

Heteroatoms in Organic Chemistry

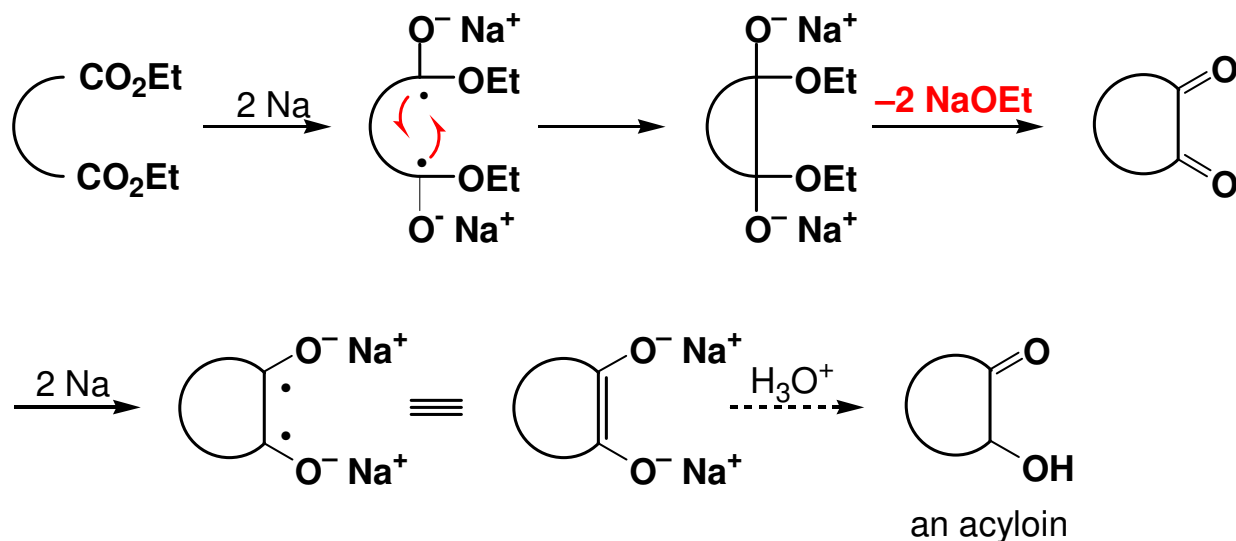
Second Year

Professor T. J. Donohoe (lectures 1-4)

HT 2006 : 8 Lectures: Thursday at 10 am (weeks 1-8)

DP: Lecture Theatre

HANDOUT 2: Silicon Reagents in Organic Synthesis



A copy of this handout is available at:

<http://users.ox.ac.uk/%7Emagd1571/finalpage/teaching2.html>

Heteroatoms in Organic Chemistry

Synopsis

Lectures 3 & 4 Silicon

- 1) General Features of Organosilicon Compounds
- 2) Use of Silicon as a Protecting Group for Organic Synthesis
- 3) Allyl Silanes in Organic Synthesis
- 4) Vinyl Silanes in Organic Synthesis
- 5) Utilising Silyl Stabilised Carbanions in Synthesis: the Peterson Reaction
- 6) Silyl Enol Ethers as enolate equivalents and protecting groups

Recommended books:

General: Organic Chemistry (Warren et al)

Organic Synthesis: The Role of Boron and Silicon, S. E. Thomas (Oxford Primer)

Some Modern Methods of Organic Synthesis, W. Carruthers (Cambridge)

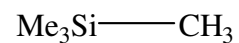
1) General Features of Organosilicon Compounds

a) Electronic configuration is

Carbon: $1s^2 2s^2 2p^2$

Silicon:

b) An electropositive



c) Bond Strengths are informative:

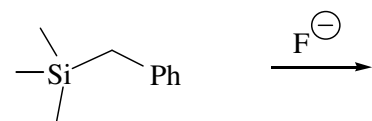


Some atoms are excellent nucleophiles for Si:

