

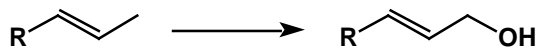
OXIDATION OF C-H BONDS

Allylic Oxidation

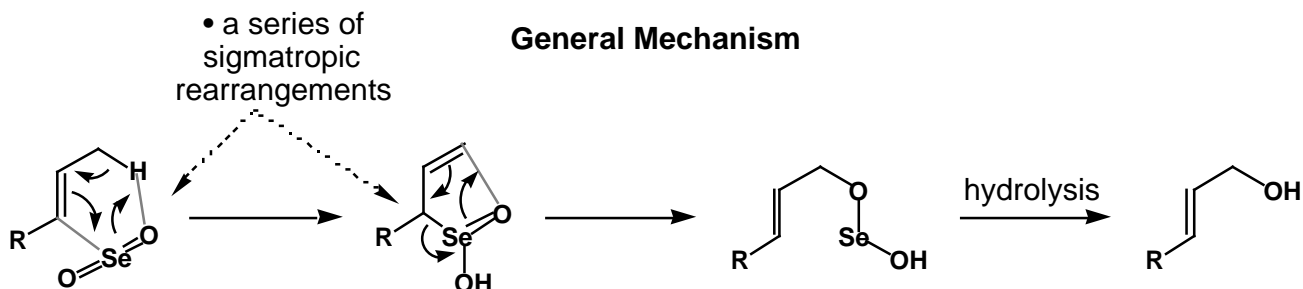
Reagent:



Transformation:



General Mechanism

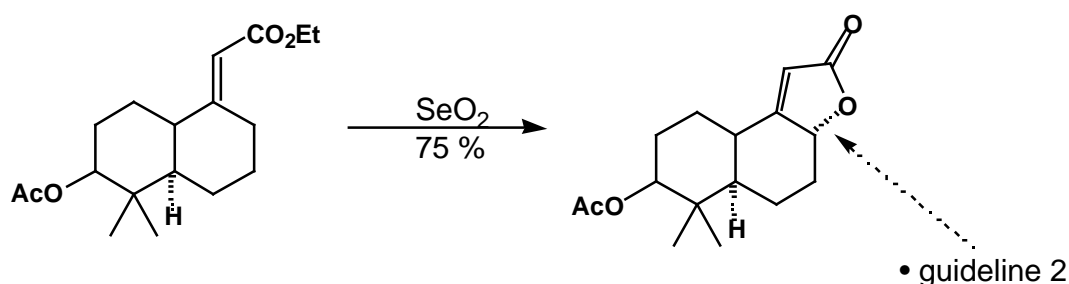
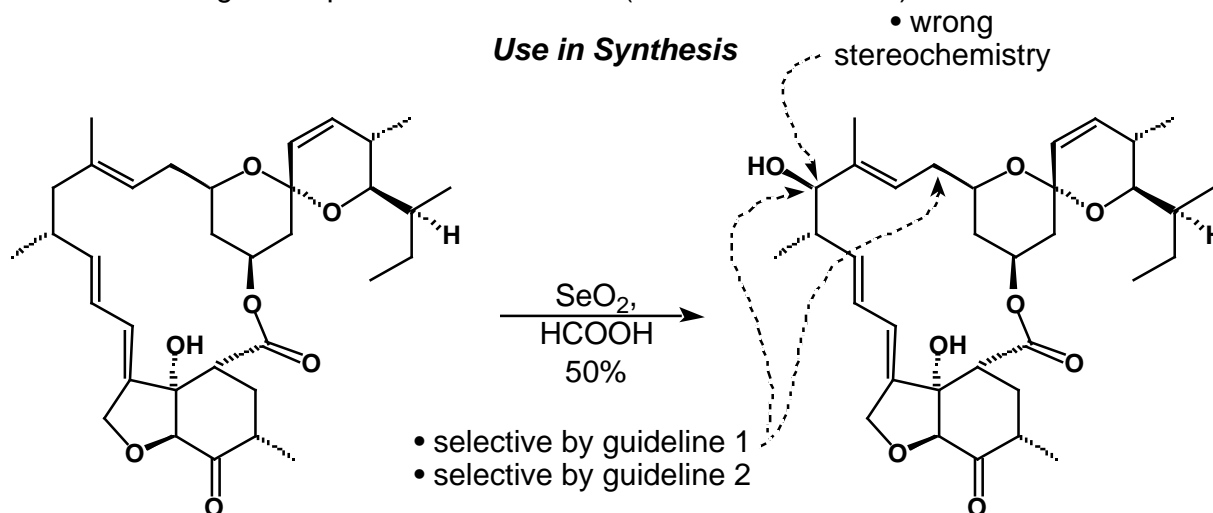


- SeO_2 toxic and hard to remove from product
- Catalytic variant developed using TBHP as stoichiometric co-oxidant
- Problem of side-reactions especially if alkene in ring
- Reaction also functions with other reagents such as PDC

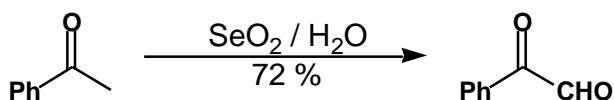
Guidelines for Predicting Product

1. Hydroxylation occurs to the most substituted end of alkene
2. Order of oxidation is $\text{CH}_2 > \text{CH}_3 > \text{CH}$
3. If alkene in ring, oxidation will occur in ring if possible (but Bredt's rule applies)
4. Rearrangement products can and will (more often than not) be formed

