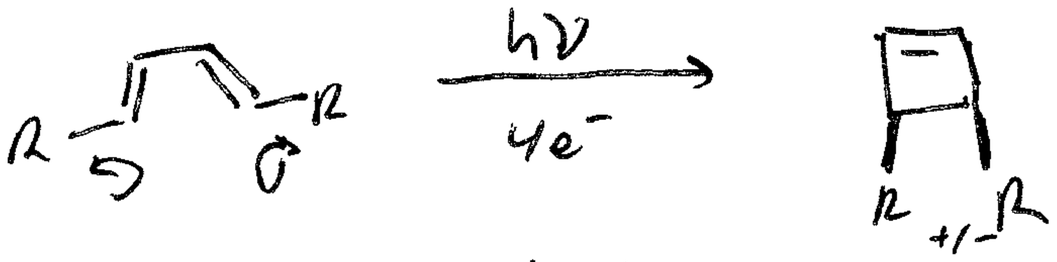


4, 8, 12 e⁻ etc thermal is conrotatory

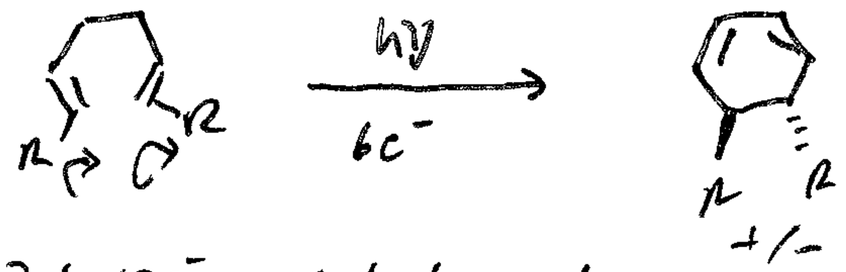


2, 6, 10 e⁻ ... thermal Disrotatory

(6 points for a touch Down)
(6 e⁻ thermal disrotatory)



photochemical 4, 8, 12e⁻ is disrotatory



2, 6, 10e⁻ photochemical conrotatory

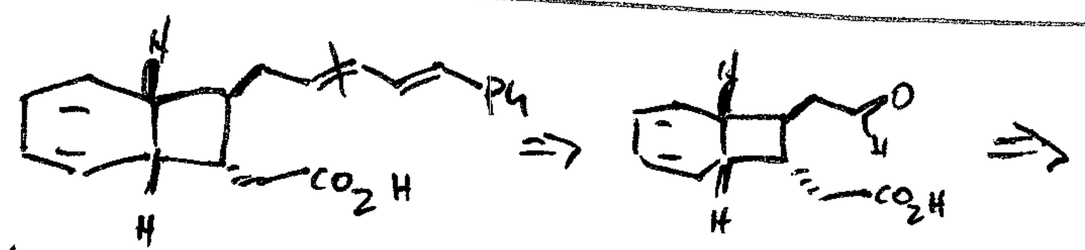
Woodward Hoffman Rules:

JACS, 1965, 87, 395
ACIE, 1969, 8, 781

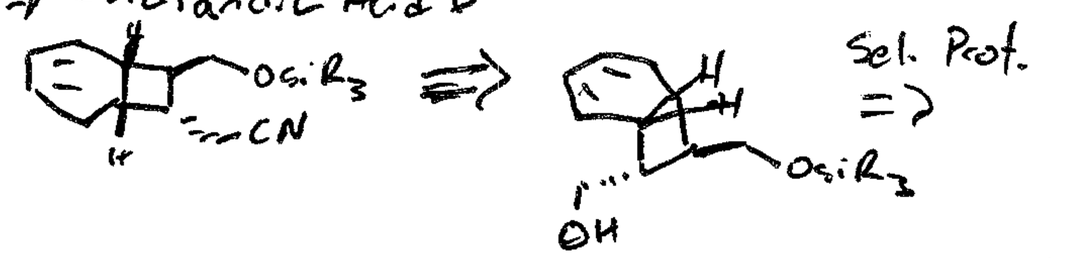
examples next

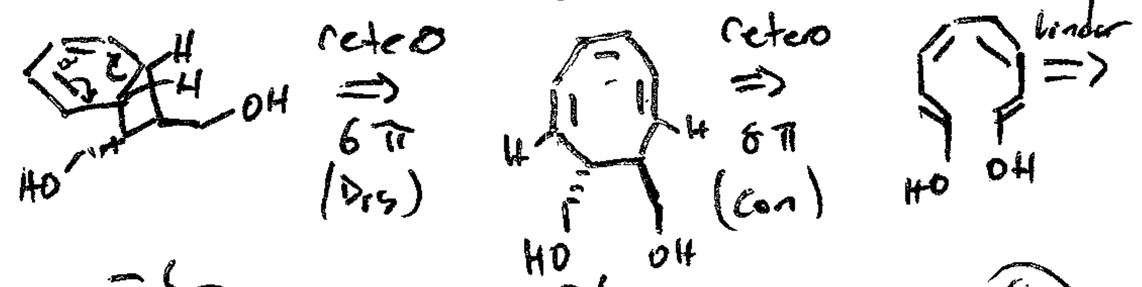
KC Nicolaou ⟹

JACS, 1982, 104, 5555

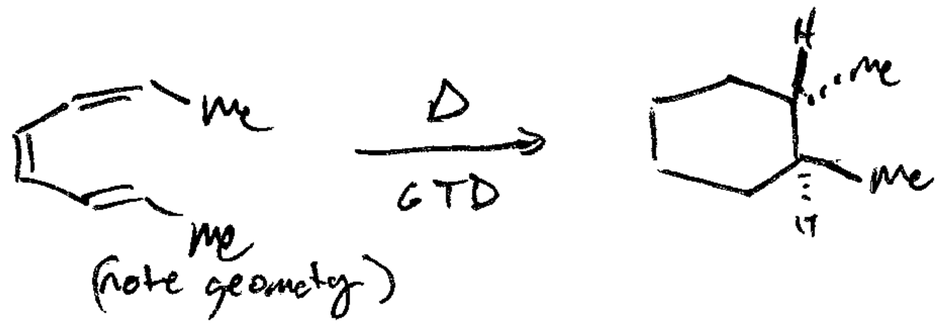


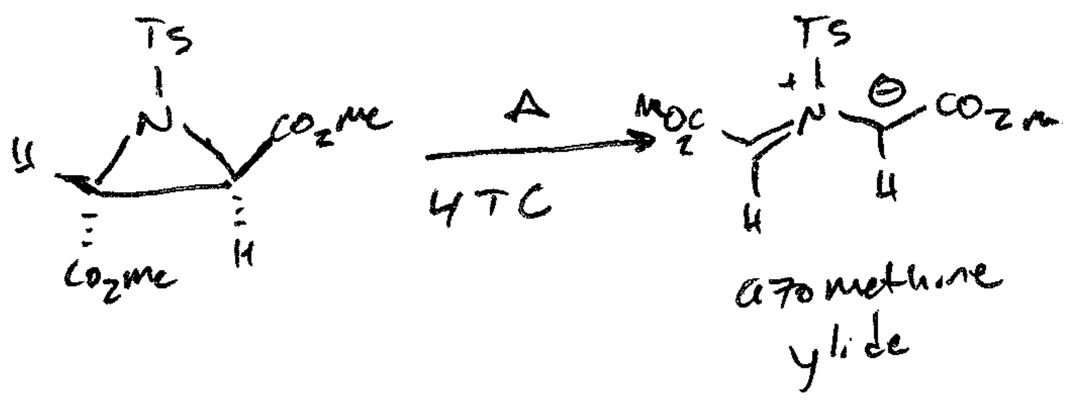
(+) Endiandric Acid D





examples of Electrocyclic Rxns





Cycloadditions

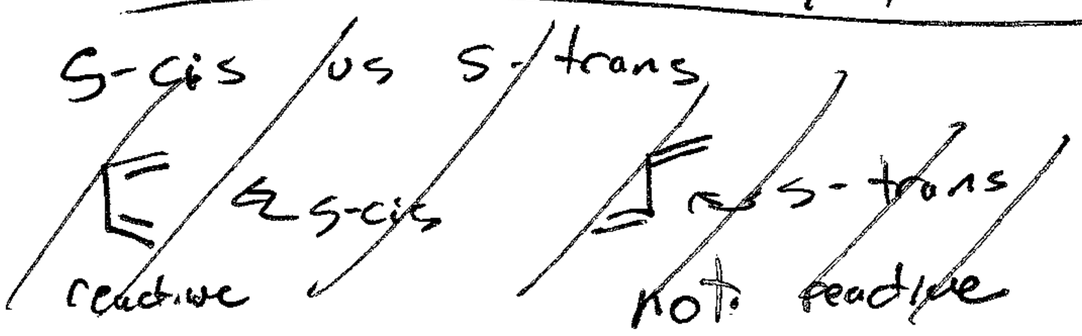
[4+2] - Diels Alder Rxn

4 atom 2 aton

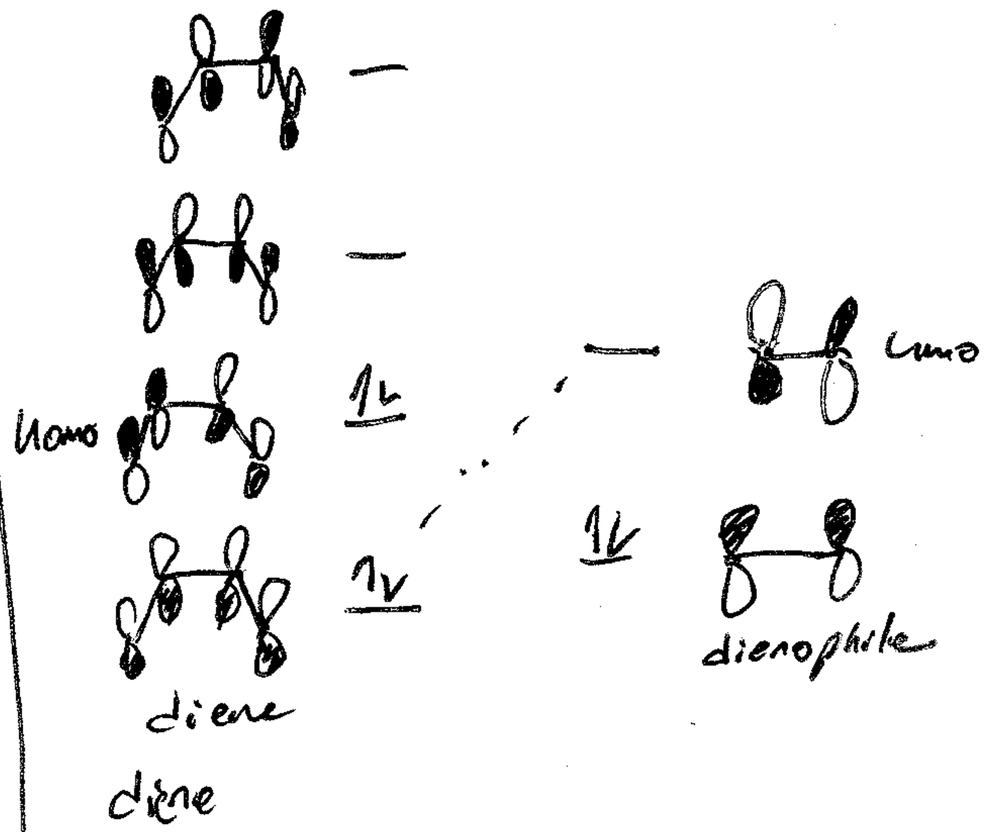
(note 6e⁻)

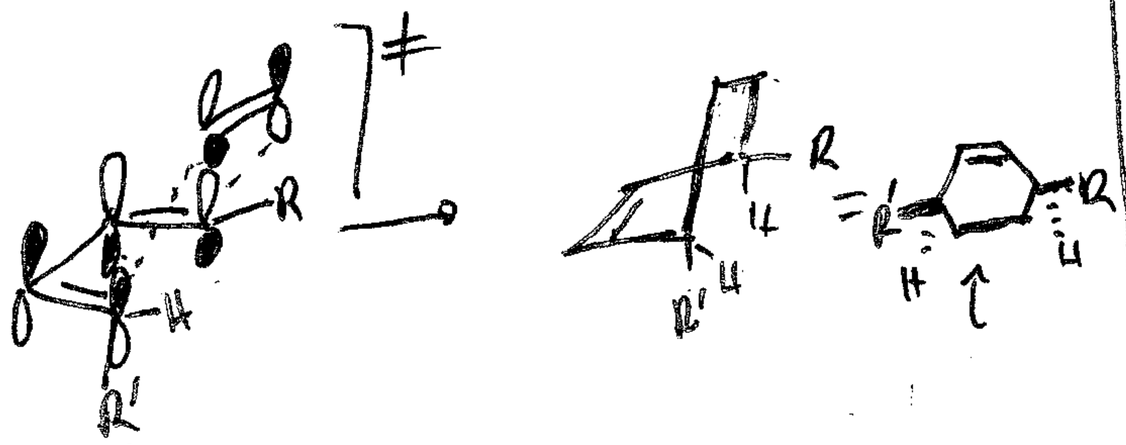
great way to make cyclohexenes & cyclohexanes