d) As are bond lengths



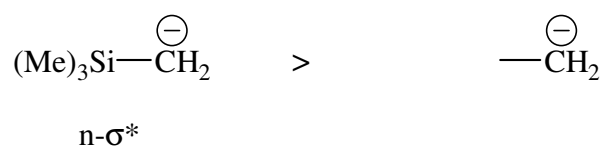
e) Substitution reactions are extremely



Consider CCl₄ versus SiCl₄

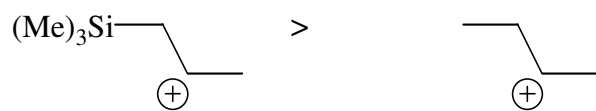
f) Two effects to think about

1) That Silicon stabilises ALPHA

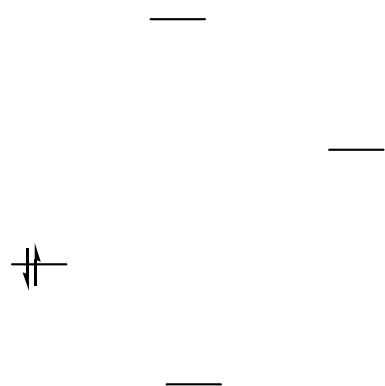


n 

2) Silicon also stabilises BETA



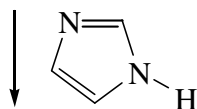
There are geometric constraints for this to happen:



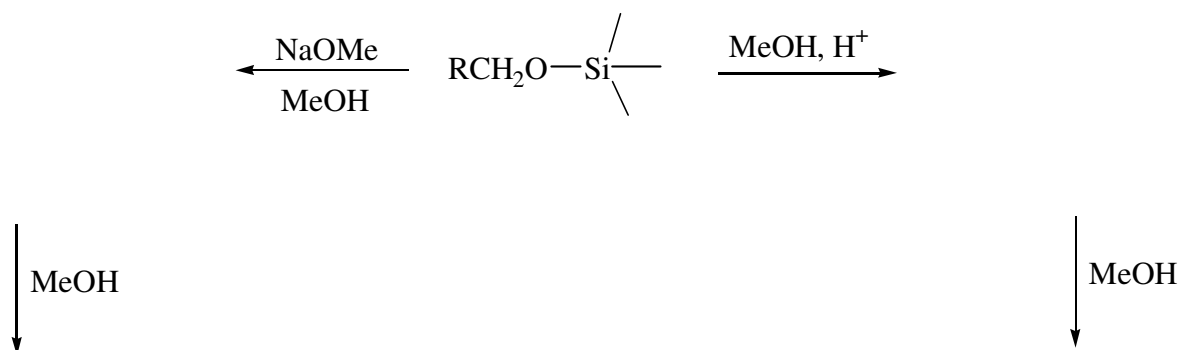
2) Use of Silicon as a Protecting Group for Organic Synthesis

What is a protecting group?

PROTECTION



DEPROTECTION



Also,



Often OTMS groups are too

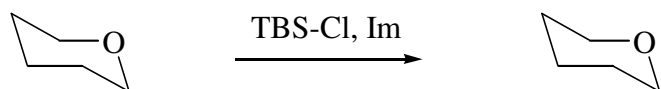
So, replace Me with bulkier groups

ROTMS

10^4

ROTBS

Can use this to silylate selectively



3) Allyl Silanes in Organic Synthesis

Undergo regioselective reaction with



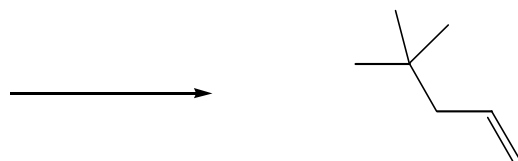
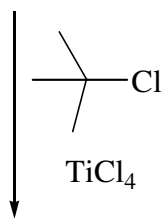
Electrophile can be:

Overall result is electrophilic

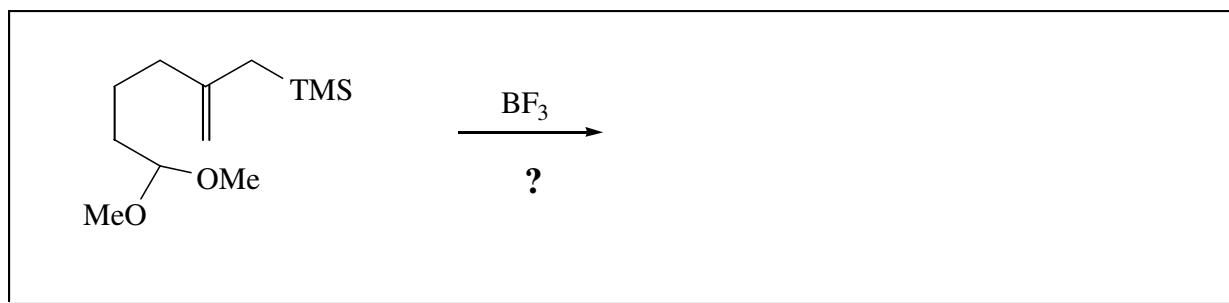
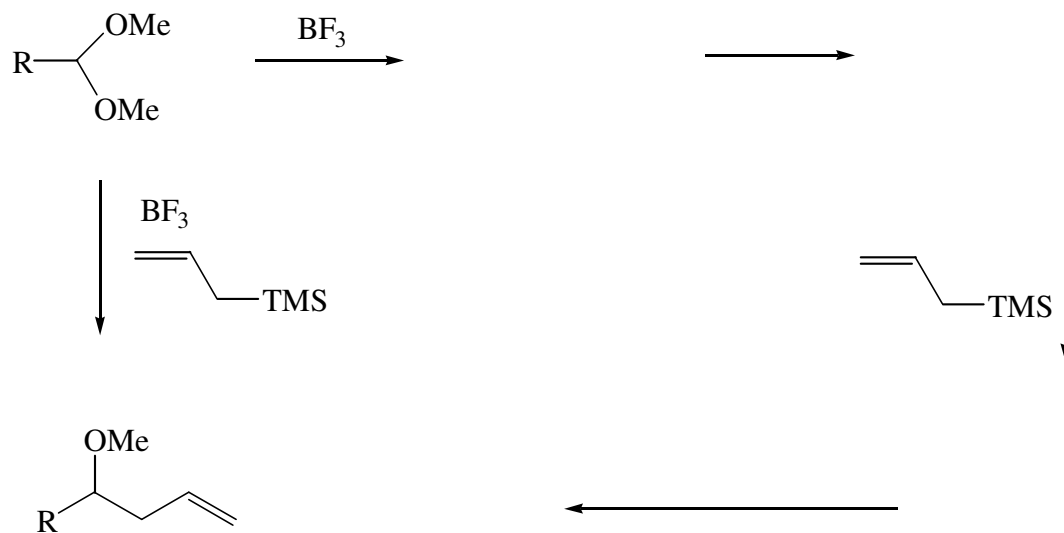
Synthesis



Reactivity



Acetals are potent electrophiles



4) Vinyl Silanes in Organic Synthesis

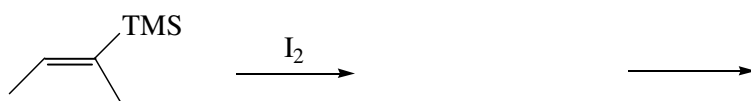
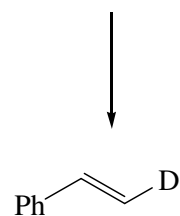
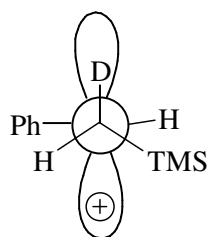
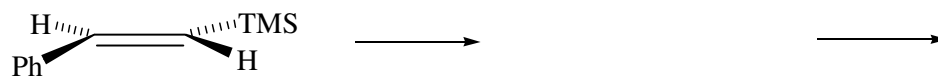
Again, the formation of a beta



retention is v. useful for

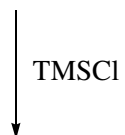


mech.

