

Organic Chemistry-4  
Semester-4, CBCS  
Course: CEMA CC-4-8-TH

Course taught by: Kaushik Basu, Department of Chemistry, SPCMC, Kolkata  
email: [chiralkaushik@gmail.com](mailto:chiralkaushik@gmail.com)

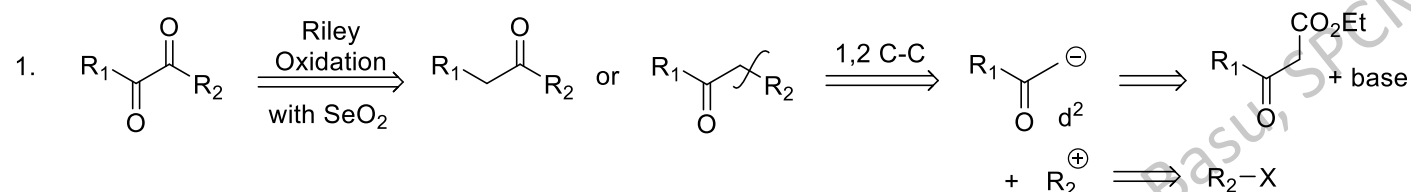
Recommended texts:

1. Study Guide to Organic Chemistry, Volume 2, by Saha, Chakraborty, Saha & Basu, Techno World, ISBN 9788192669588,
2. Organic Chemistry, Second Ed. by Clayden, Greeves & Warren, OUP, ISBN 9780198728719

**The Logic of Organic Synthesis: Analysis of bifunctional target molecules:**
**A] 1,2-bifunctional (1,2-diX) compounds:**

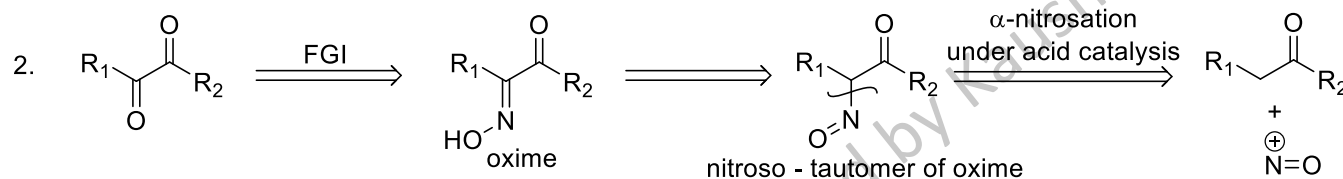
The following is a summary of the retrosynthetic strategies one can adopt commonly when the target molecule contains two heteroatom-based functional groups at *vicinal* carbons, i.e. a 1,2-bifunctional compound.

Note that umpolung strategy is necessary as these classes of target molecules are dissonant in nature.

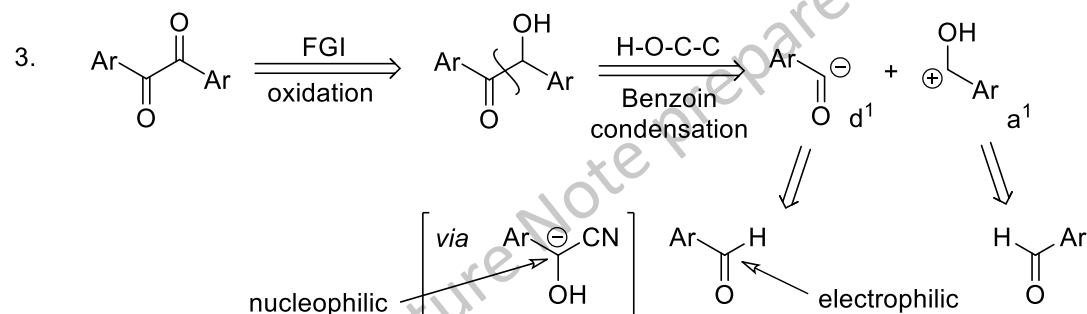
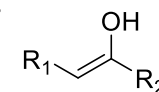