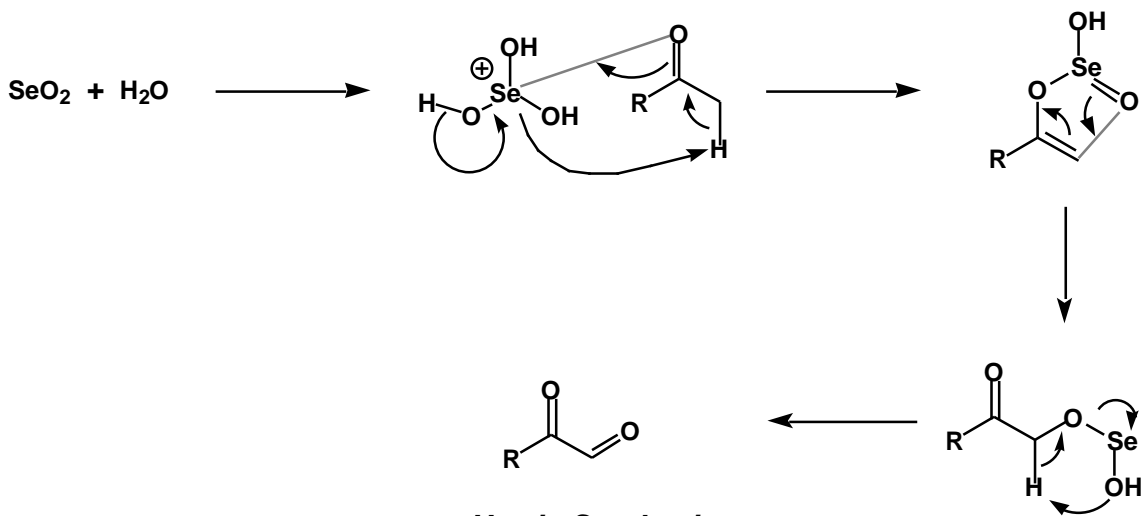
Use in Synthesis



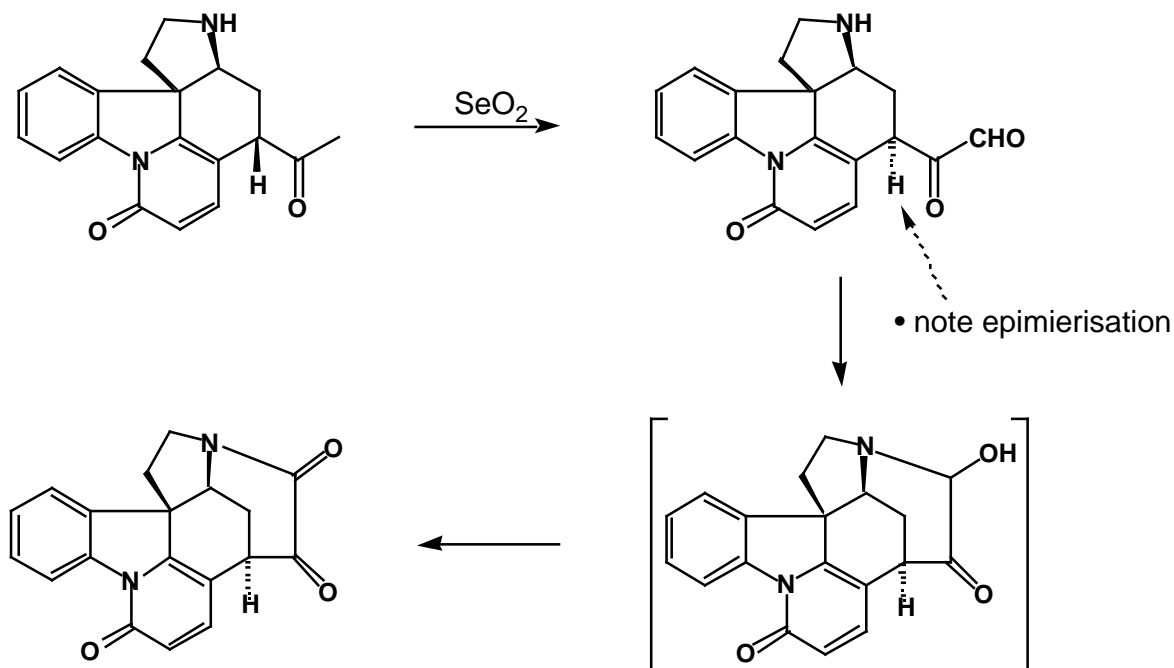
Related reaction: Formation of Dicarbonyl Compounds Transformation:



Mechanism



Use in Synthesis



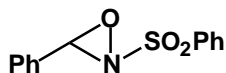
What have we learnt?

- The position - to a double bond can be oxidised
- A set of guidelines allow some degree of predictability to this reaction
- The reaction proceeds *via* a series of sigmatropic rearrangements
- A related reaction results in the synthesis of dicarbonyl compounds

Oxidation of Activated C–H Bonds α -Hydroxylations

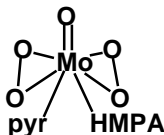
Reagent:

Davis' Oxaziridine

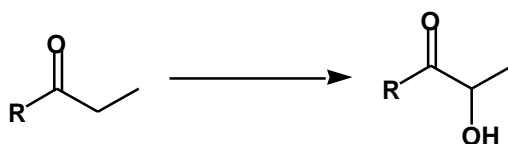


*Oxidodiperoxymolybdenum(pyridine)-
(hexamethylphosphoric triamide)*

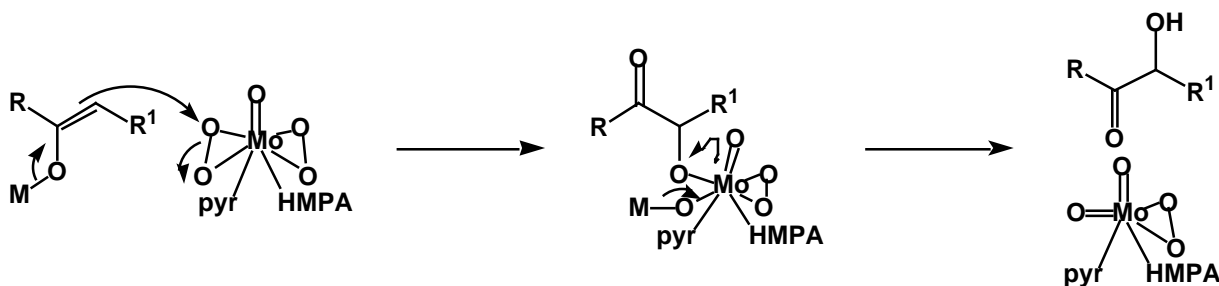
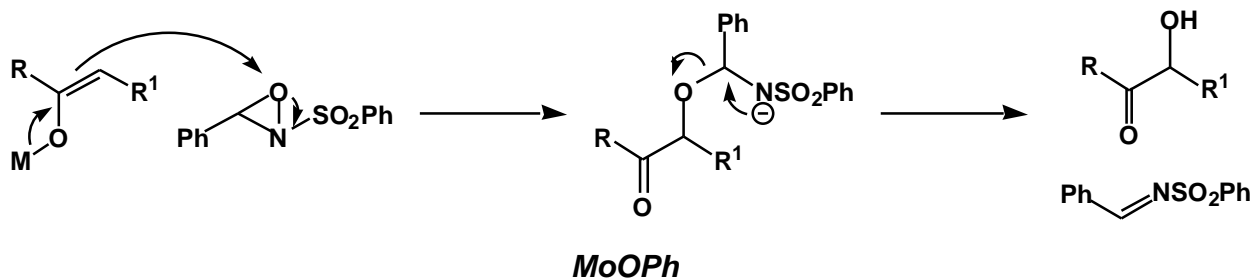
MoOPh



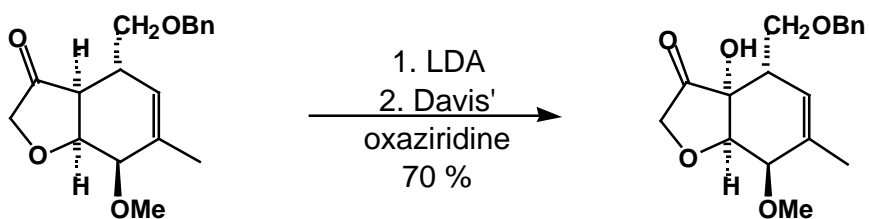
Transformation:



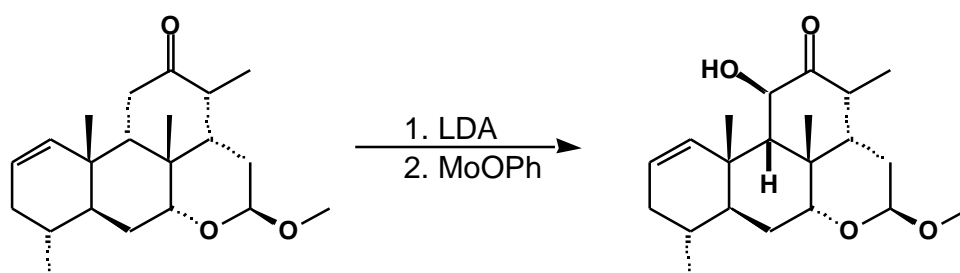
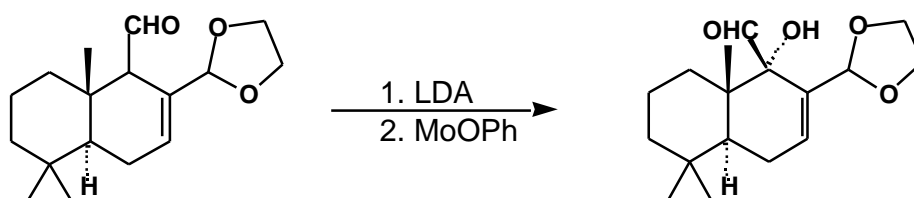
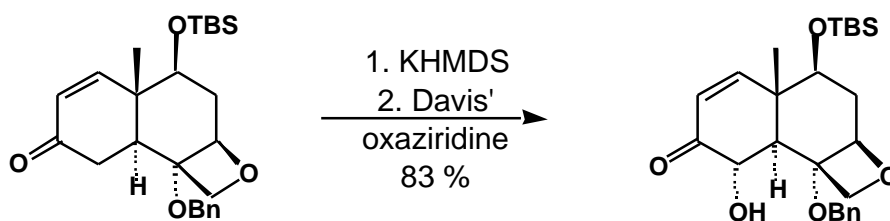
General Mechanism
Oxaziridine



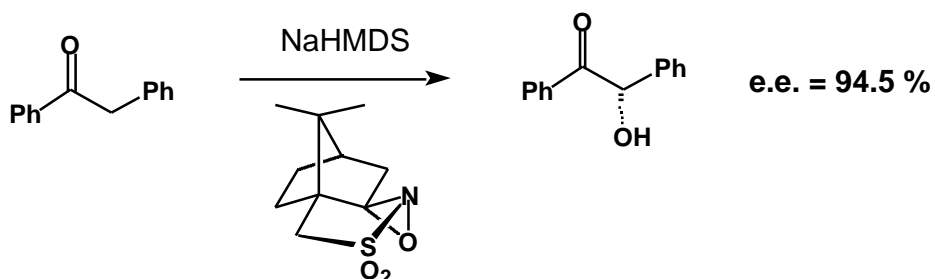
Use in Synthesis



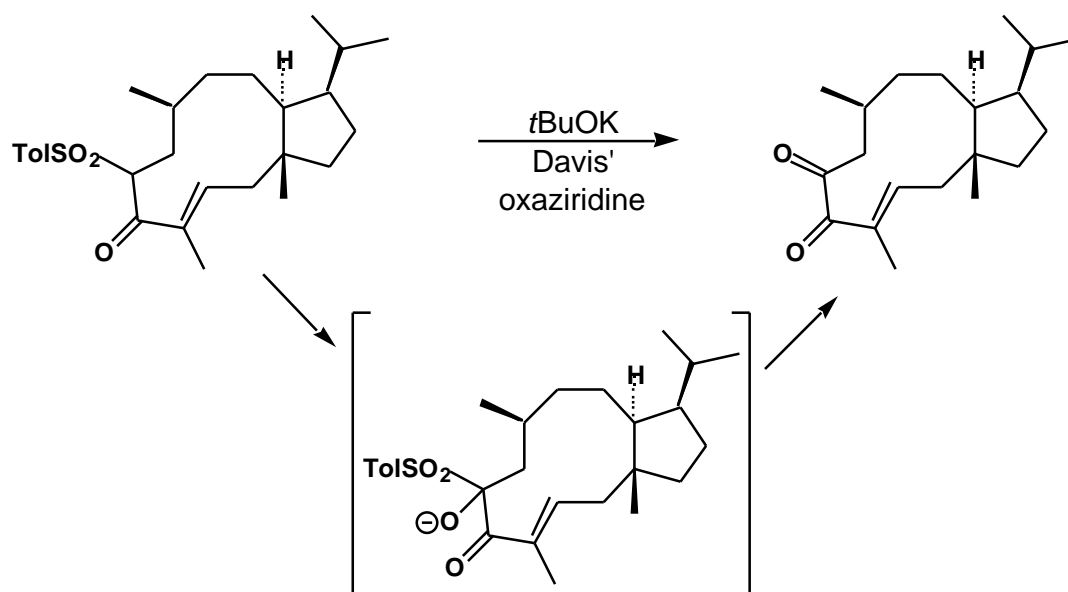
Use in Synthesis



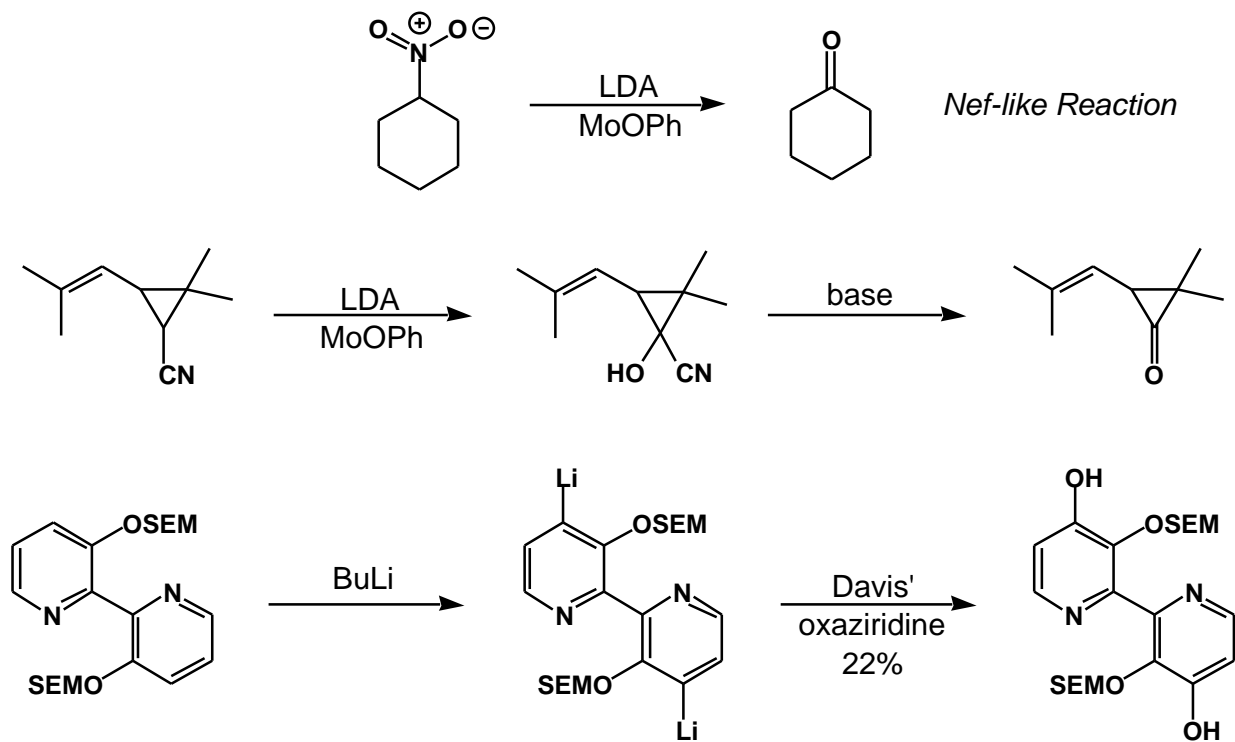
- Chiral oxaziridines can be prepared allowing *reagent control* asymmetric reactions