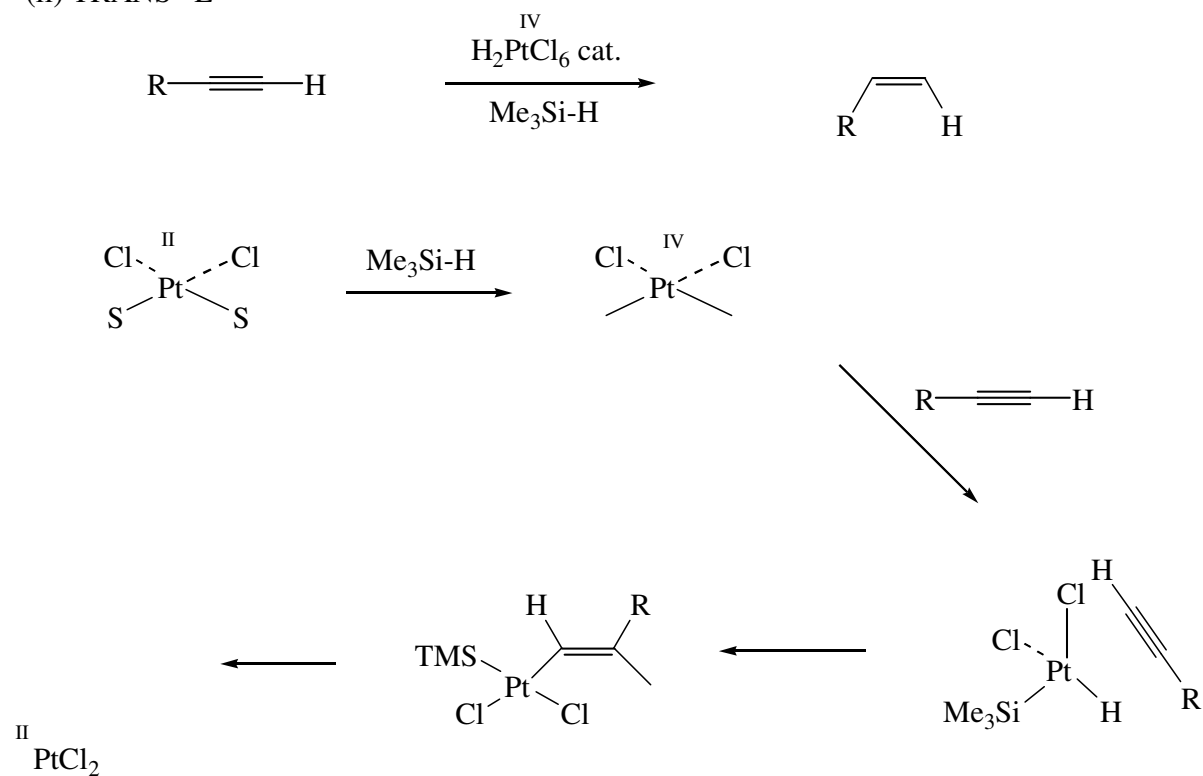


This reactivity is only useful if we can easily prepare the starting vinyl silanes as single

(i) CIS Z



(ii) TRANS E



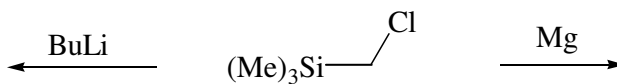
5) Utilising Silyl Stabilised Carbanions in Synthesis: the Peterson Reaction

Step 1: form the anion

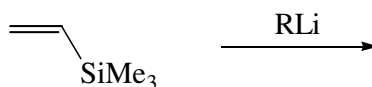
(i) Deprotonation



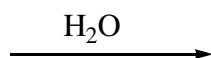
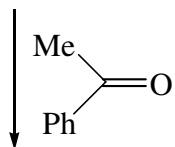
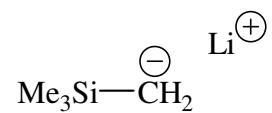
(ii) Halogen-Metal Exchange