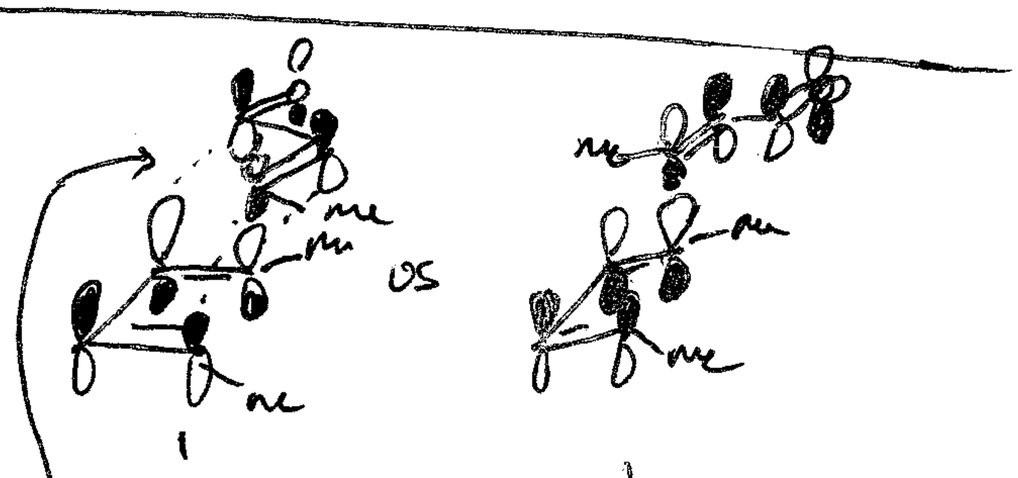
S-cis vs S-trans



FMO control -

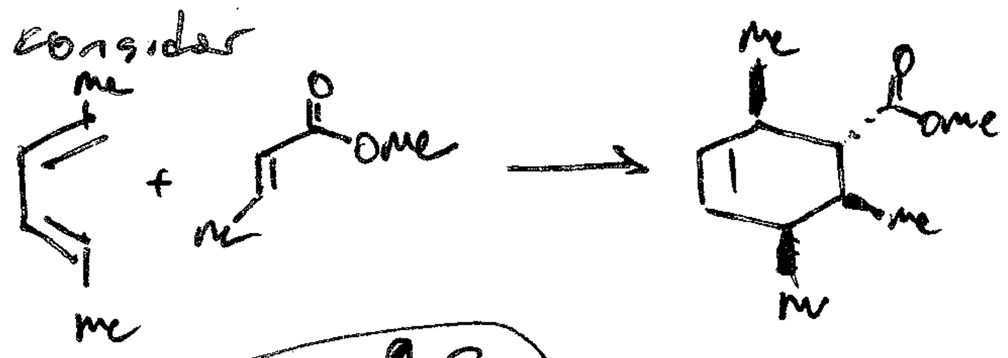


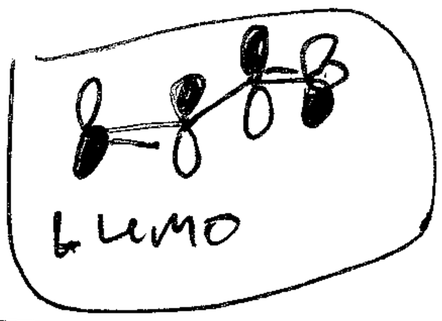


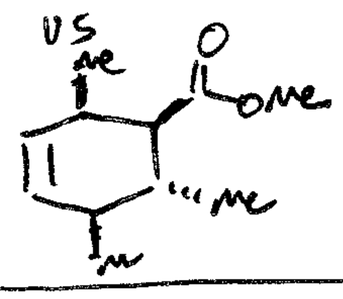


Endo vs Exo

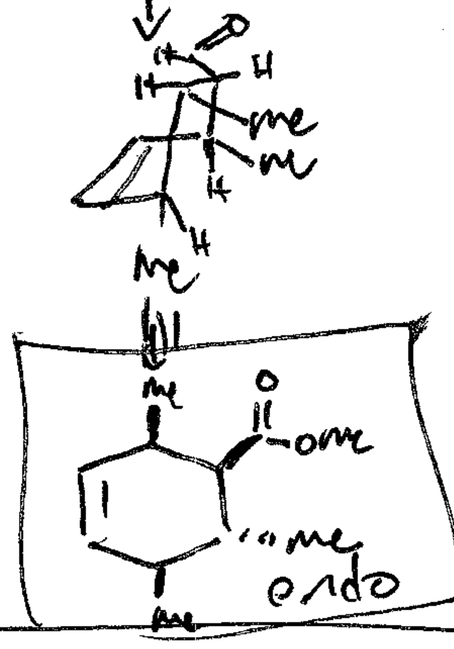
Consider

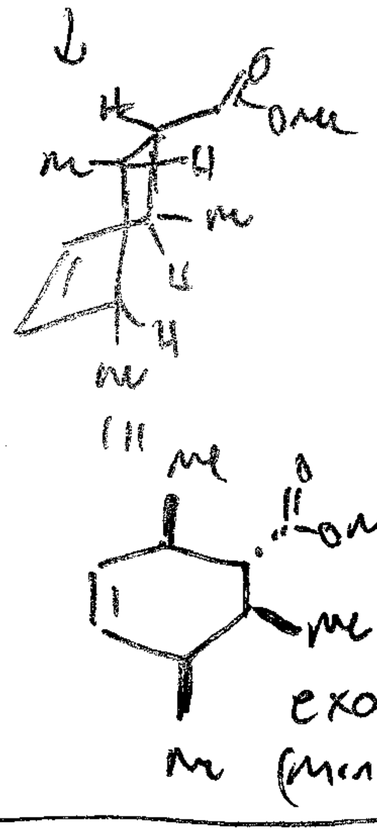




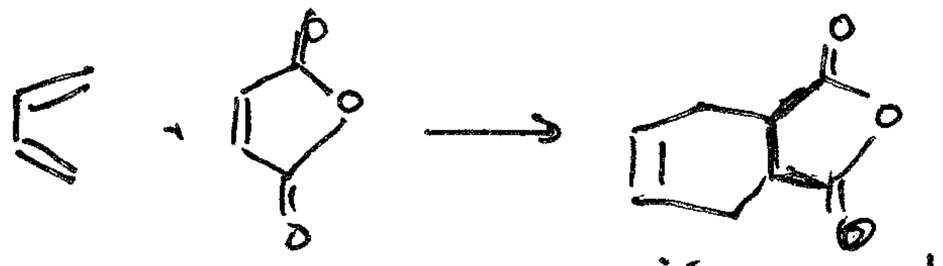


2nd orbital overlap preferred





EWG - Accelerate Rxn - Lumo Lowering

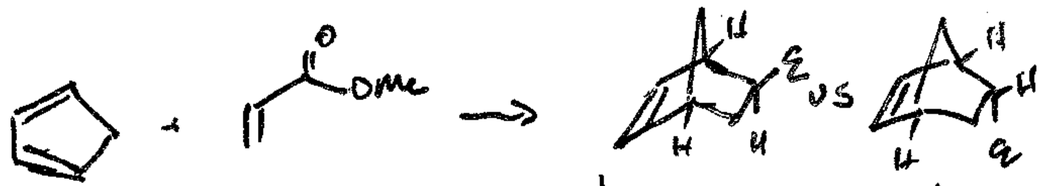


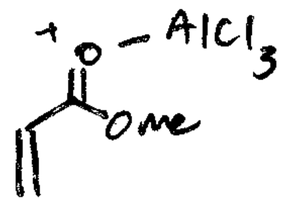
100% 24h, rt

78% 17h, 165°C, 12600 psi !