Comments:

1,2-diketone TM  
(polarity inversion by oxidation)  
# potential regioselectivity issue

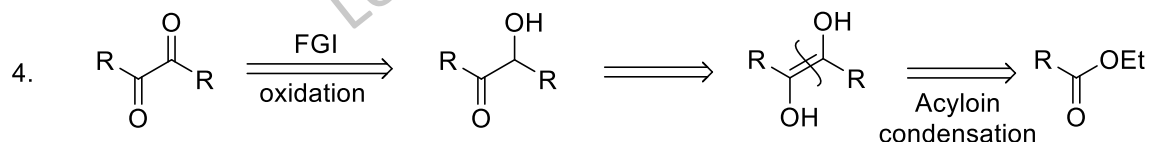


1,2-diketone TM  
(polarity inversion by nitrosation)  
# via more substituted enol under acid catalysis



Symmetrical, aromatic 1,2-diketone TM,  
can be revised to  $\alpha$ -hydroxyketone TM  
- benzoin is an easy option.

$d^1$  synthon illogical -  
accessed through cyanohydrin



Symmetrical, aliphatic 1,2-diketone TM,  
can be revised to  $\alpha$ -hydroxyketone TM  
- acyloin an easy option.

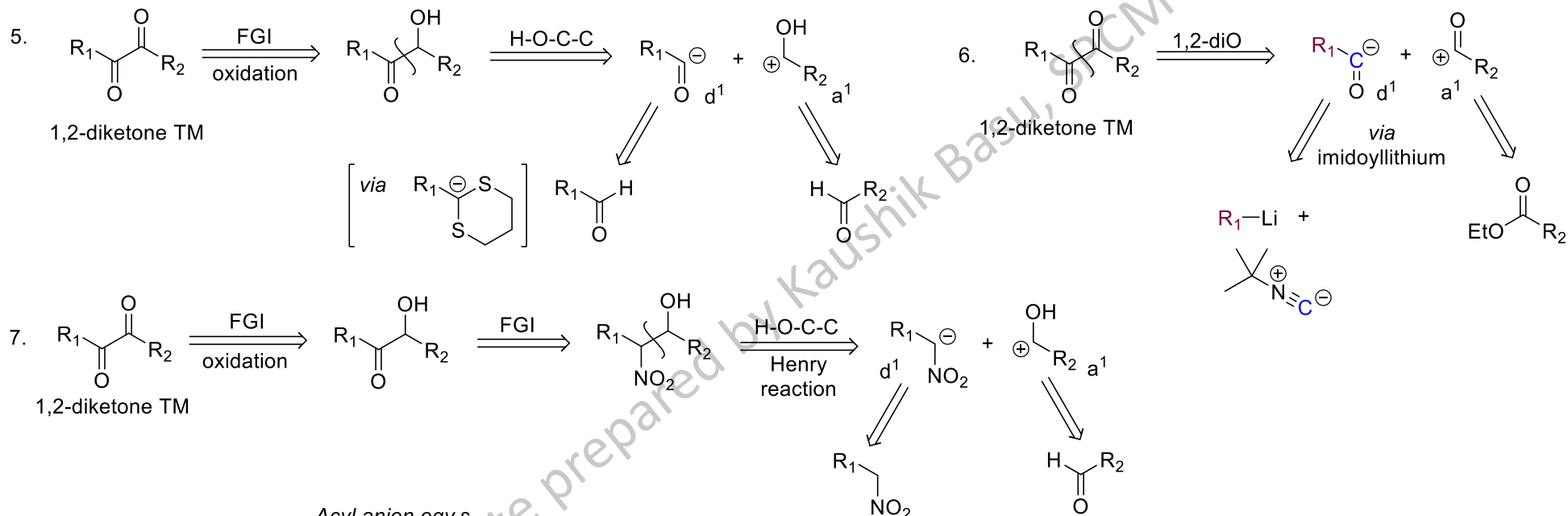
radical coupling to achieve 1,2-diX relation