(iii) Conjugate Addition

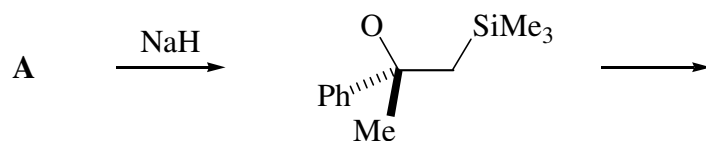


Step 2: react the anion with an aldehyde or ketone

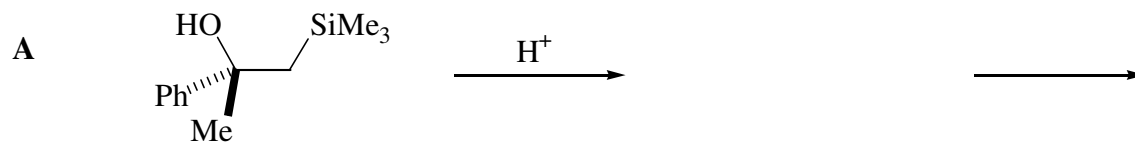


A

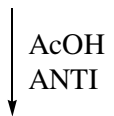
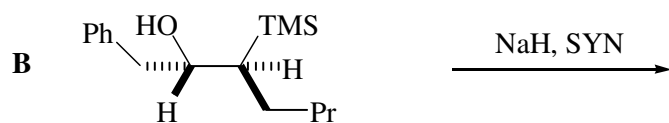
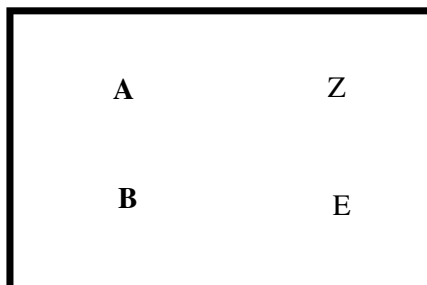
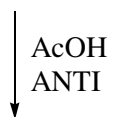
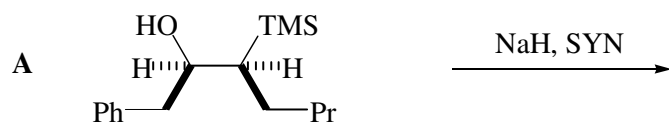
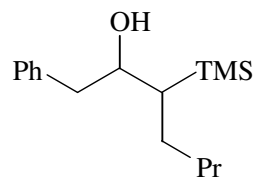
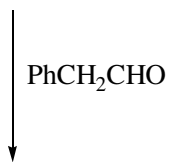
Step 3: collapse the intermediate to form an alkene



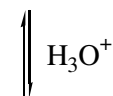
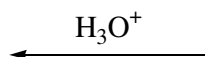
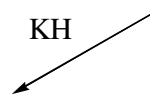
OR, Alternatively



This option gives high flexibility wrt the alkene geometry formed:

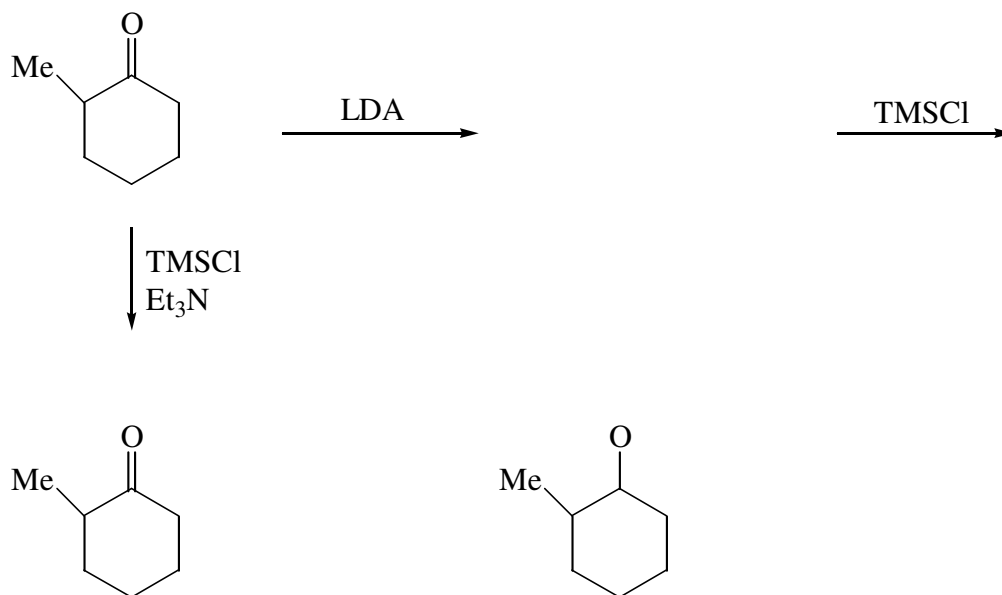


Homologation of aldehydes using the Peterson reaction



6) Silyl Enol Ethers as enolate equivalents and protecting groups

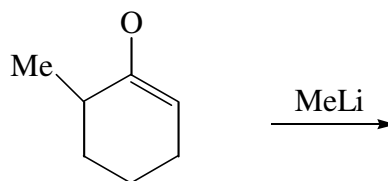
Synthesis



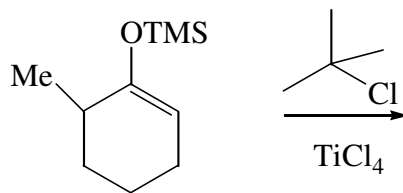
So, either isomer

Reactivity

(i) Stable Precursors for enolates

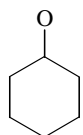


(ii) React with electrophiles
(usually with Lewis acidic conditions)



Compare the types of electrophiles that Li enolate and Si enol ethers prefer.