EWG - lowers Lumo

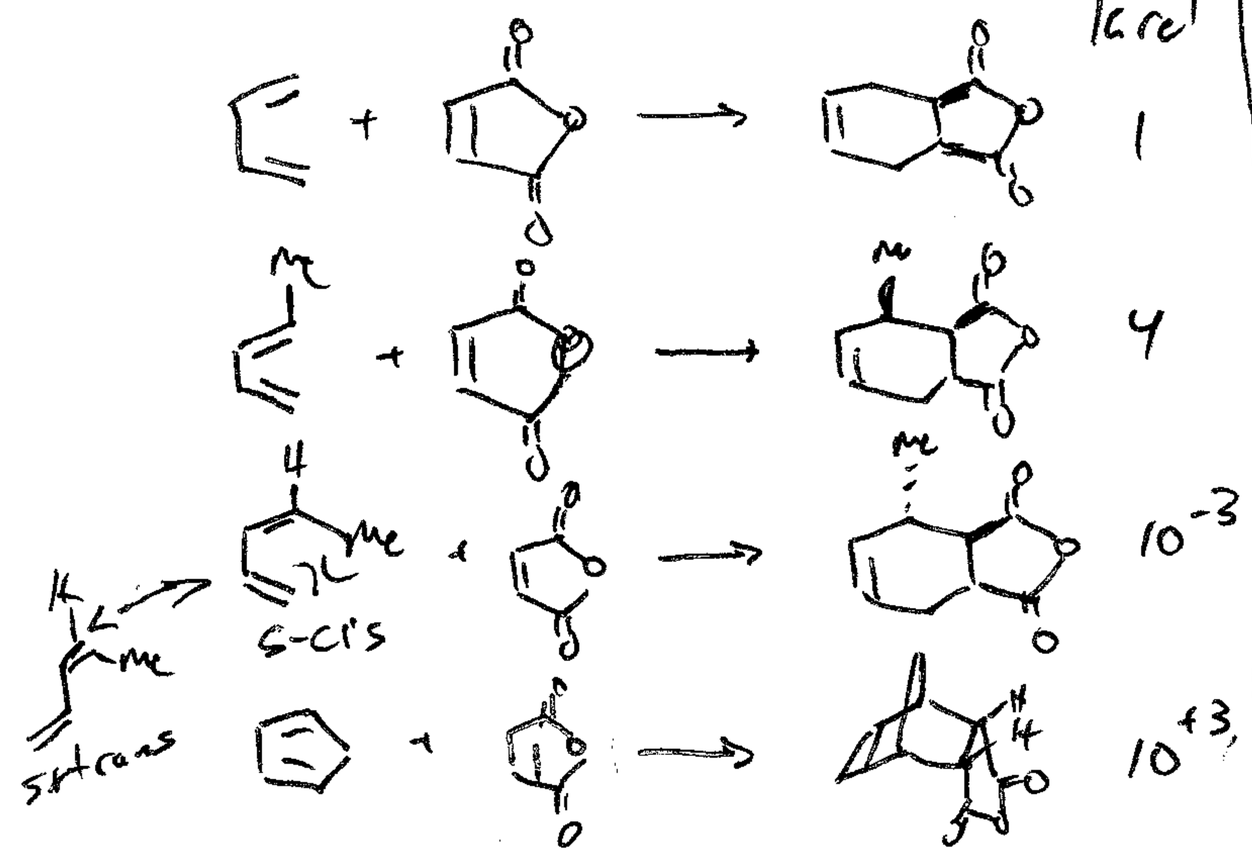
Lewis acid catalysis



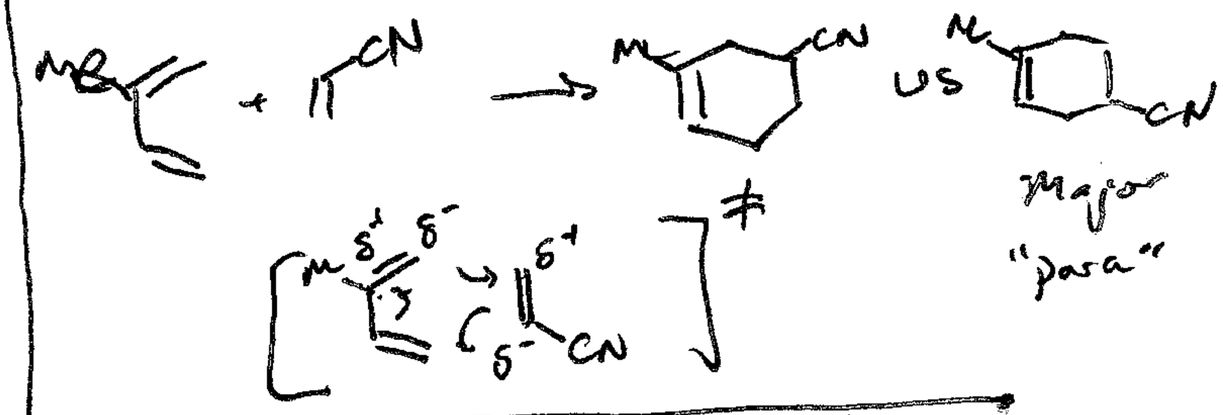


↑ lower Lumo

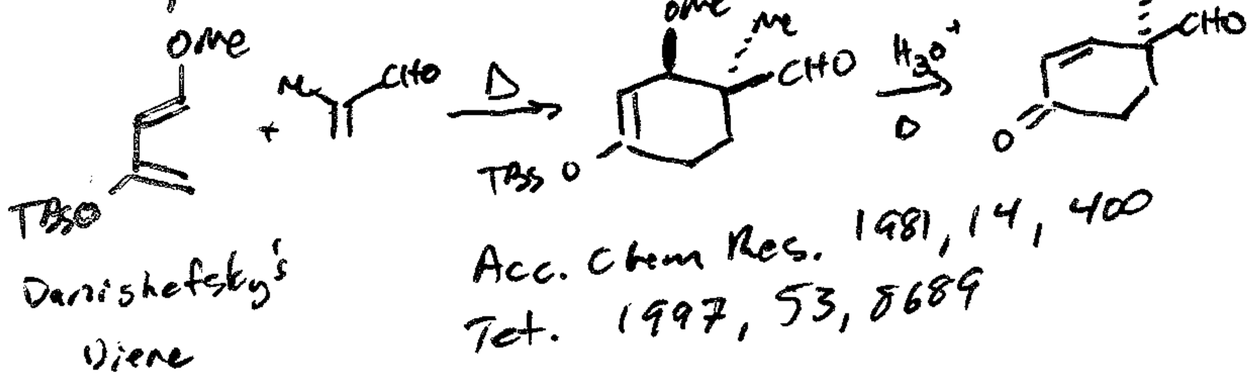
S-cis vs s-trans : S-cis is reactive



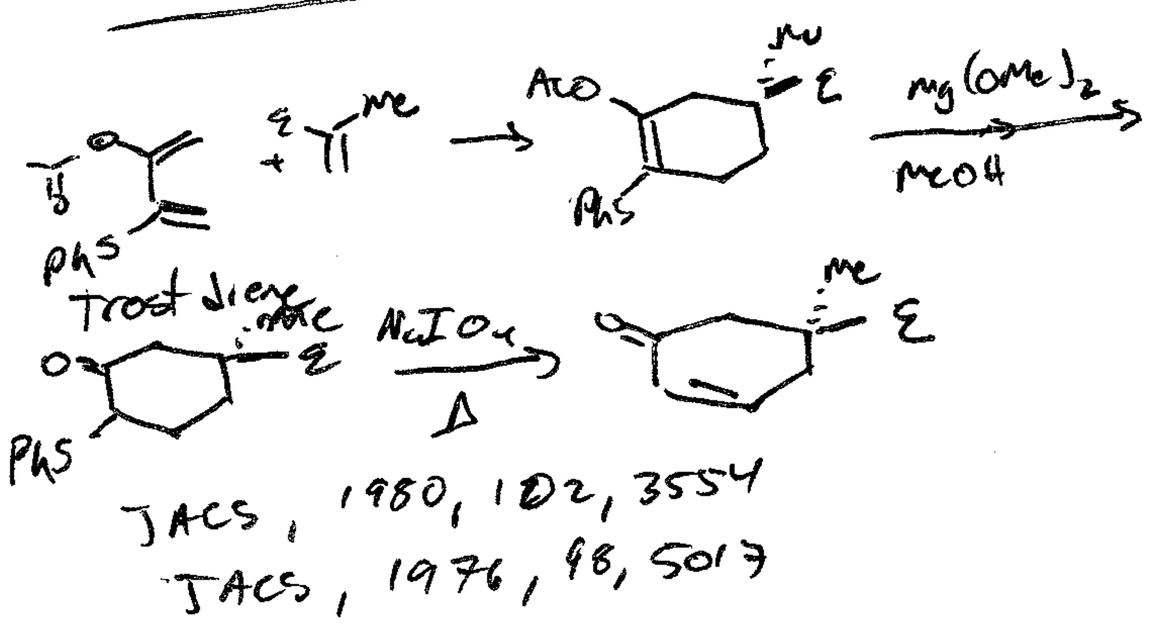
Regioselectivity - polorazation



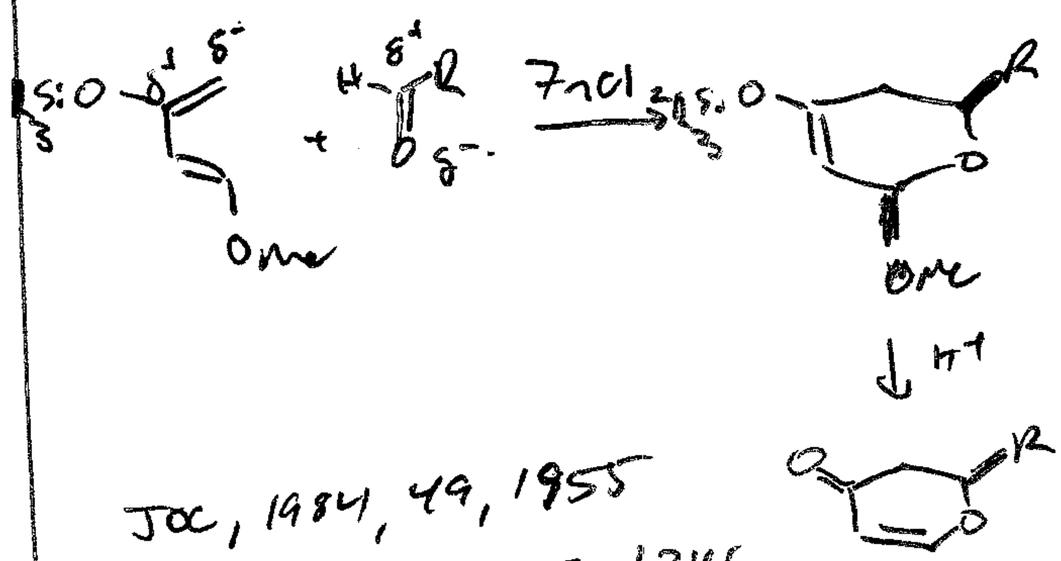
Important Dienes



Acc. Chem Res. 1981, 14, 400
Tet. 1997, 53, 8689

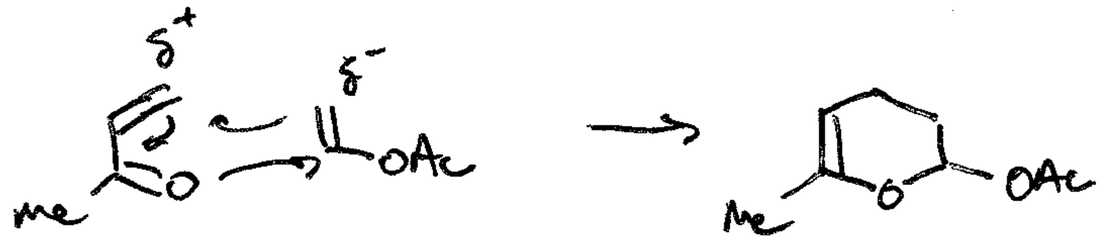


Hetero Diels Alder Rxns

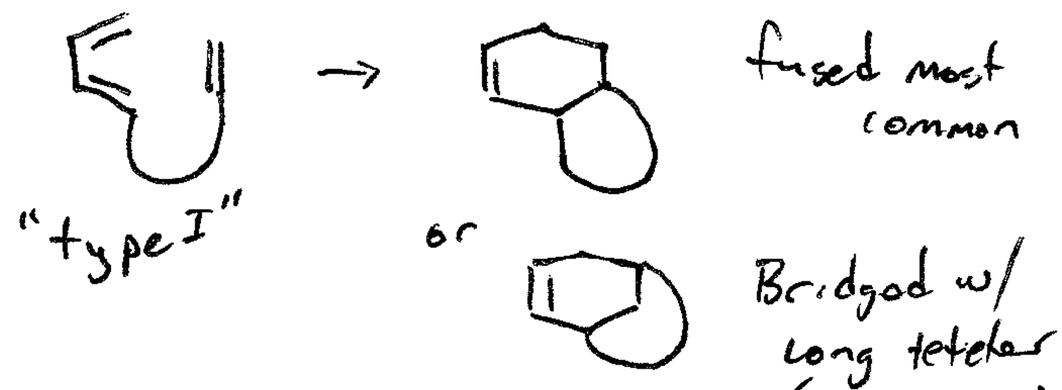


JOC, 1984, 49, 1955
JACS, 1985, 107, 1246

Inverse demand DA



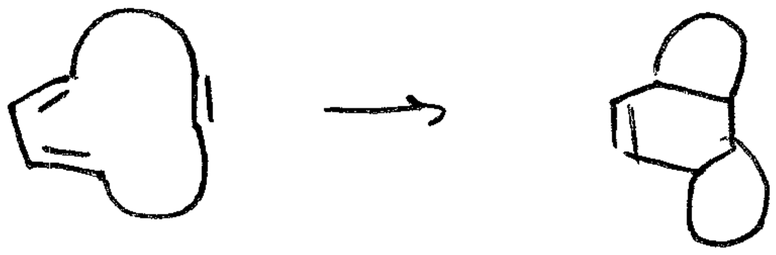
Intramolecular Diels Alder Rxns



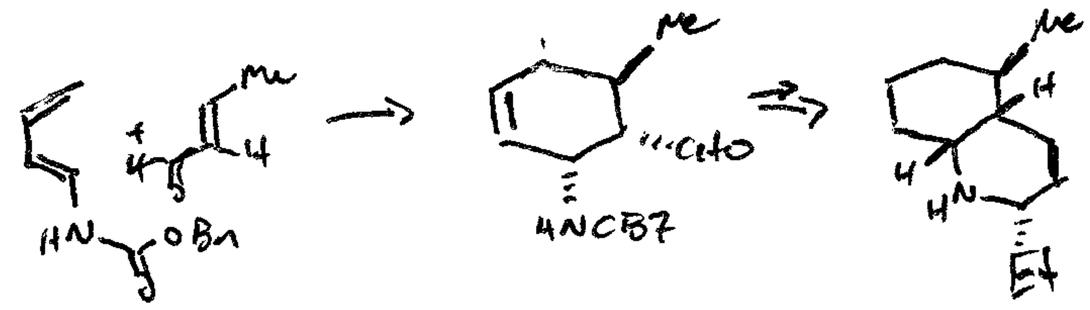
"Type II"

Need long tether to avoid anti-Bredt olefine

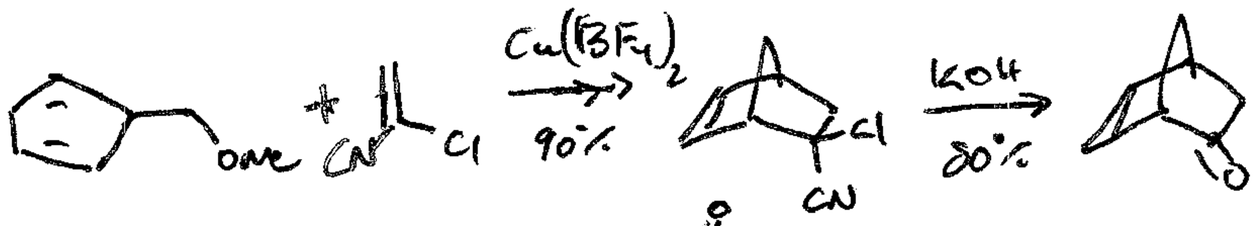
Trans annular DA

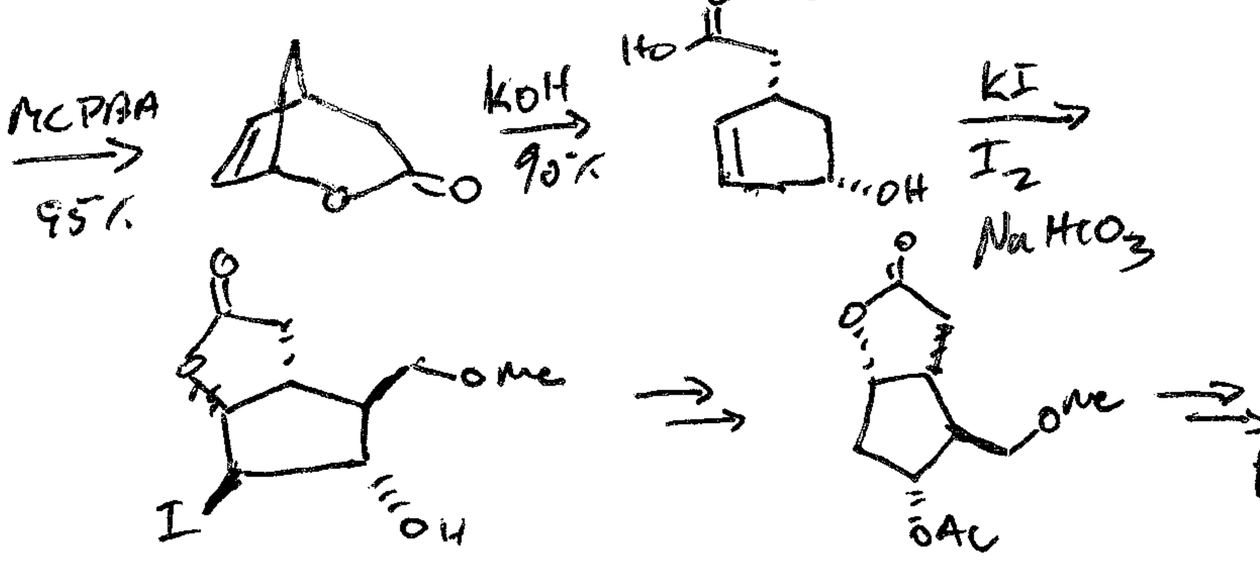


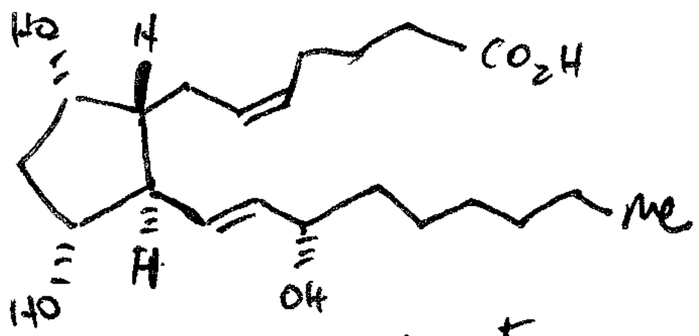
Examples of DA in Synthesis



(±) Pumiliotoxic C
Org Syn Coll Vol. 6, 95

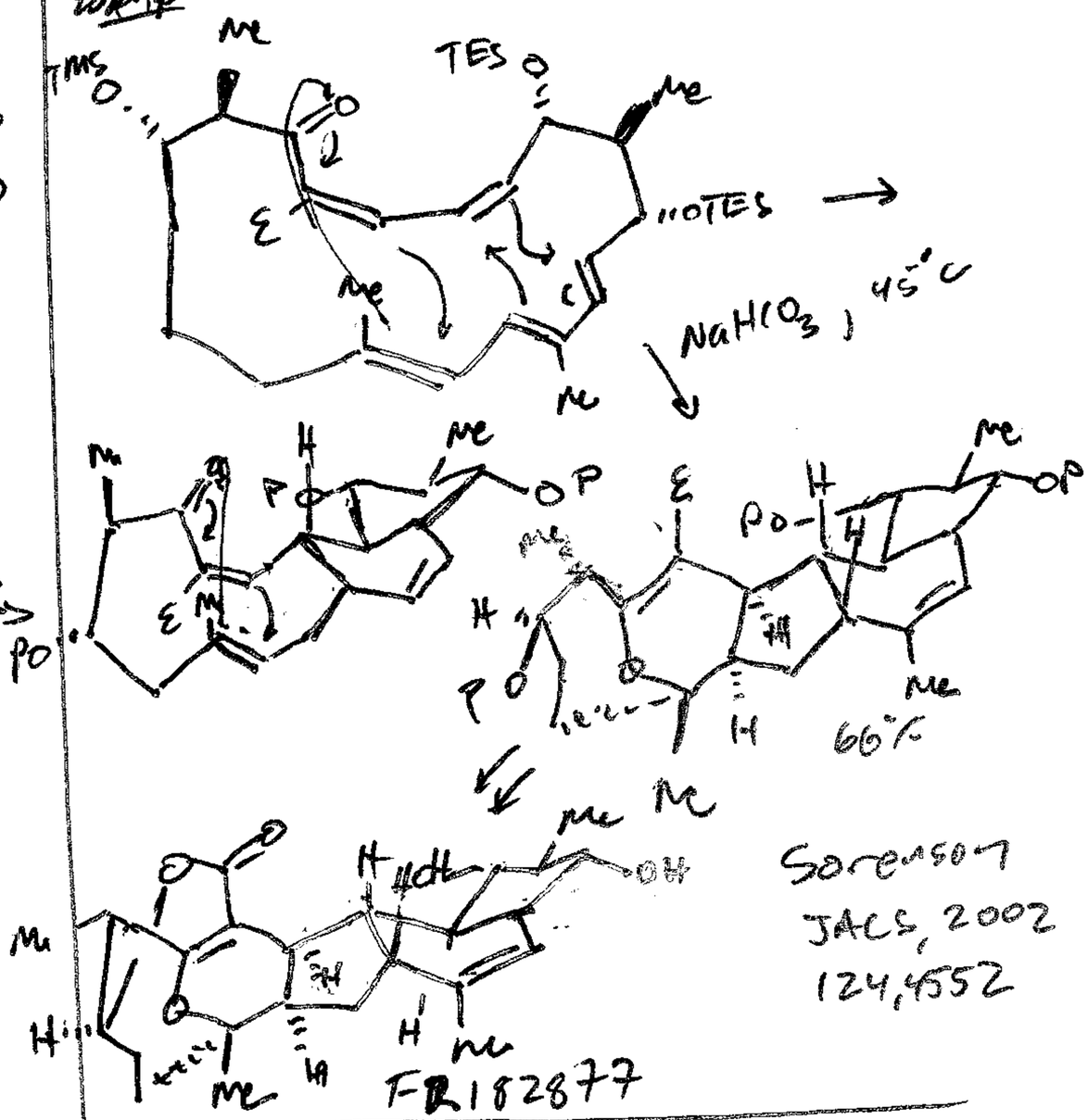






Prostaglandin $F_{2\alpha}$

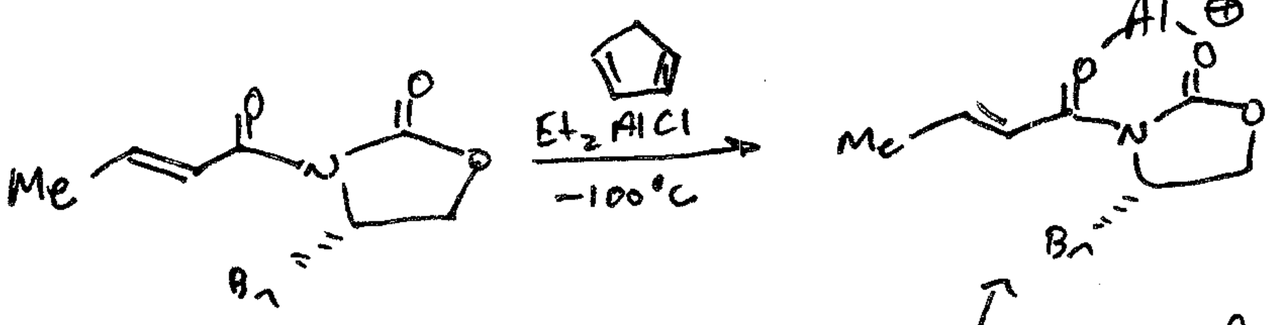
Corey



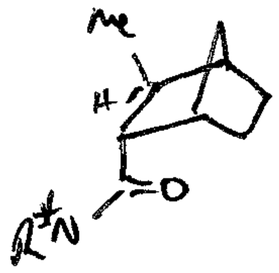
Sorensen
JACS, 2002
124, 4552

FR182877

Chiral Aux. control. - see Carreira Chp 17.