Reaction with other Stabilised Anions



Reaction with other Stabilised Anions



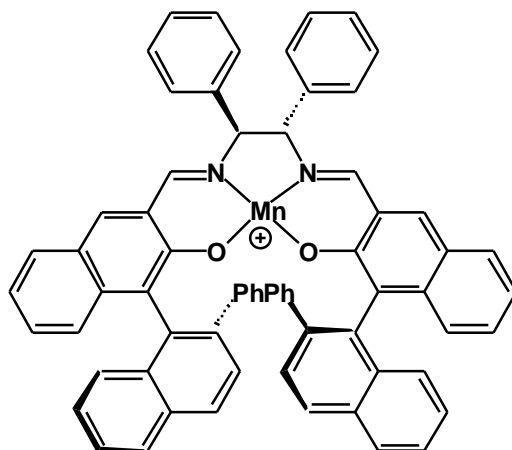
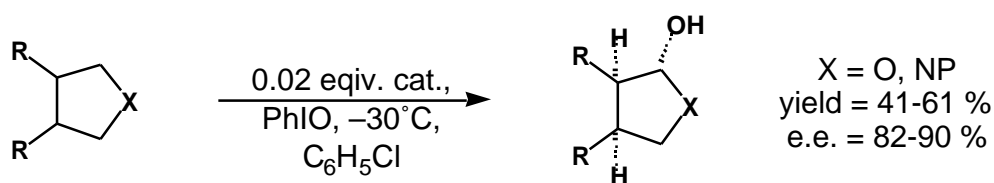
- Use of **oxaziridines** preferable to MoOPh (results & toxicity) but this is **substrate dependant**

What have we learnt?

- You can readily introduce hydroxyl group -to functionality
- Reaction can be achieved asymmetrically
- Reaction can be used to oxidatively cleave functionality

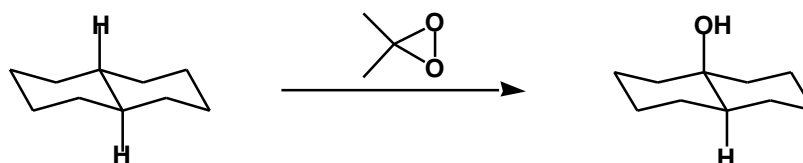
Miscellaneous C–H Oxidations

- Some recent developments in C–H oxidation
- Katsuki has used Mn-salen complexes to perform enantioselective C–H oxidations

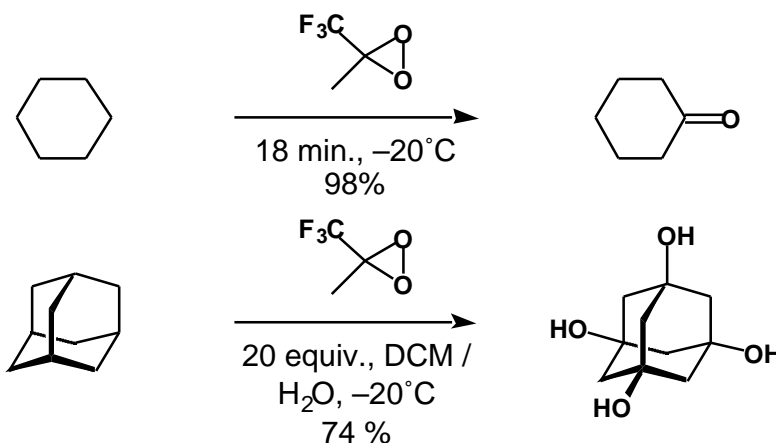


Oxidation of Unactivated C–H Bonds Dioxirane Strikes Back

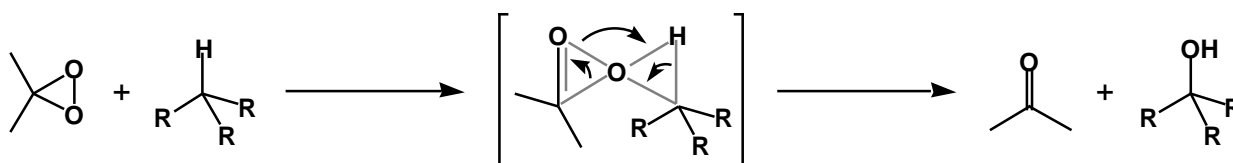
- Dioxiranes are amazingly reactive (sometimes)



- Can be quite slow so more reactive dioxiranes have been developed:



Possible Mechanism



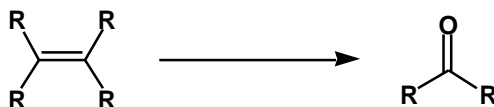
MISCELLANEOUS OXIDATIONS

Ozonolysis

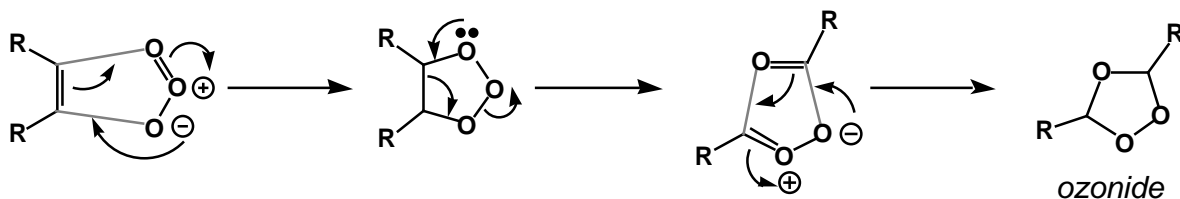
Reagent:

O₃, DMS or PPh₃ or LiAlH₄

Transformation:

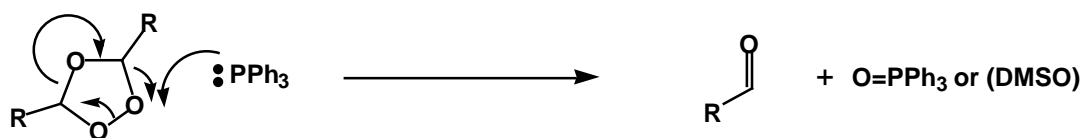


General Mechanism



- Ozonide then has to be broken down (they can be isolated but not advisable)

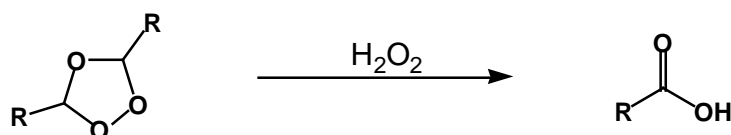
Decomposition with DMS, PPh₃ or H₂ Pd / C



Reductive Decomposition with LiAlH₄, NaBH₄

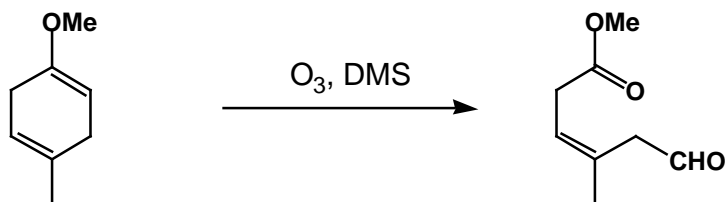
- Quite shockingly this gives the alcohol

Oxidative Decomposition with peracids or hydroperoxides

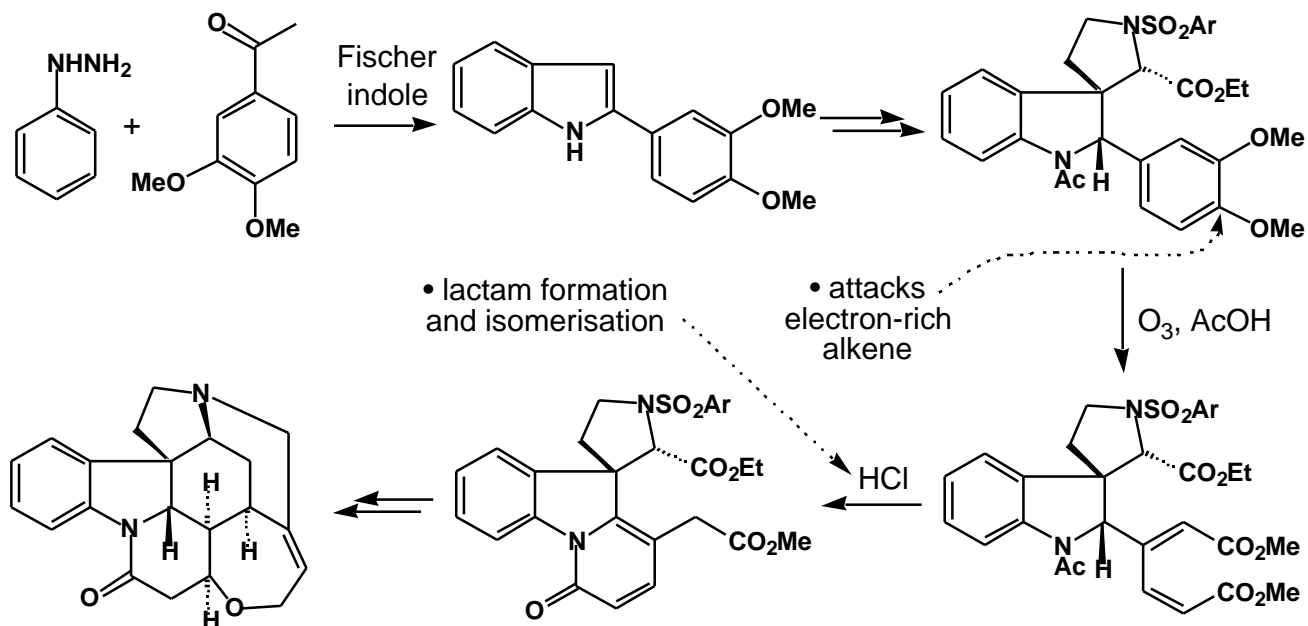


Selectivity

- More **electron-rich** alkenes react faster
- Enol ethers give esters on ozonolysis



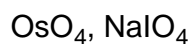
Use in Synthesis



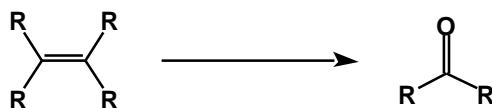
• Alternatively...

The Lemieux–Johnson Reagent

Reagent:

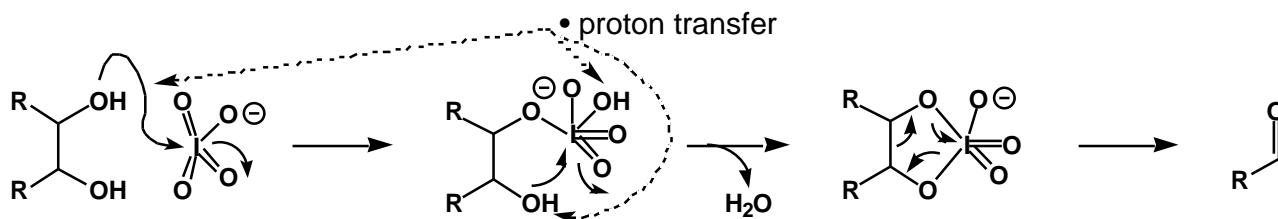


Transformation:



General Mechanism

- Use catalytic quantities of osmium which is reoxidised by the periodate
- Dihydroxylation as before (*vide supra*)
- NaIO₄ cleaves the diol...



What have we learnt?