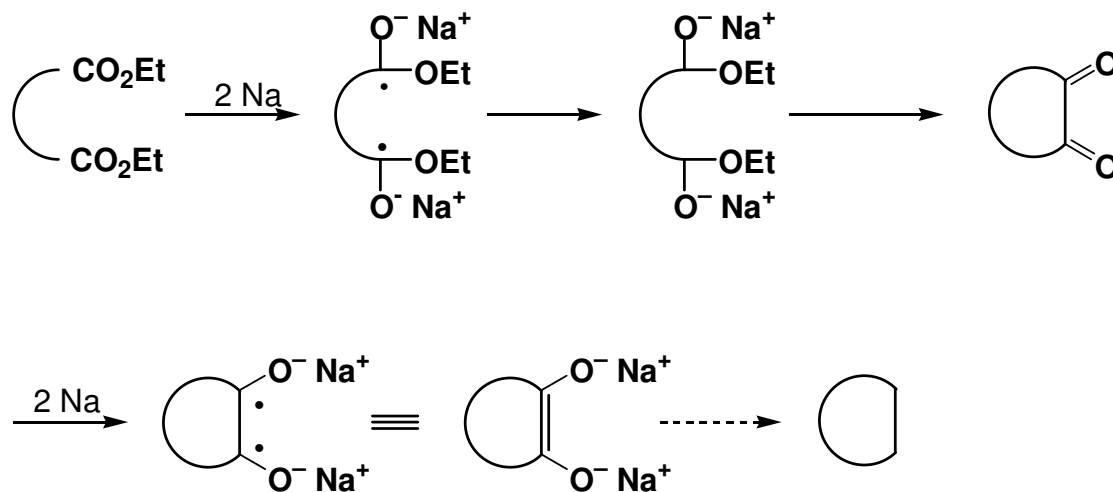
Li-enolate:



Silyl enol ether:

In situ protection of ketones: the ACYLOIN reaction

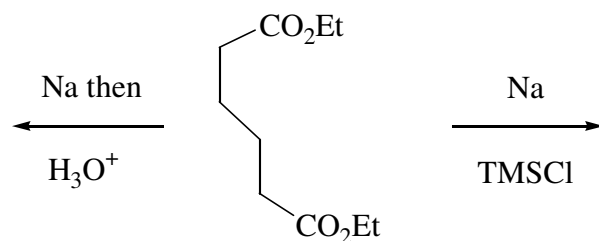
The basic reaction:



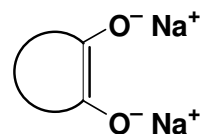
Good for a variety of ring sizes:

One of the problems with this reaction is that

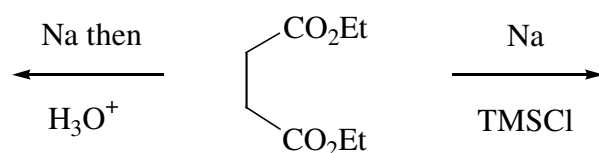
Solution is to add TMSCl to the reaction.

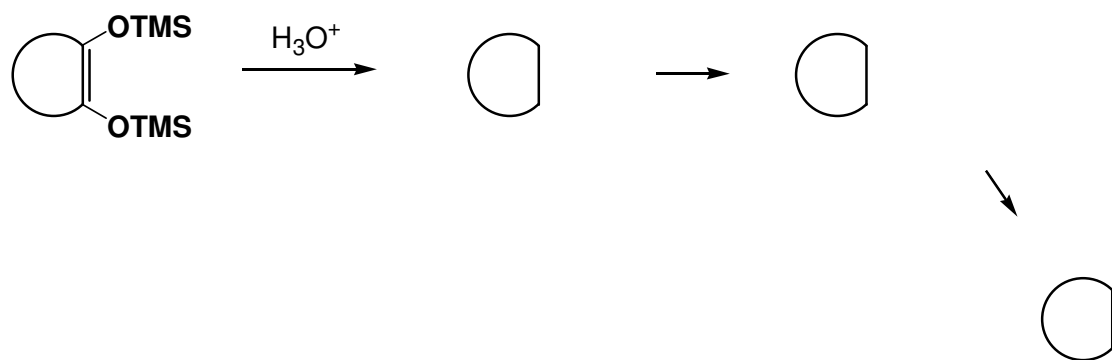


1) TMS-Cl reacts with EtO



2) It also reacts with the alkoxide product.





OR