Block rear-face



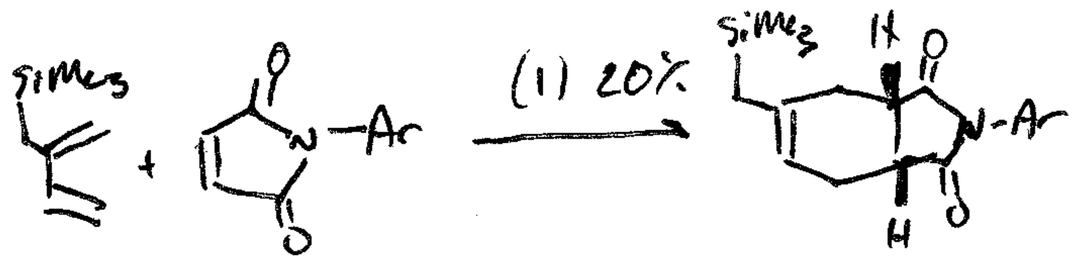
dr = 97:3
endo exo 55:1

many other Aux.'s

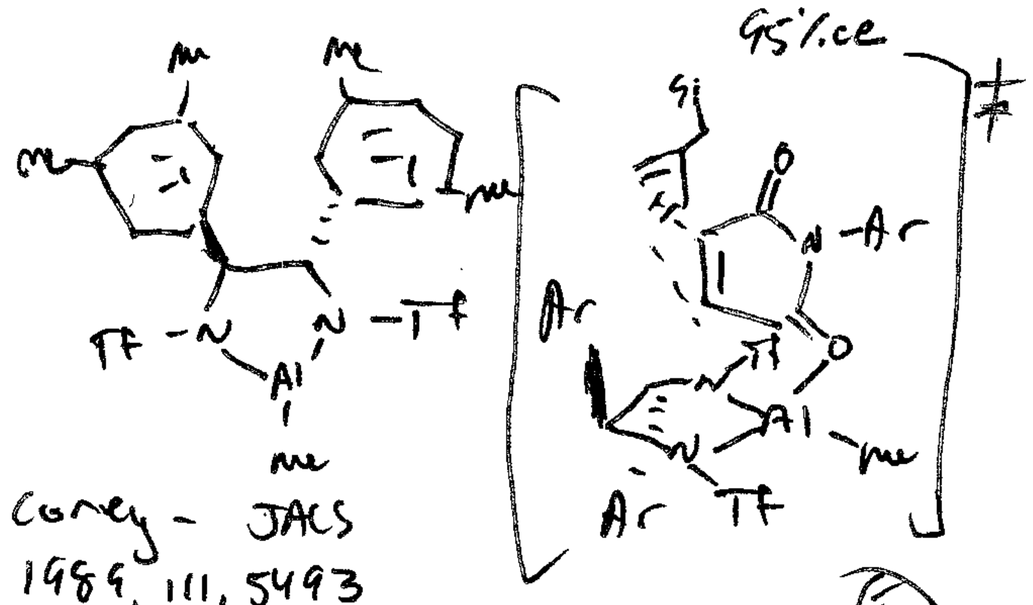
this ~~example~~ example

Evans, JACS, 1984, 106, 4261

Asy. Catalysis - many cats

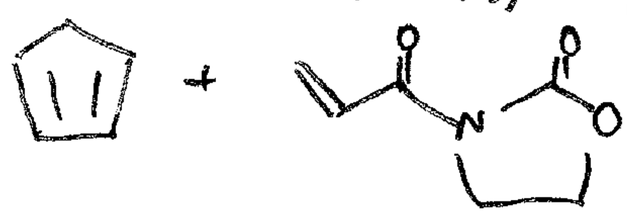


95% ee

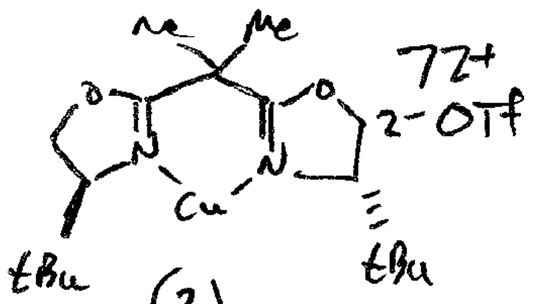


Corey - JACS 1989, 111, 5493

Evans JACS, 1993, 115, 6460

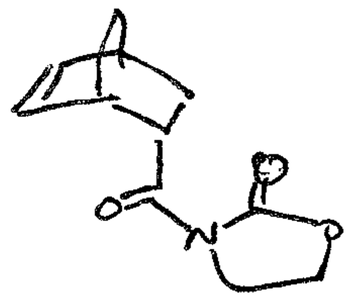


(2) 10%

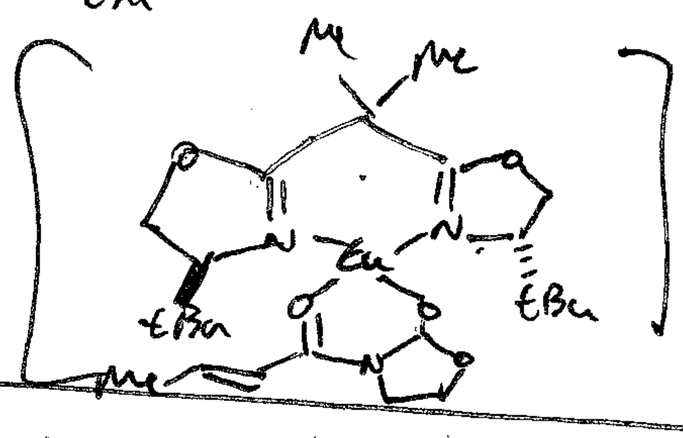


72+
2-OTf

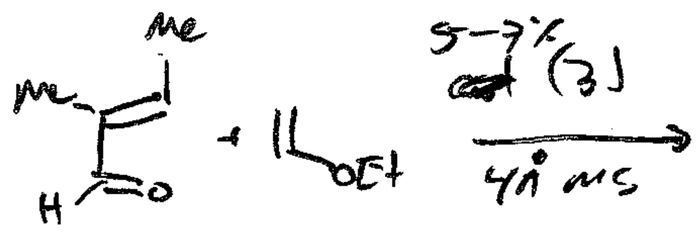
(2)



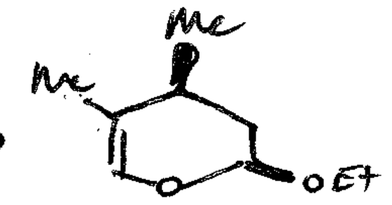
≠



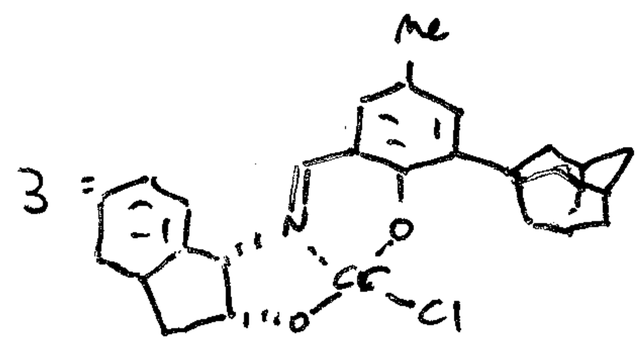
JACOBSEN, ACIE, 2002, 114, 3185



5→7% (3)
4Å MS



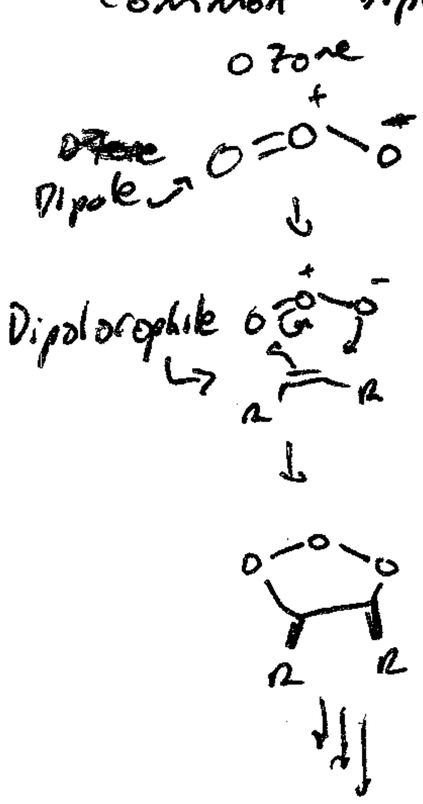
75% i., 94% ee

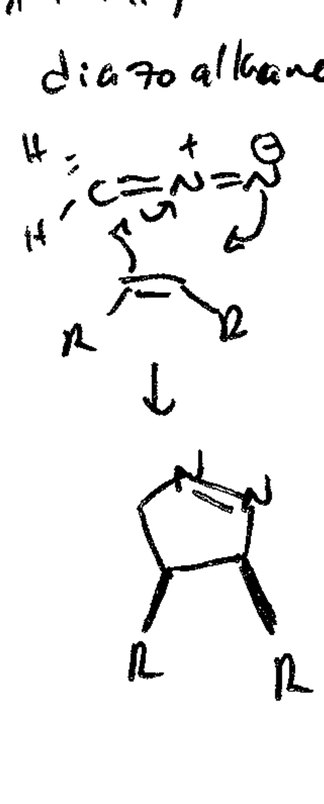


3 =

[3+2] - most common (useful) are 1,3-dipolar cycloadditions

Common Dipoles (note 5 ll 2π + 4π)

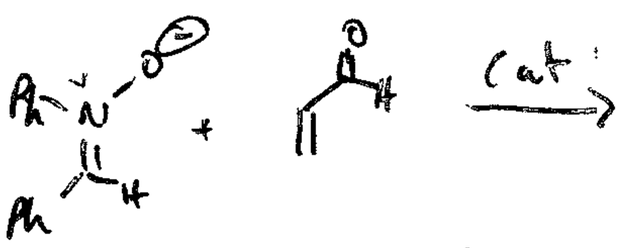




w/ Cu^I cat
"Click Rxn"
Fast, used for bioconjugation
Sharpless

Note acrolein somewhat complex.
See CES B 6-2

Lewis Acid Cat



Cat	yield		
None	5 %	80	: 20
Ar_3Al	100%	91	: >99

Asy. Cat also possible

Carreira Ch. 18 / CES B 6-2

[2+2] - w/ strained rings

Sigmatropic Rxns

3,3 - Sigmatropic Rearrangements

Cope

~~ΔG‡ ~~

as drawn ΔG = 0

Claisen

ΔG‡ ↓

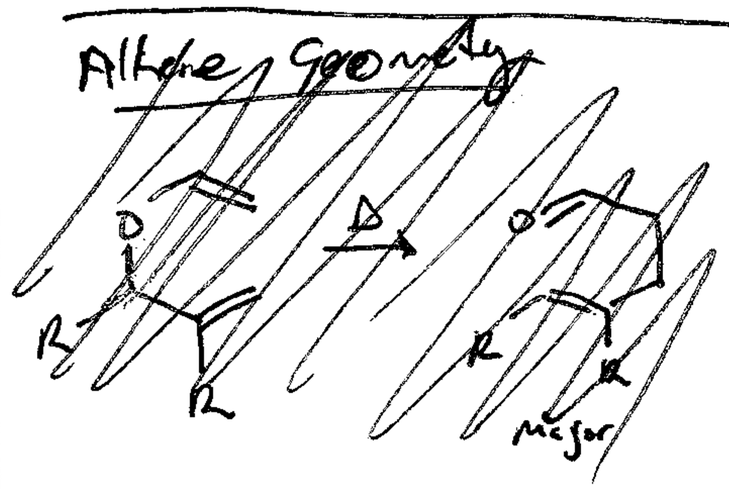
C-O π > C-C π

Highly Predictable TS - Both Rxns

Chair-like

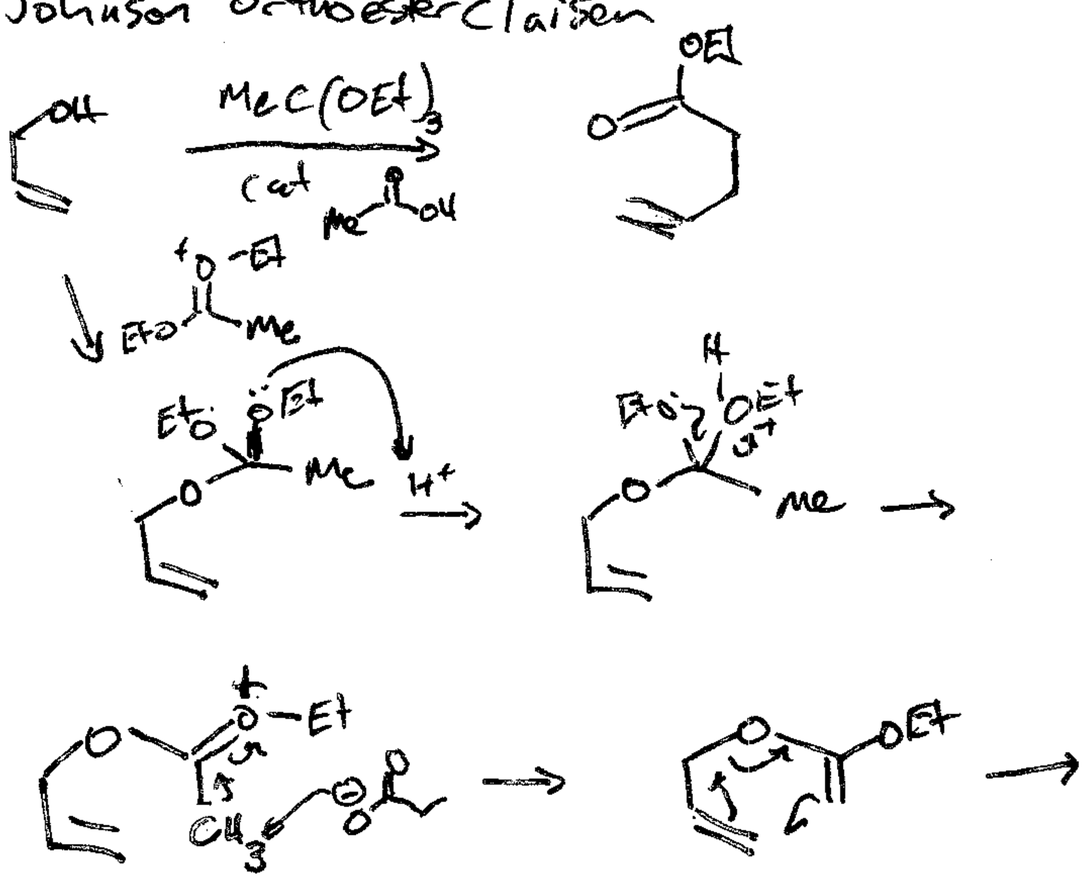
(most often)