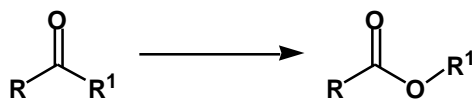
- Alkenes can be oxidatively cleaved in a number of ways

Baeyer-Villiger Oxidation

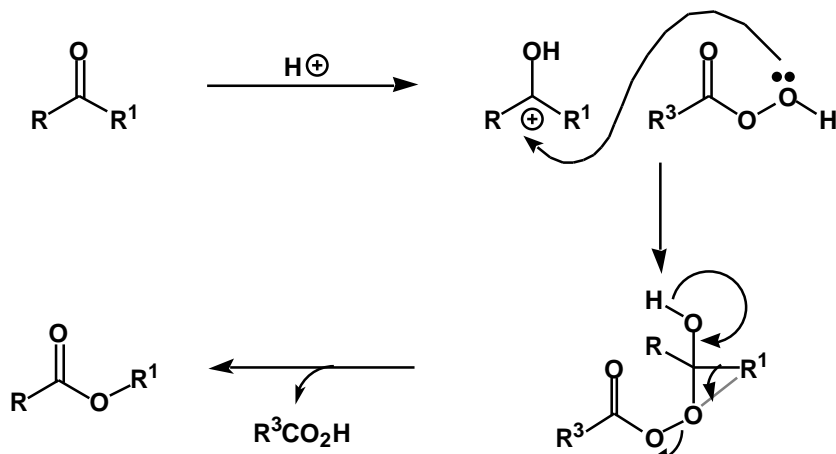
Reagent:



Transformation:

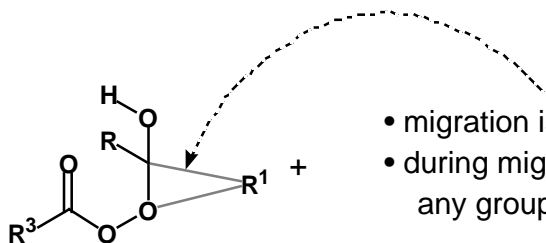


General Mechanism



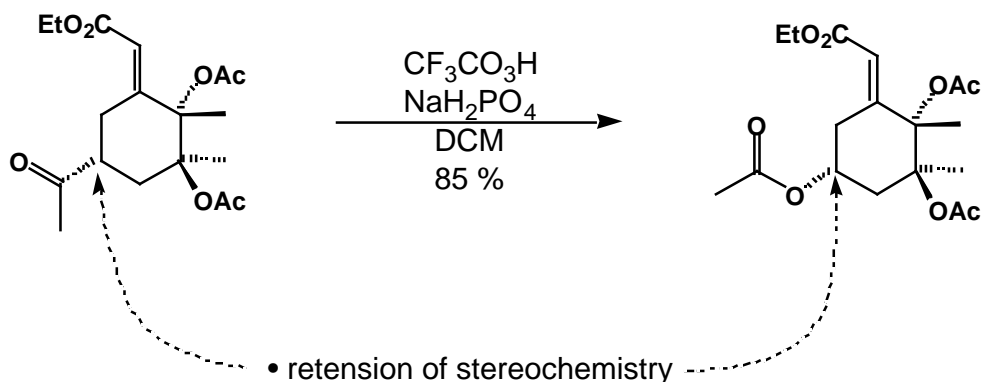
Migratory aptitude

- Unsymmetric ketones have a choice of which substituent will migrate
- Normally most nucleophilic group / group that can stabilise + charge best migrates
t-alkyl > cyclohexyl secondary alkyl benzyl > vinylic > primary alkyl > methyl
- Reason...

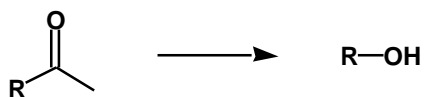


- migration is concerted
- during migration 2 e⁻ spread over 3 atoms
any group stabilising the electron deficiency will be favoured

- As the migration is concerted (bonds broken and formed at same time) it occurs with **retention of stereochemistry**

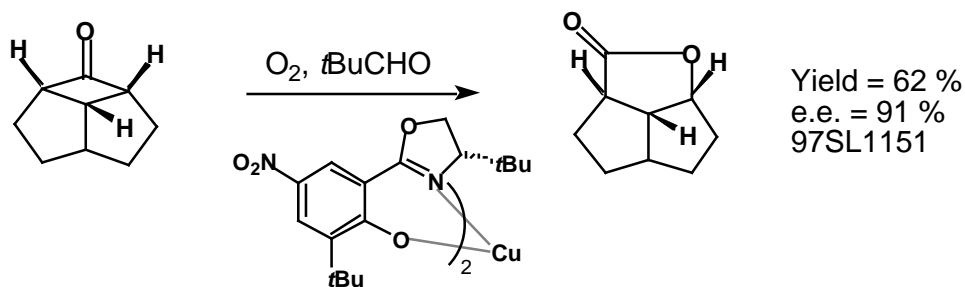
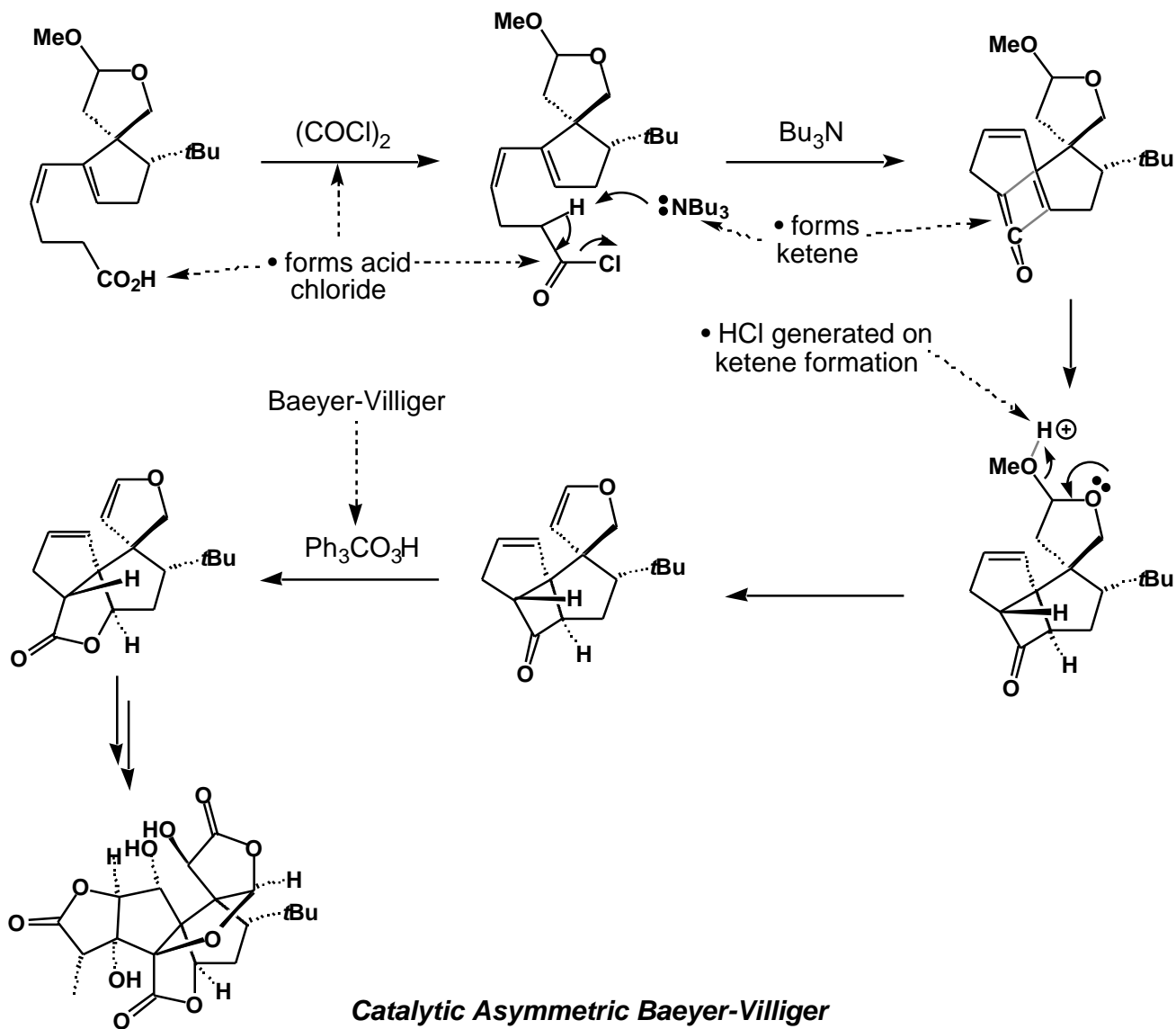


- The methyl group has a very poor migratory aptitude, consequently the Baeyer-Villiger reaction is an excellent way to make acetates
- Acetates are readily cleaved, therefore the Baeyer-Villiger is equivalent to:



Use in Synthesis

- **Problem:** if alkenes are present a possible competitive reaction is *epoxidation*
- **Conditions:** under acidic conditions Bayer-Villiger favoured
- **Conditions:** *m*CPBA + inert solvent at low temperature encourages epoxidation

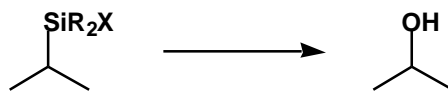


Tamao-Fleming Oxidation

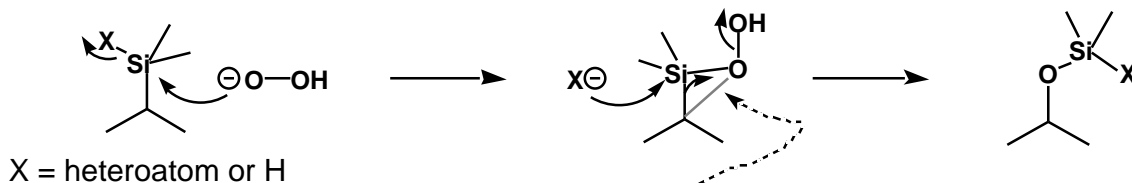
Reagent:

KF, KHCO₃, H₂O₂ or EX / RCO₃H / base

Transformation:



General Mechanism

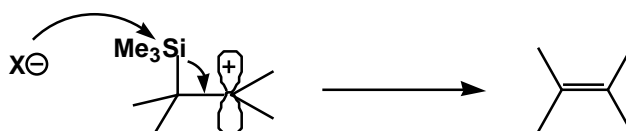


X = heteroatom or H

• concerted migration so
retention of stereochemistry

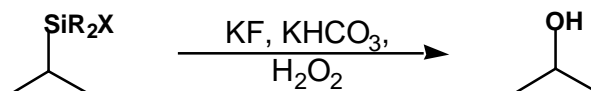
Use in Synthesis

- Silyl groups relatively unreactive
- C-Si bond only easily broken when carbon functionality allows it eg:



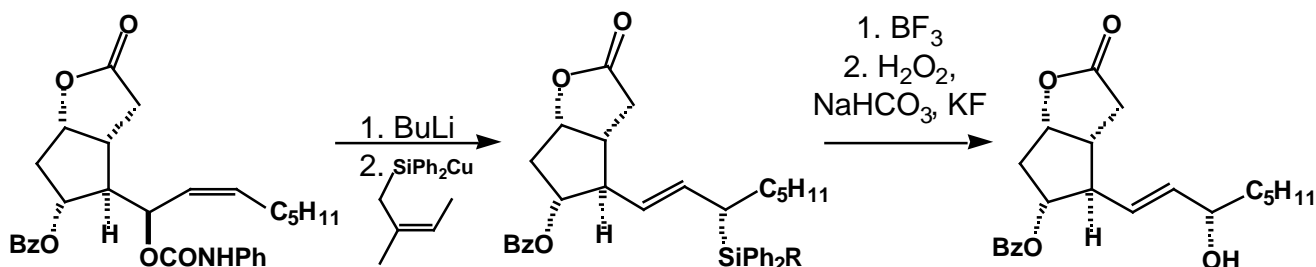
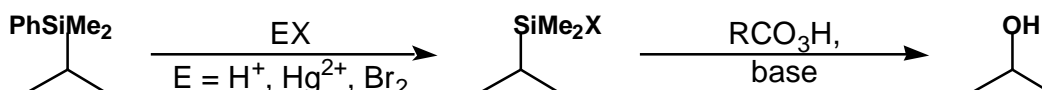
- Silyl group very useful - can be thought of as **super-proton** - it activates double bonds, encourages substitution rather than addition, controls regio- and stereochemistry (97CR2063)

Tamao Oxidation



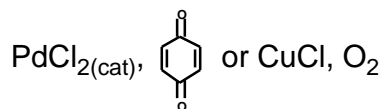
Fleming Oxidation

- More useful silyl groups BUT harsher conditions

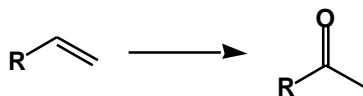


Wacker-Type Oxidations

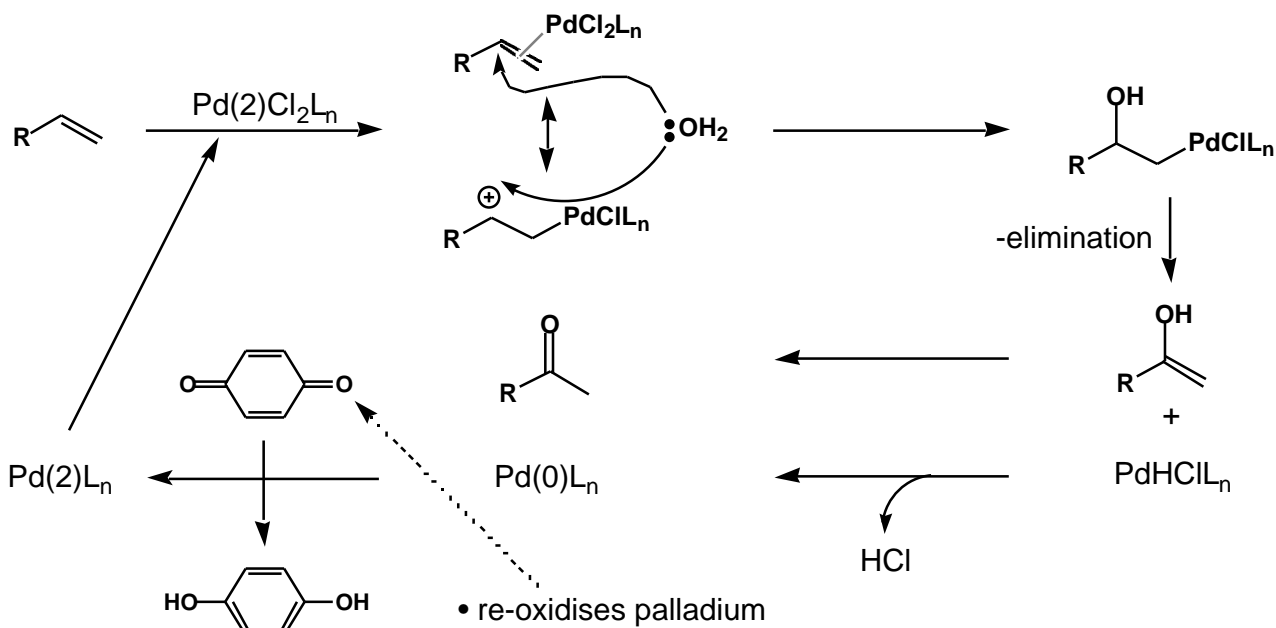
Reagent:



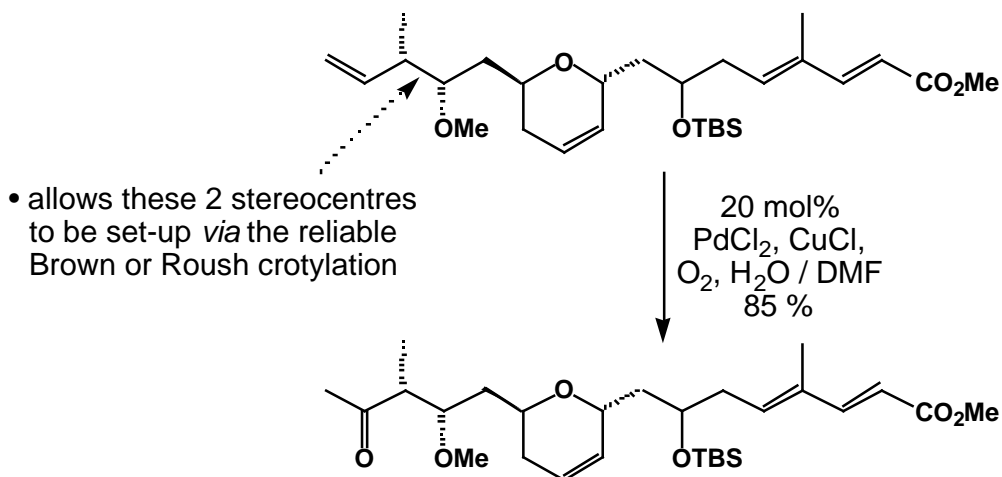
Transformation:



General Mechanism

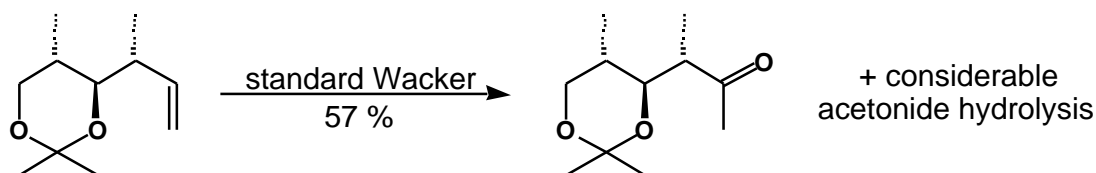


Use in Synthesis



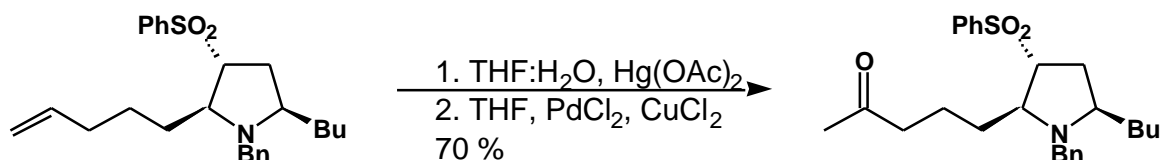
- Problems:** alkene isomerisation
chlorination (especially if CuCl_2 used)
regiochemistry
acid sensitivity of molecule as HCl produced

Modifications to the Wacker Reaction Smith's Modifications



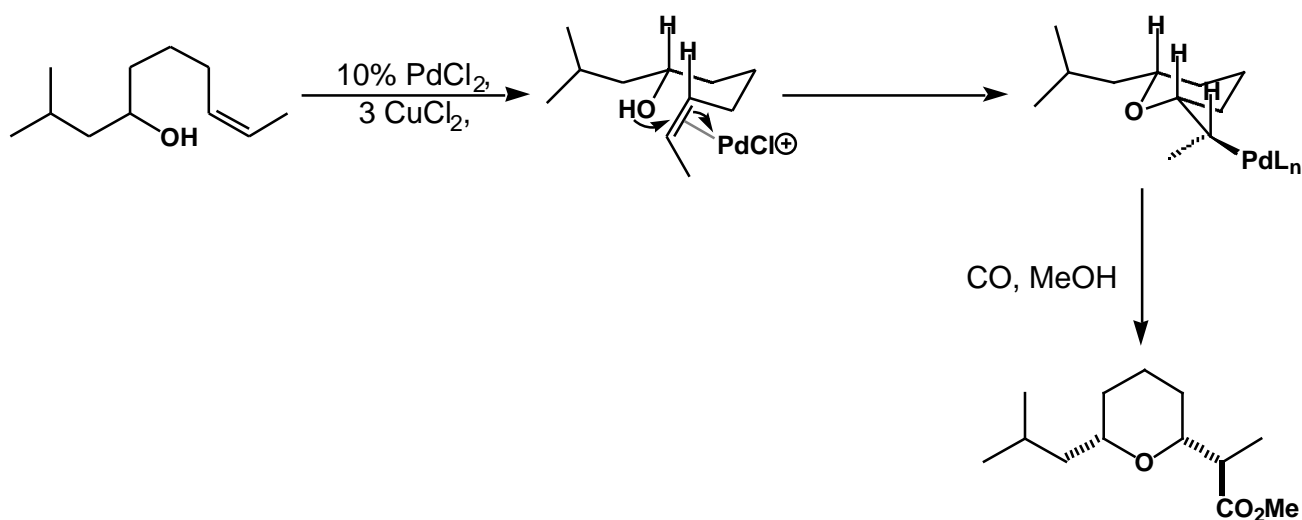
- HCl destroying product
- Replace CuCl with Cu(OAc)₂ - no HCl generated only the weaker AcOH
- allows catalytic copper to be used making work-up easier
- Yield increased to 86 %

Oxo-mercurial Variant



- Proceeds *via* oxo-mercuration then transmetalation
- Standard Wacker resulted in a maximum yield of 45 %

Intramolecular Wacker-Type Oxidation



Asymmetric Intramolecular Variant