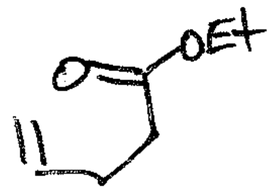
Alkene Geometry



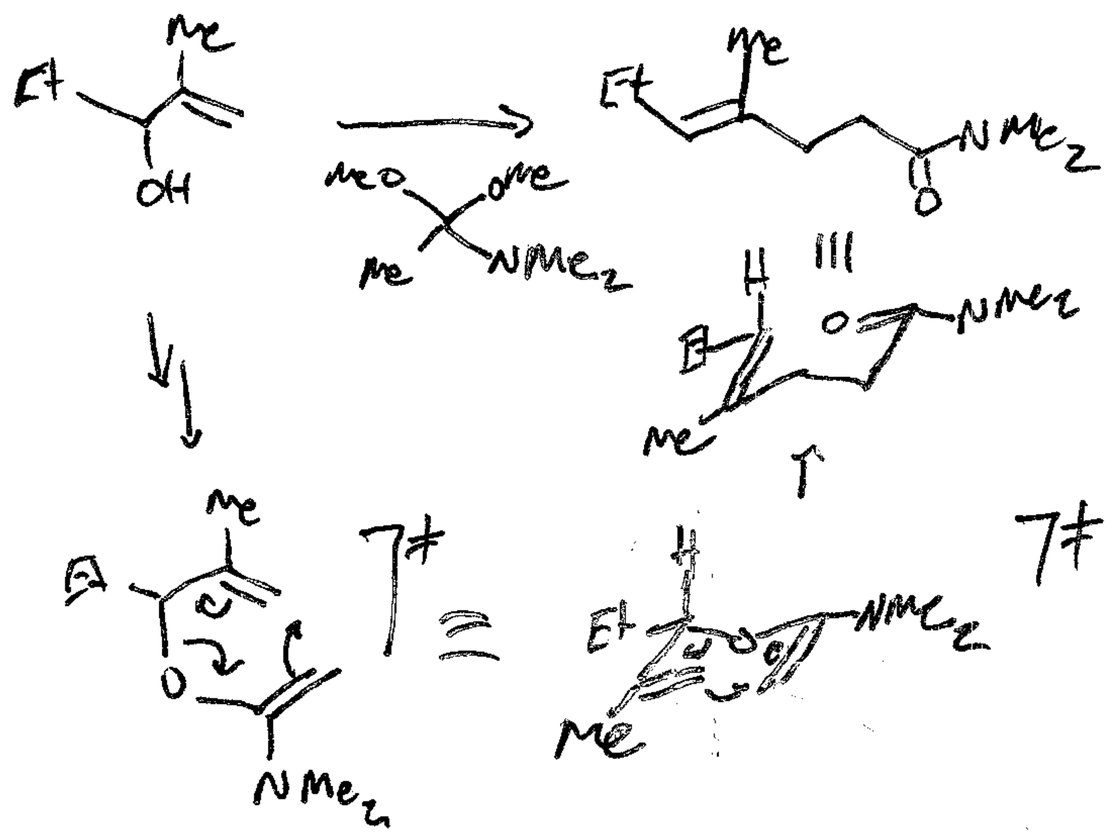
Modified Claisen Rearrangements - most often used

Johnson orthoester Claisen



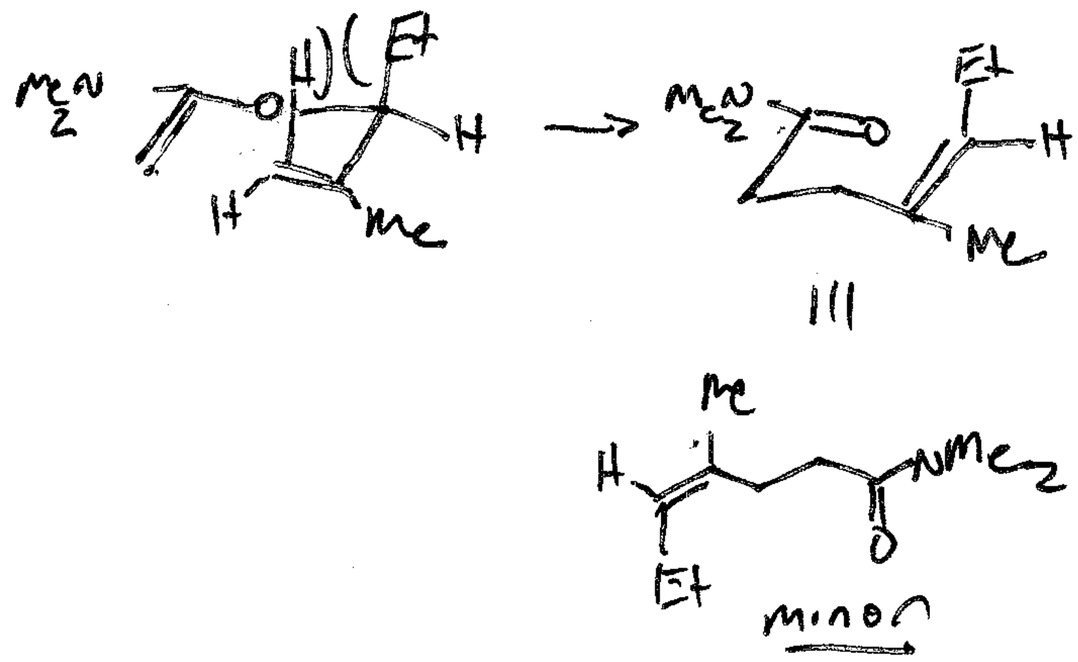


Eschenmoser - Claisen



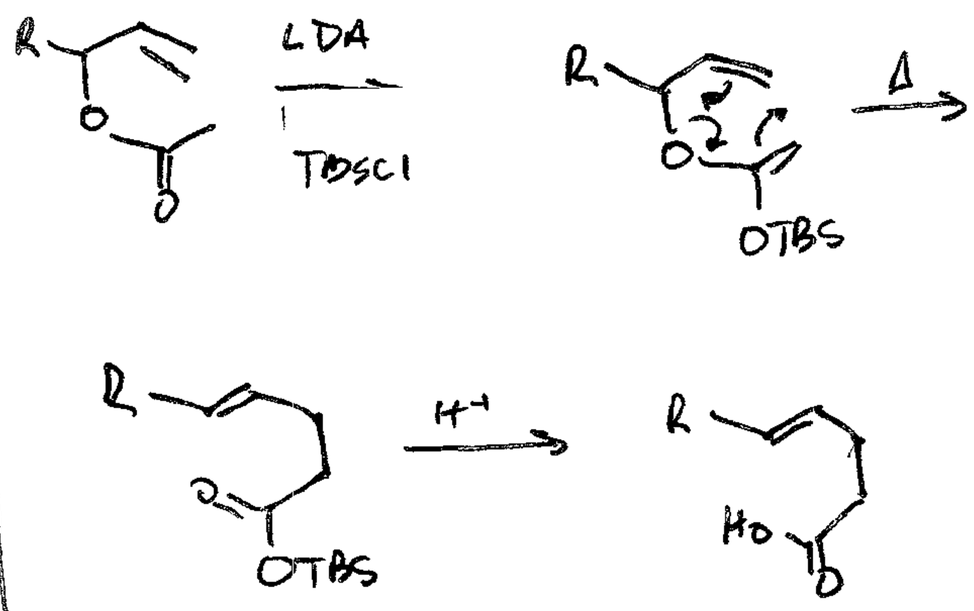
Note Alkene geometry results from lowest energy chair

alternate

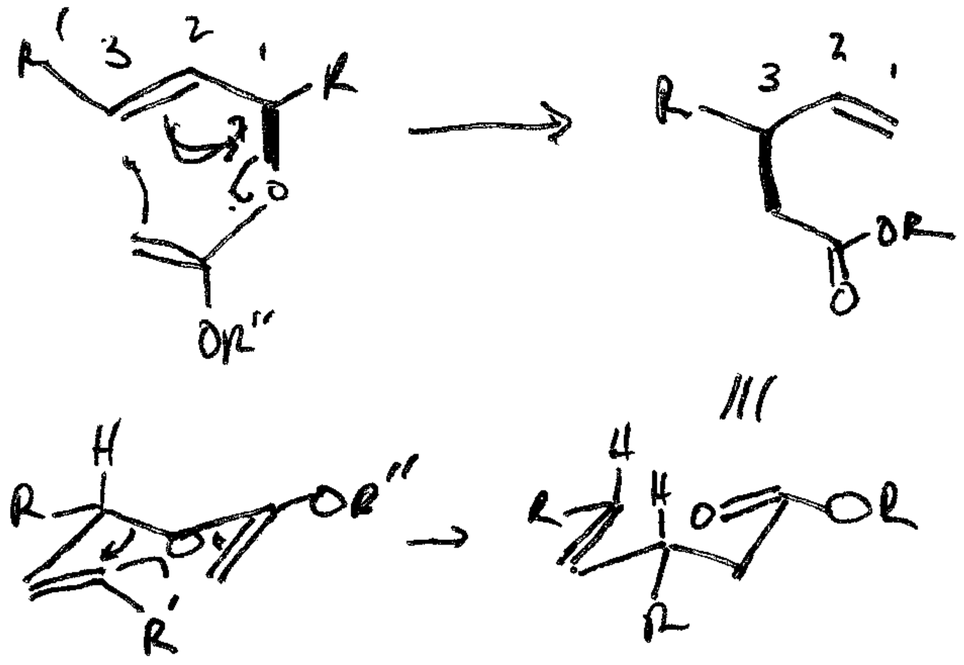


minor

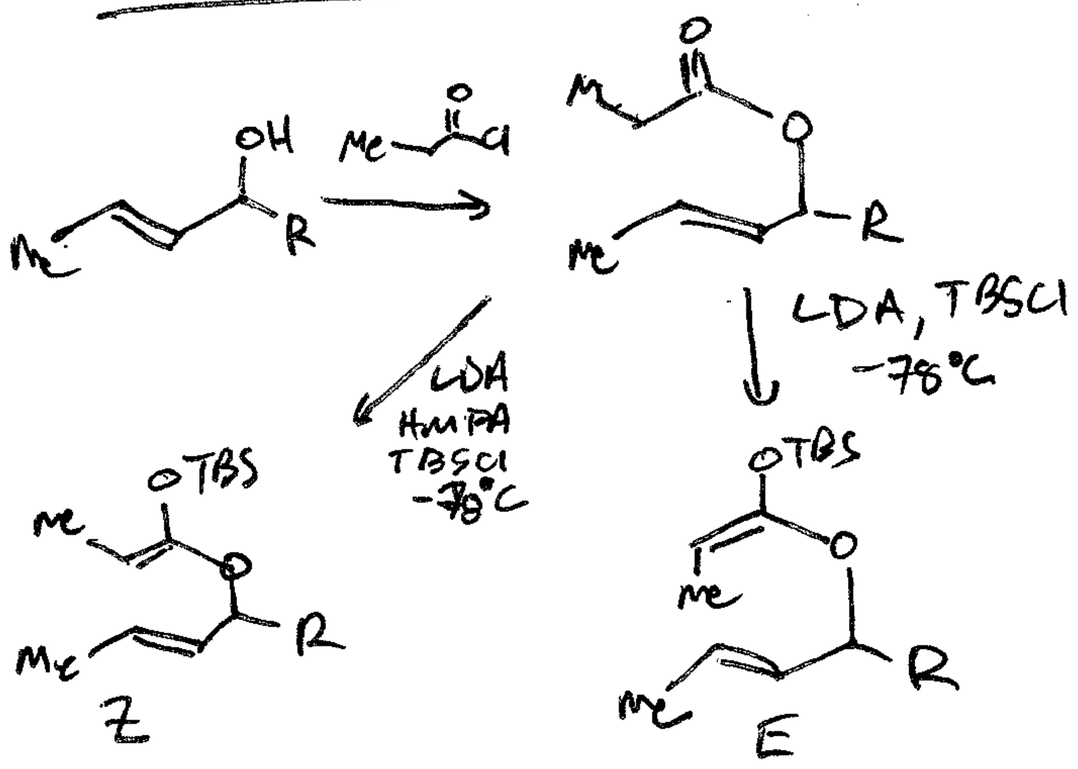
Ireland Claisen - (most useful)



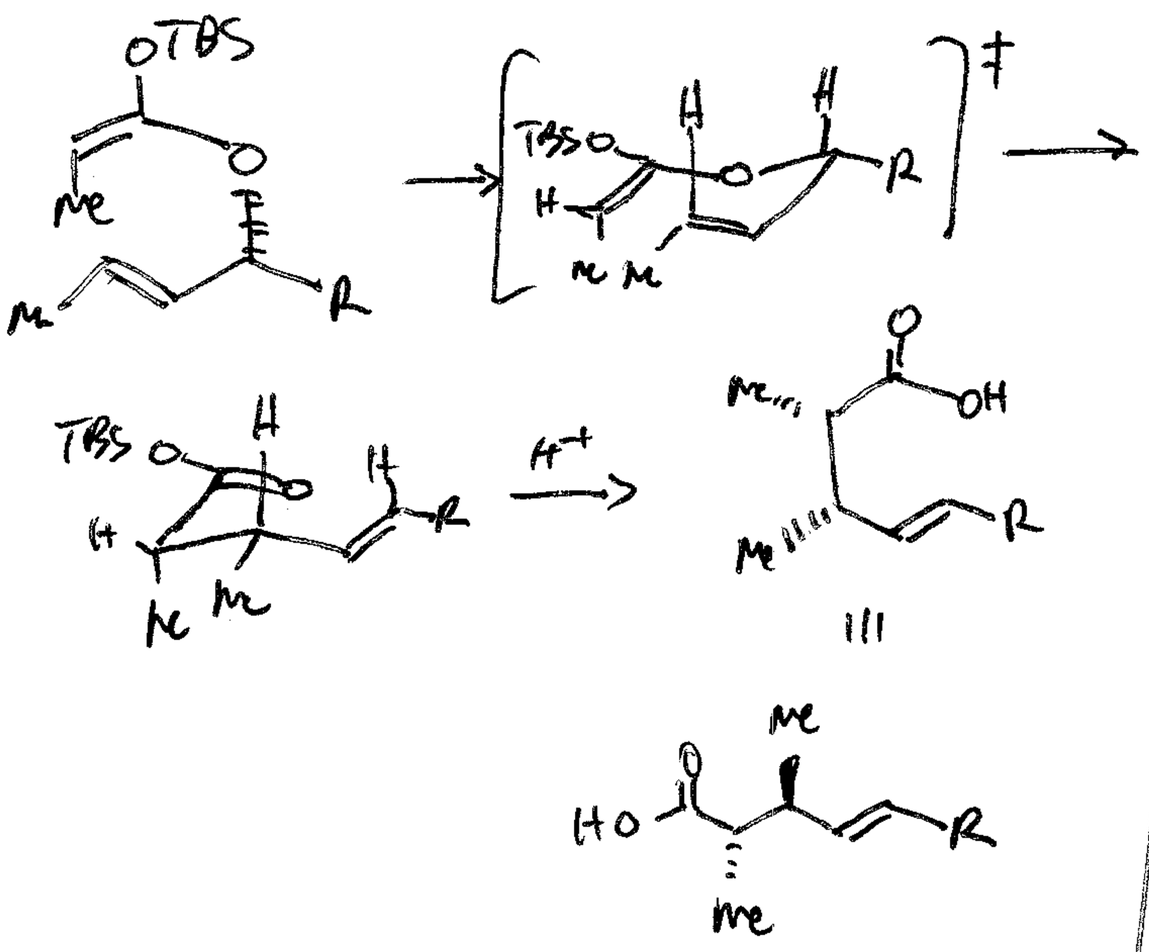
1,3-Chirality Transfer



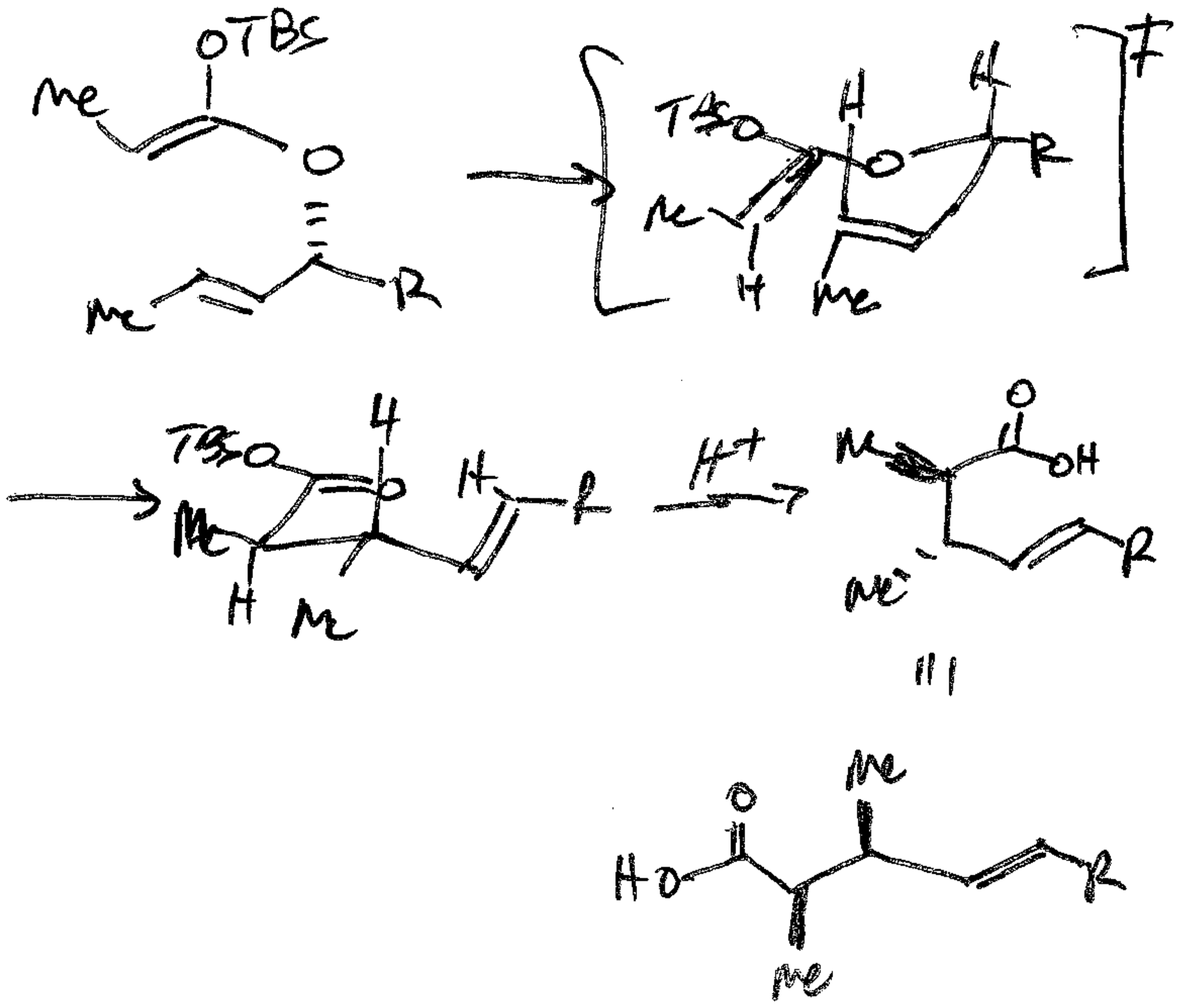
Enolate-geometry



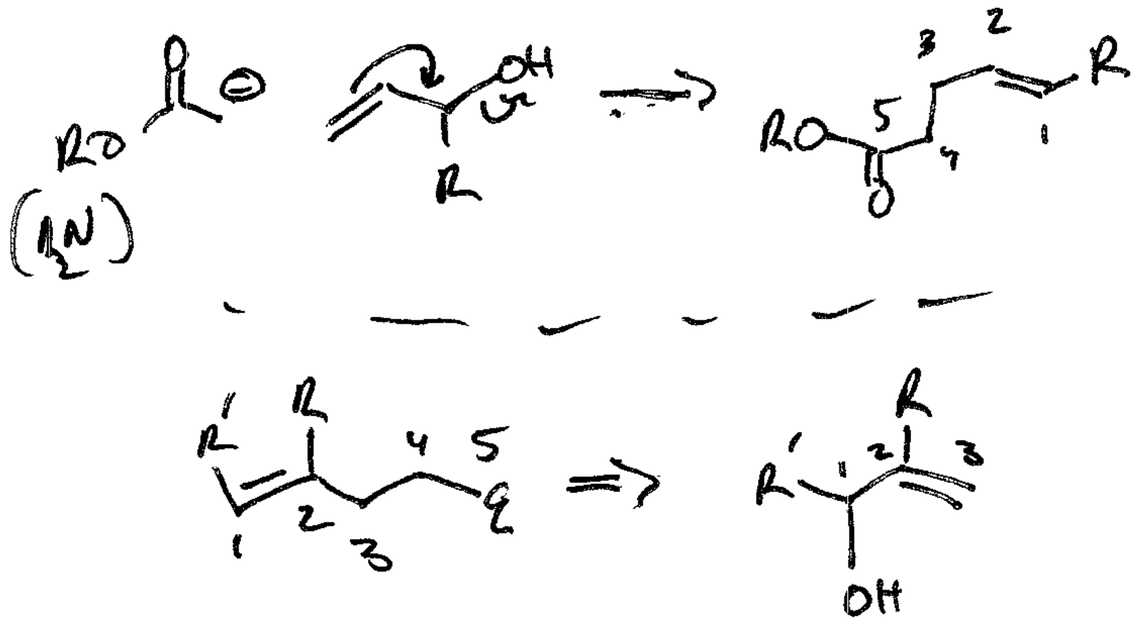
E-Enolates



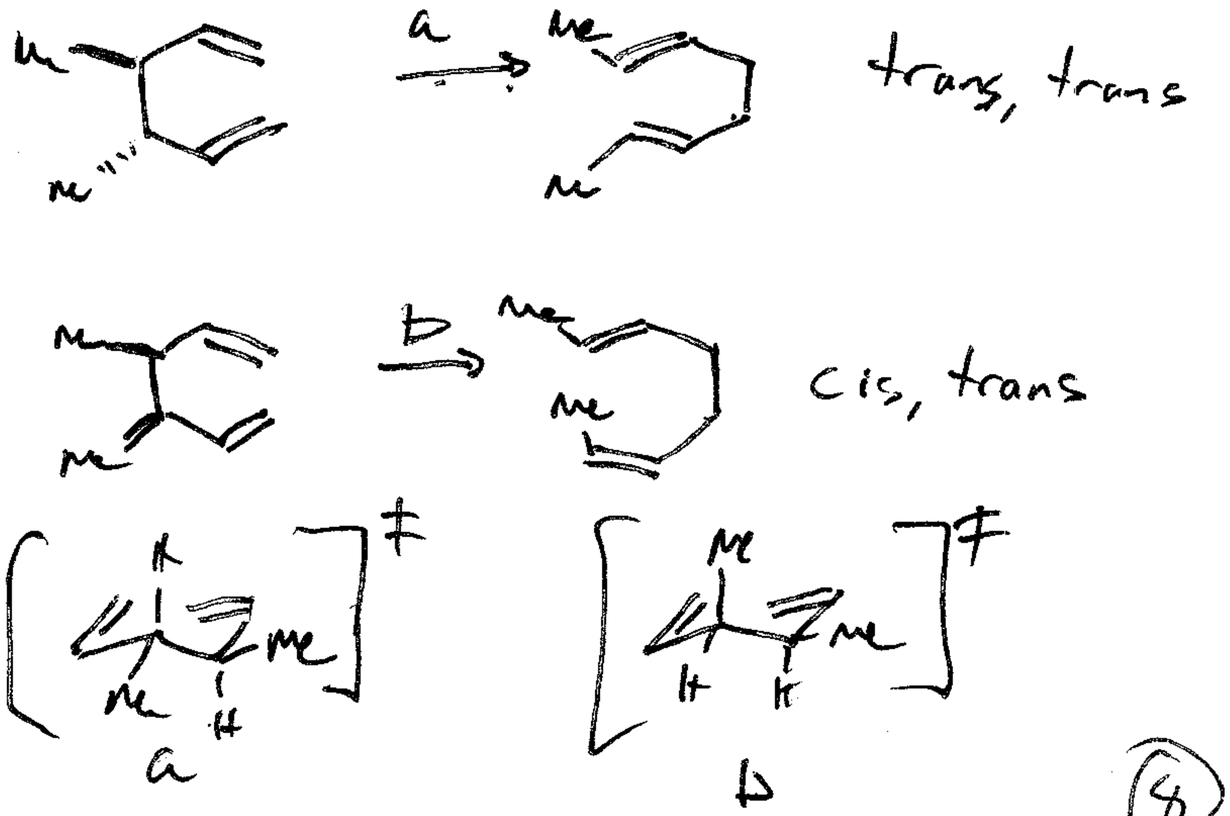
Z-Enolates



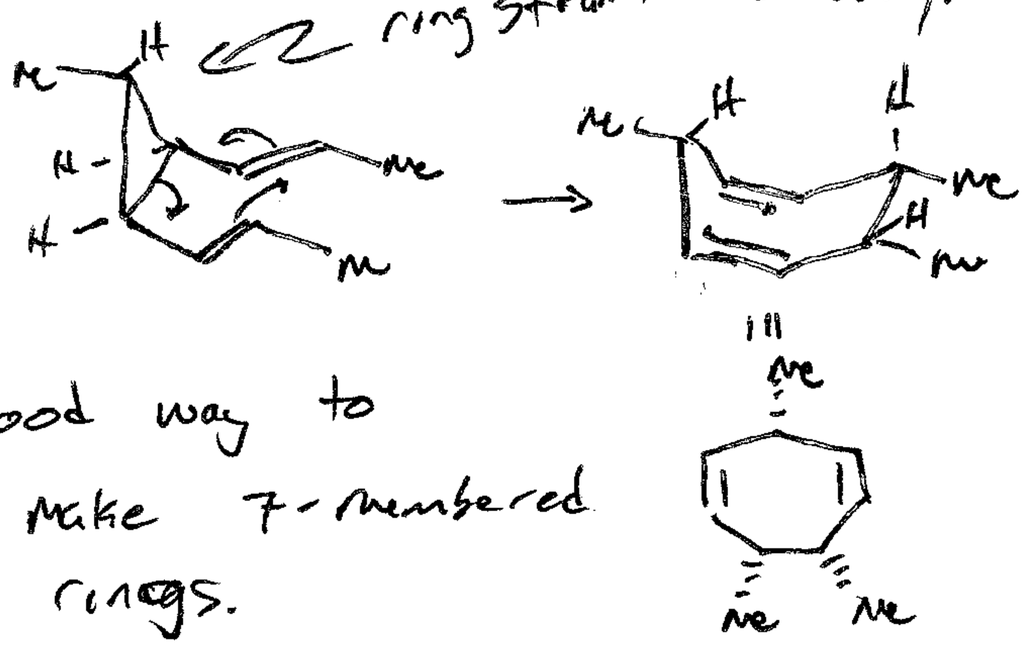
overall strategy



Cope

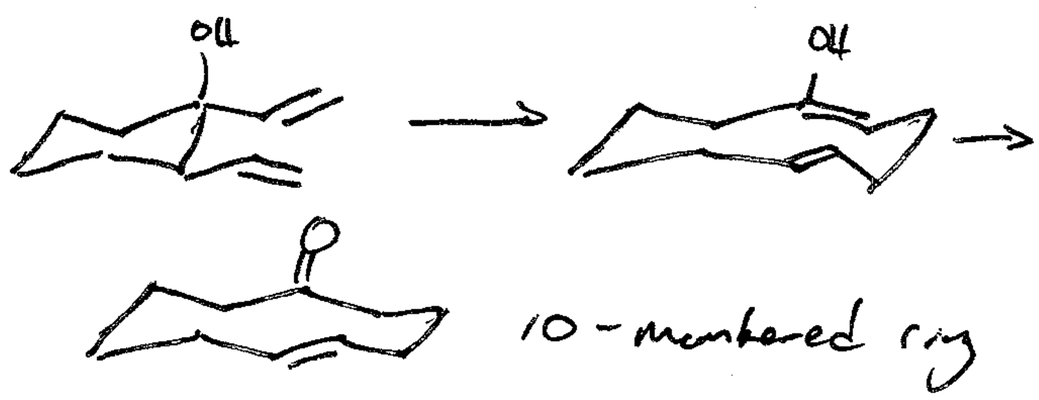


Divinyl cyclopropane - Ring strain to drive cope

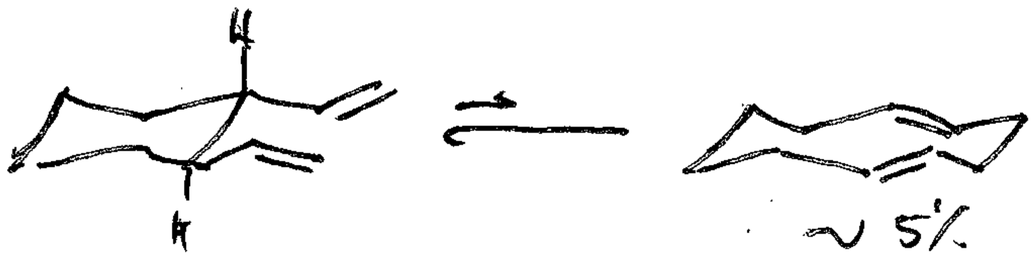


good way to make 7-membered rings.

[3,3] rearrangements good to make medium Rings

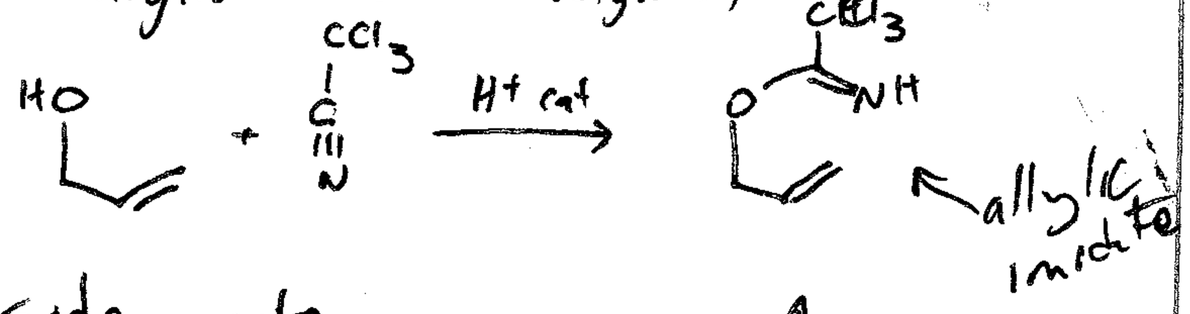


contrast however

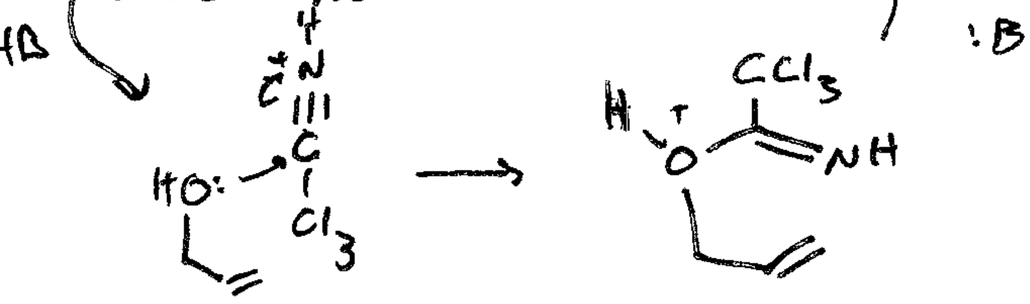


Med. Ring more strained.

Aza-Claisen (Overman Rrgmt)
(or allylic imidate Rrgmt)



(side note



this is a Pinner Synthesis

General way to make imidates

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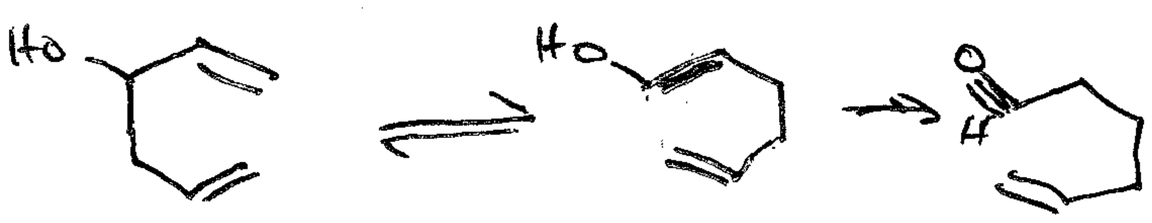
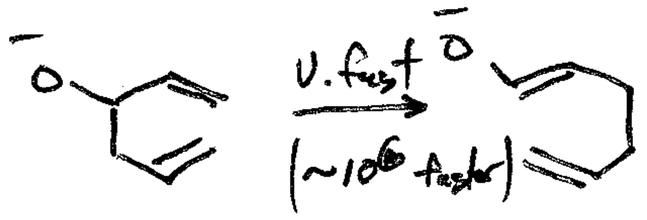
oxy-cope

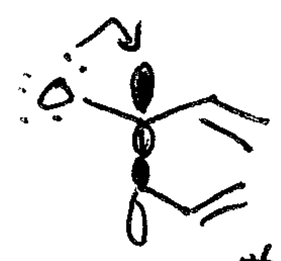


C-O π bond!

anionic oxy cope - charge accerated

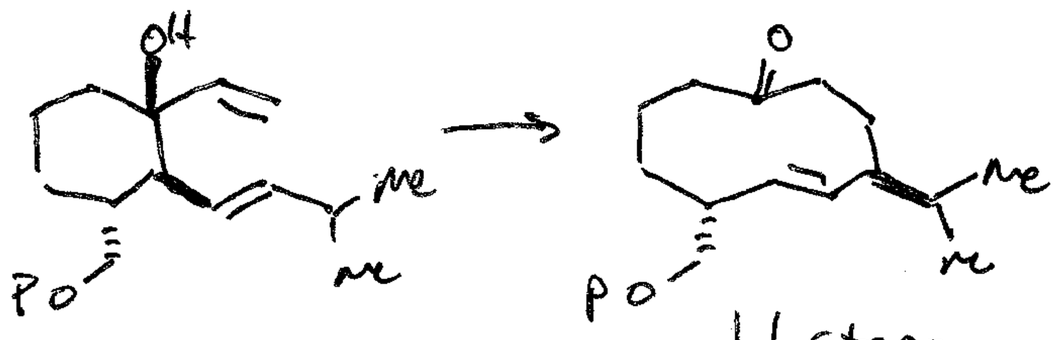


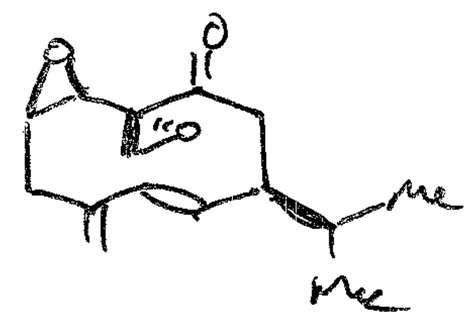
(Other charge accel. 3,3 rxns)



$n_O \rightarrow \sigma^*_{C-C}$

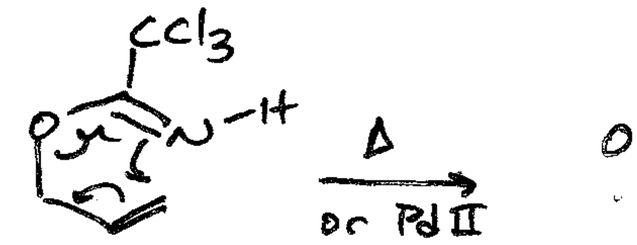
Recall



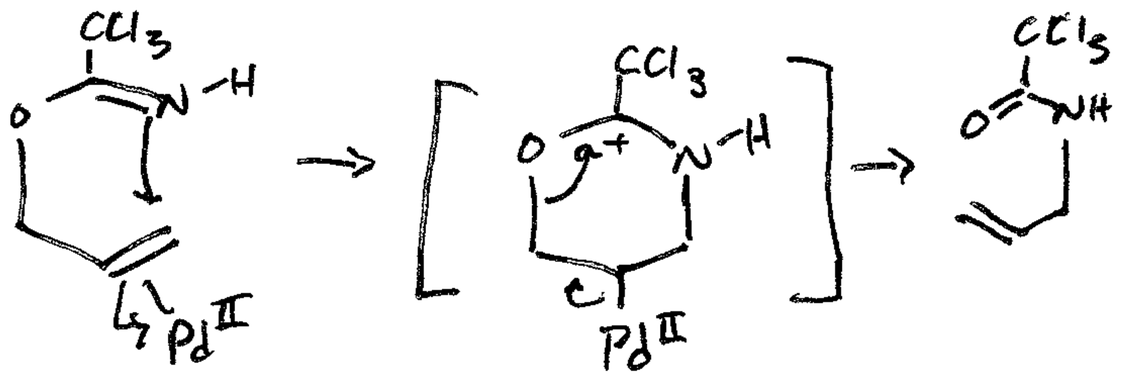


(±) Periplanone B

Still JACS, 1979, 101, 2493

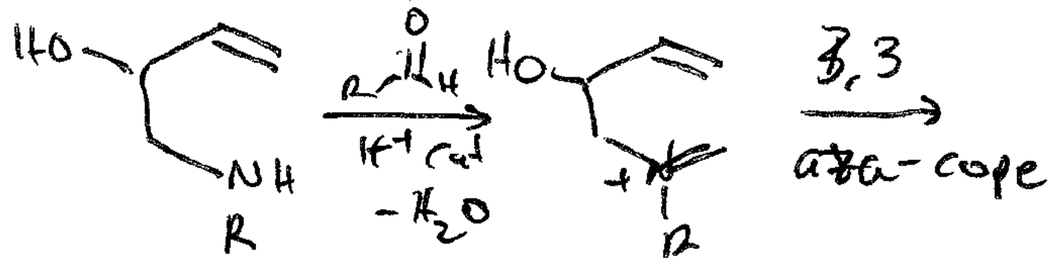


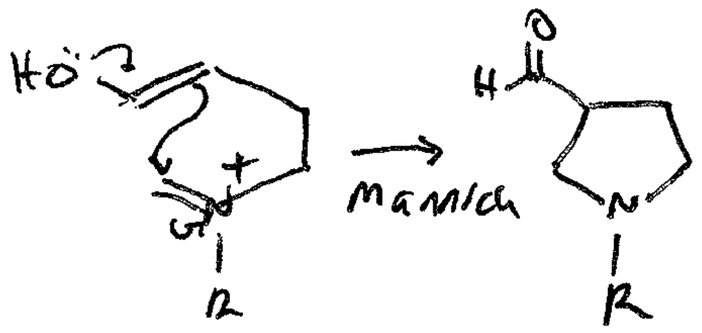
Note on Pd^{II} cat



General for Sigmatropic Rxns (9)

Tandem Rxns - overman

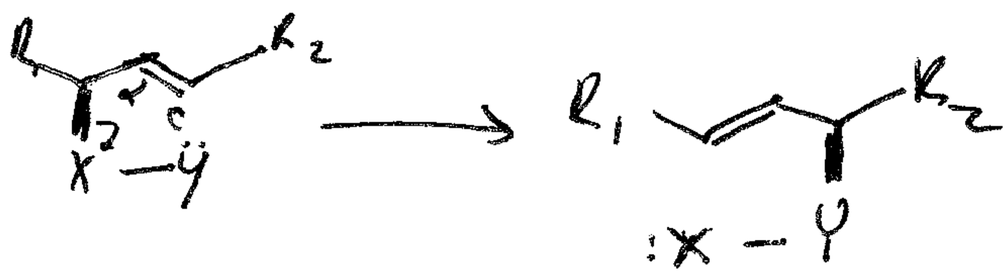




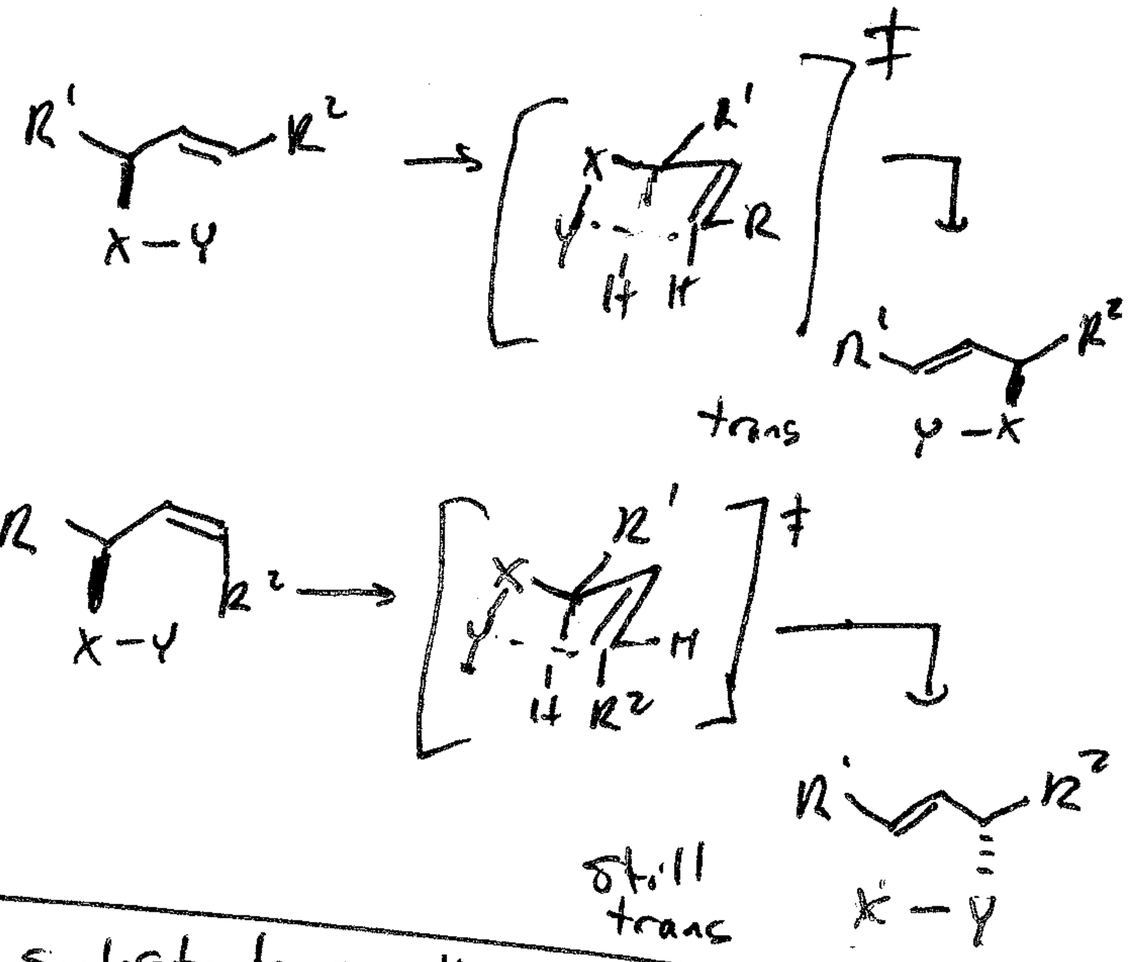
Reading Chapter 6 ~~6~~ 5 B

[2,3]- sigmatropic

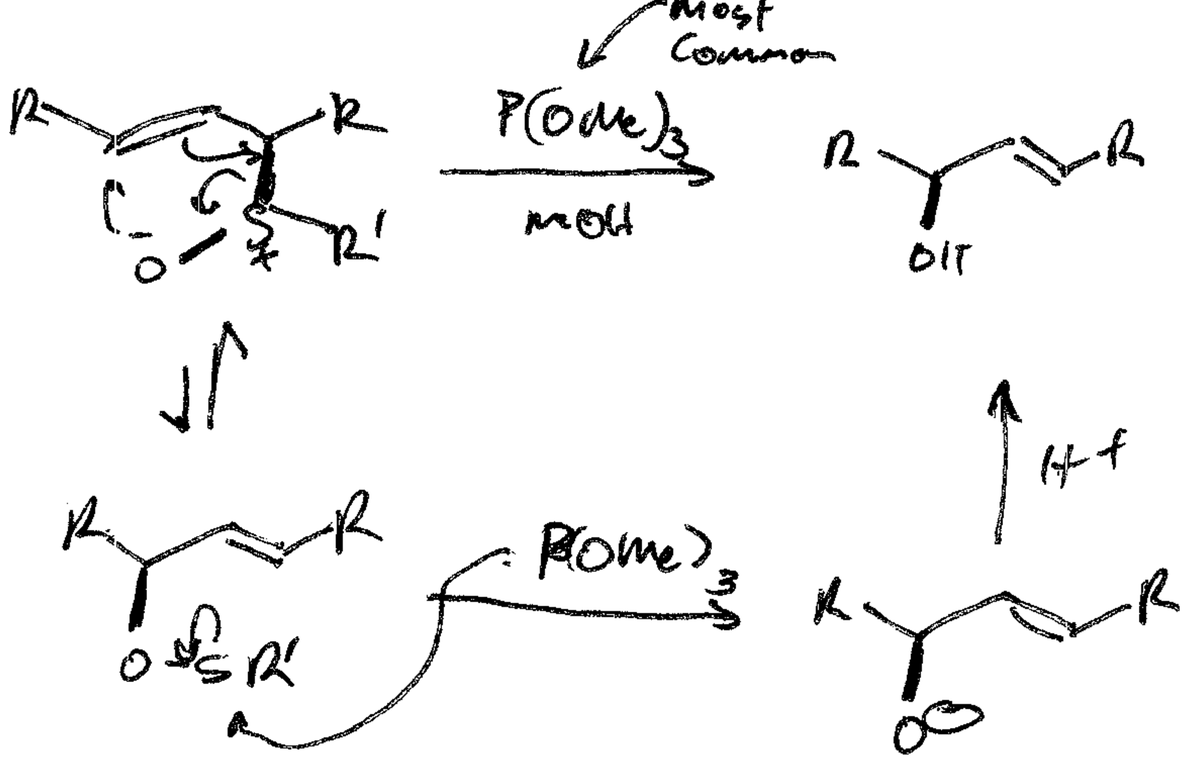
General



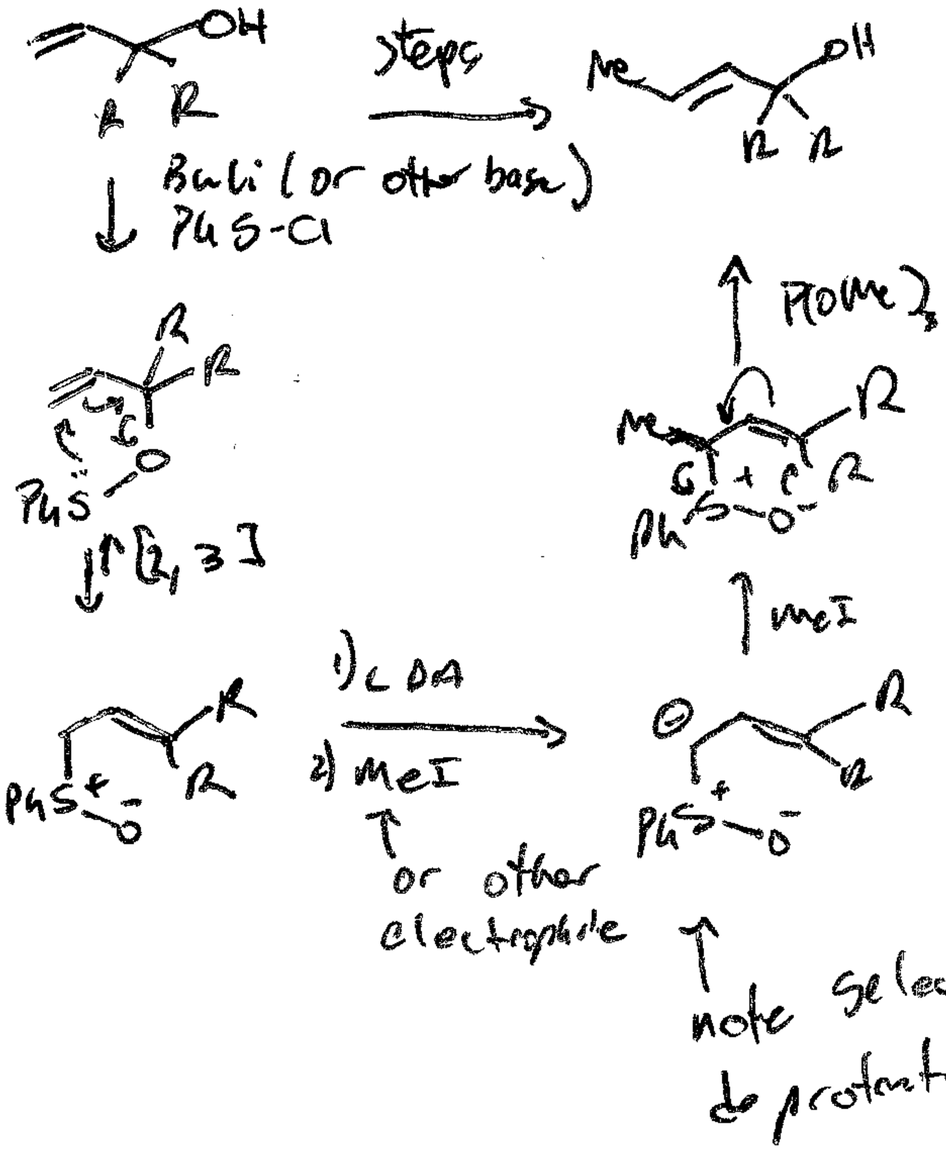
Stereotransfer - General - alkenes(s)



Mislow-Evans Rearrangement



Substrate synthesis

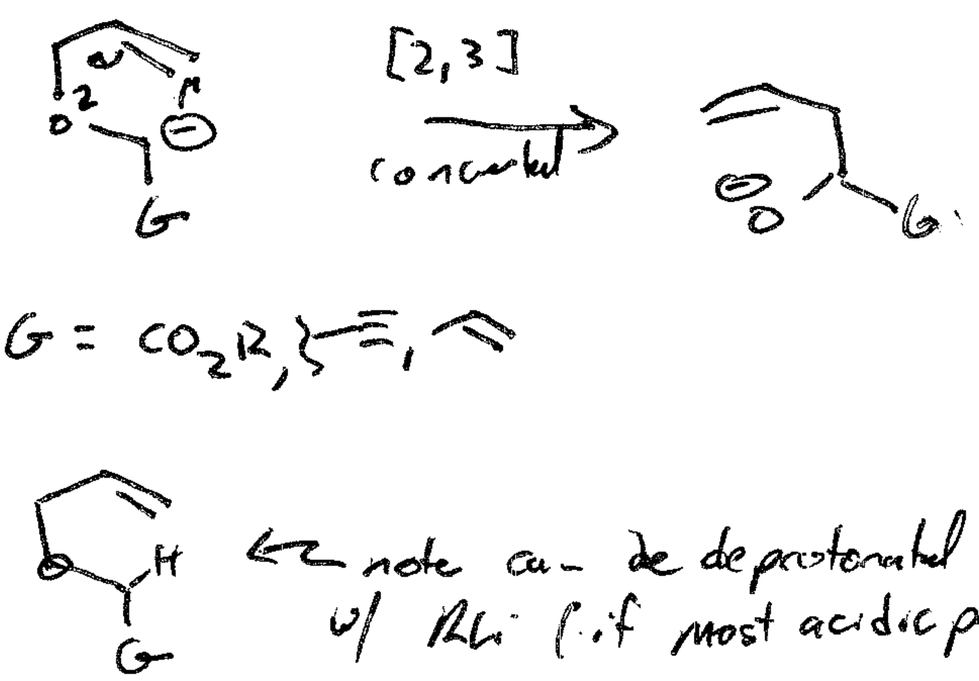


Example

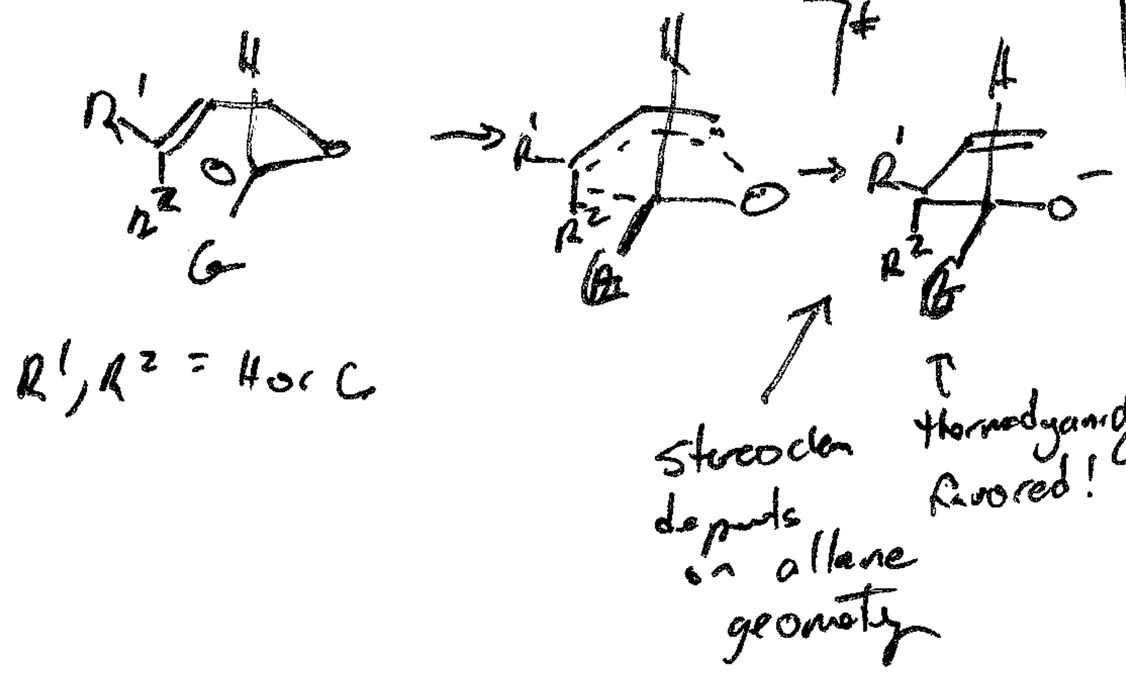
JOC, 1991, 56, 3473

(Stereochem due to steric control)

2,3 W. Hg



Nakai model

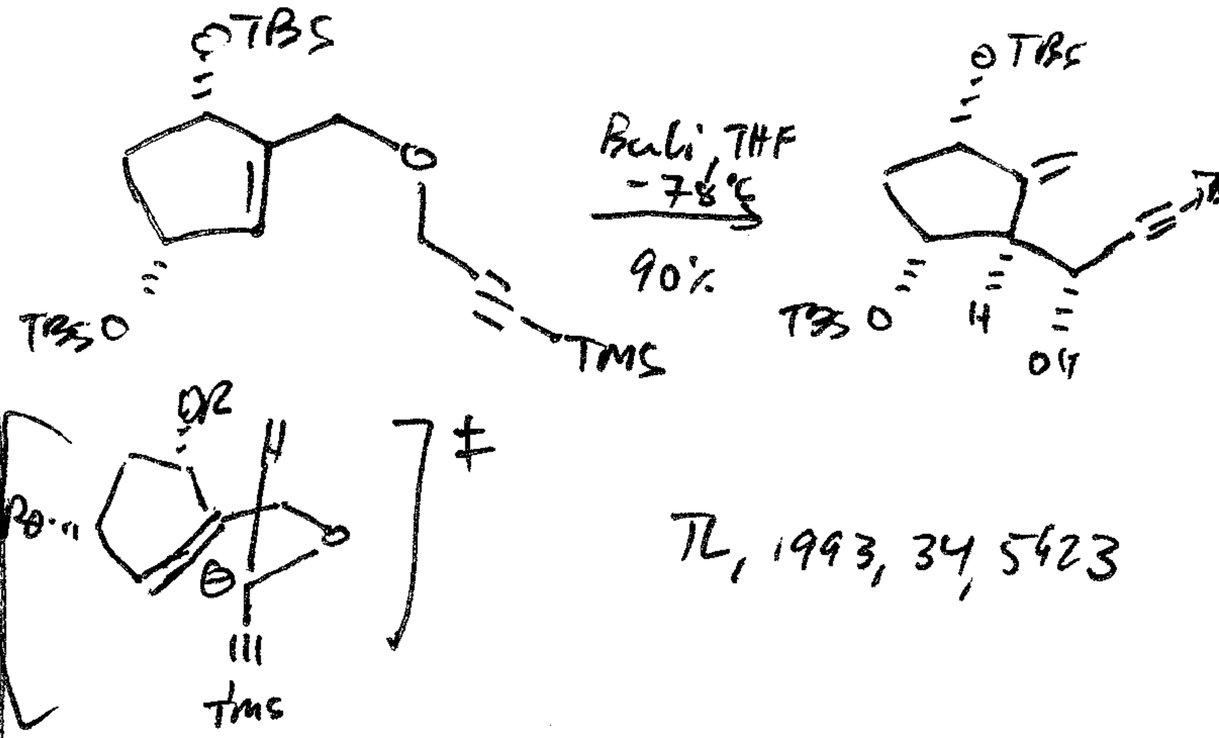


R^1, R^2 = H or C

stereochem depends on allene geometry

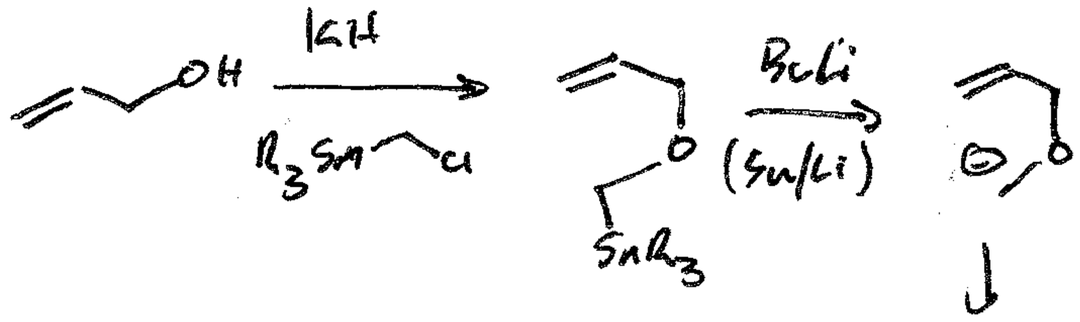
T Hammond-Curtin favored!

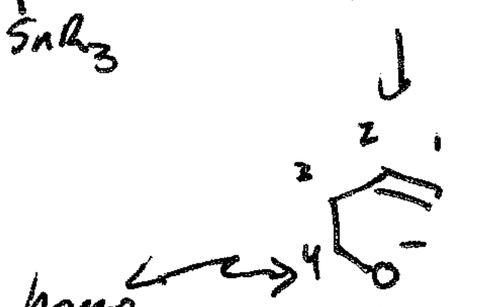
Example



TL, 1993, 34, 5423

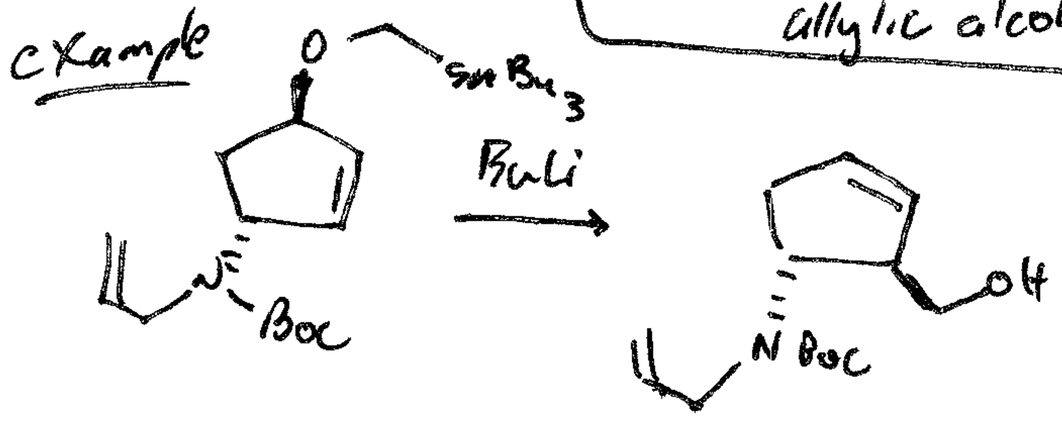
Still - Wittig





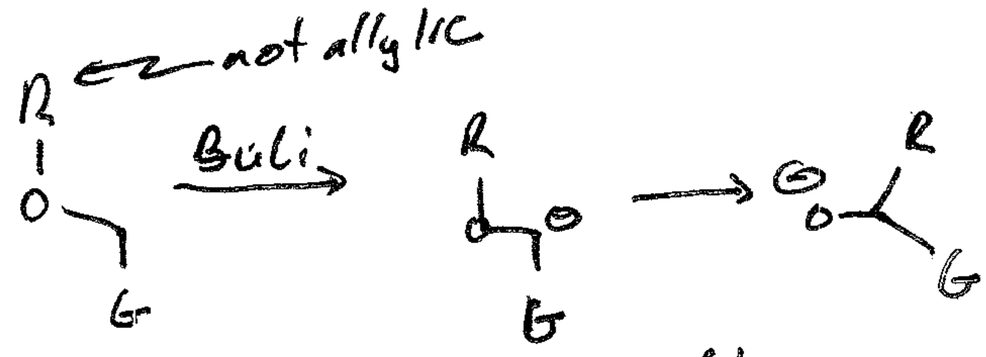
homo allylic alcohol!

example



JOC, 2003, 68, 2913

1,2 Wittig



not allylic

not concerted!