## The Logic of Organic Synthesis: Analysis of bifunctional target molecules:

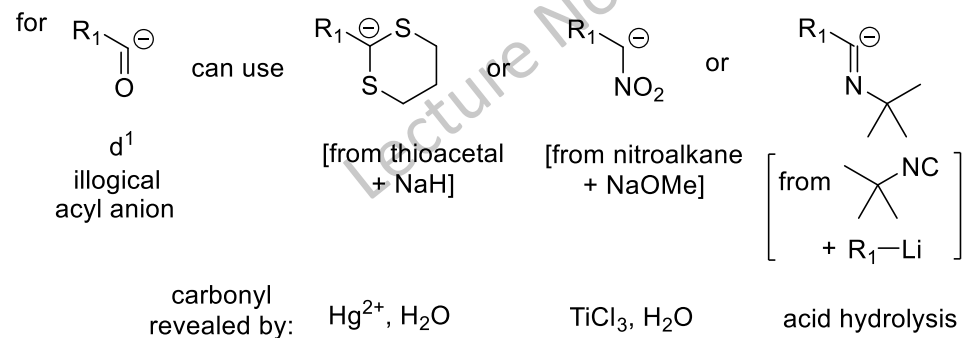
### A] 1,2-bifunctional (1,2-diX) compounds (contd.):

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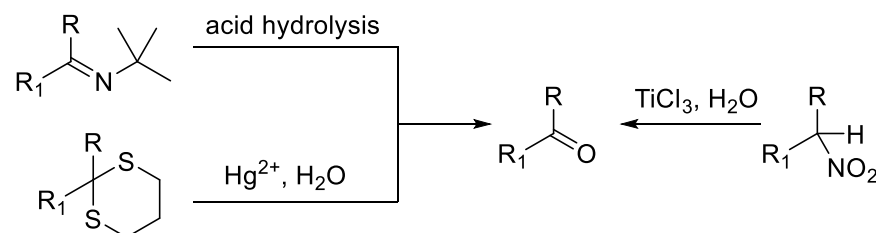
Note that umpolung strategy is necessary as these classes of target molecules are dissonant in nature.



Acyl anion eqv.s



Comments: All methods involve illogical  $d^1$  synthon  
Solved by three elegant methods as outlined below:

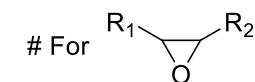
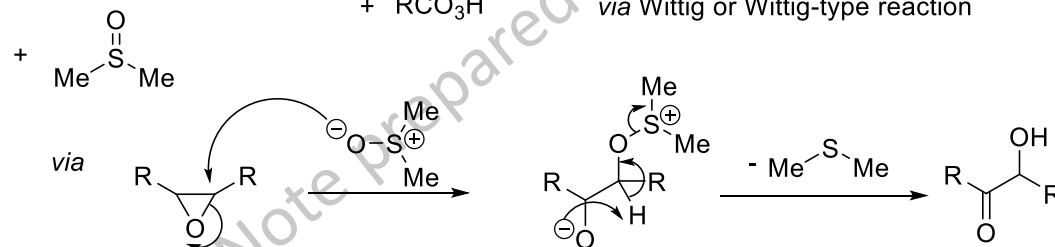
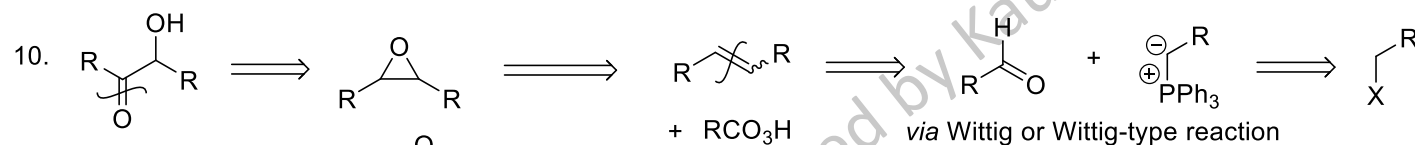
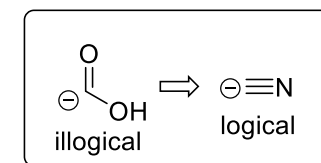
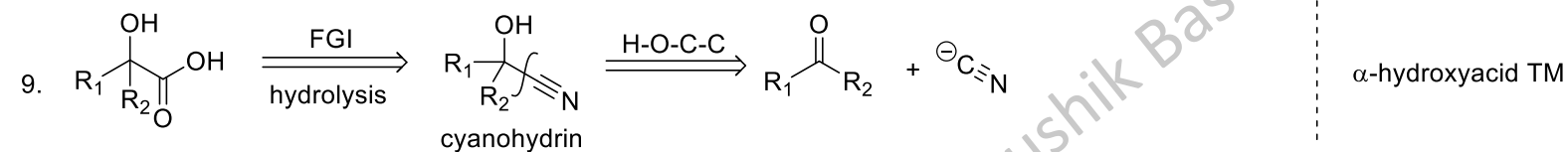
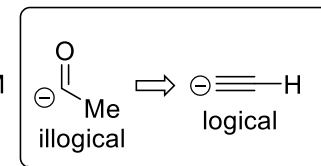
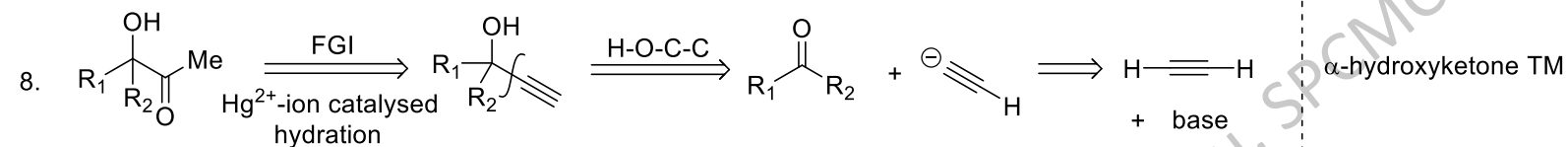


**The Logic of Organic Synthesis: Analysis of bifunctional target molecules:**
**A] 1,2-bifunctional (1,2-diX) compounds (contd.):**

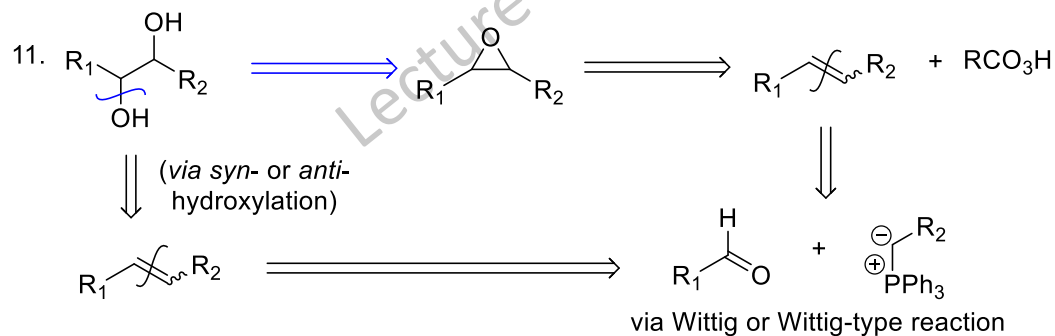
The following is a summary of the retrosynthetic strategies one can adopt commonly when the target molecule contains two heteroatom-based functional groups at *vicinal* carbons, i.e. a 1,2-bifunctional compound.

Note that umpolung strategy is necessary as these classes of target molecules are dissonant in nature.

Comments:



there will be regioselectivity issue with attack of DMSO

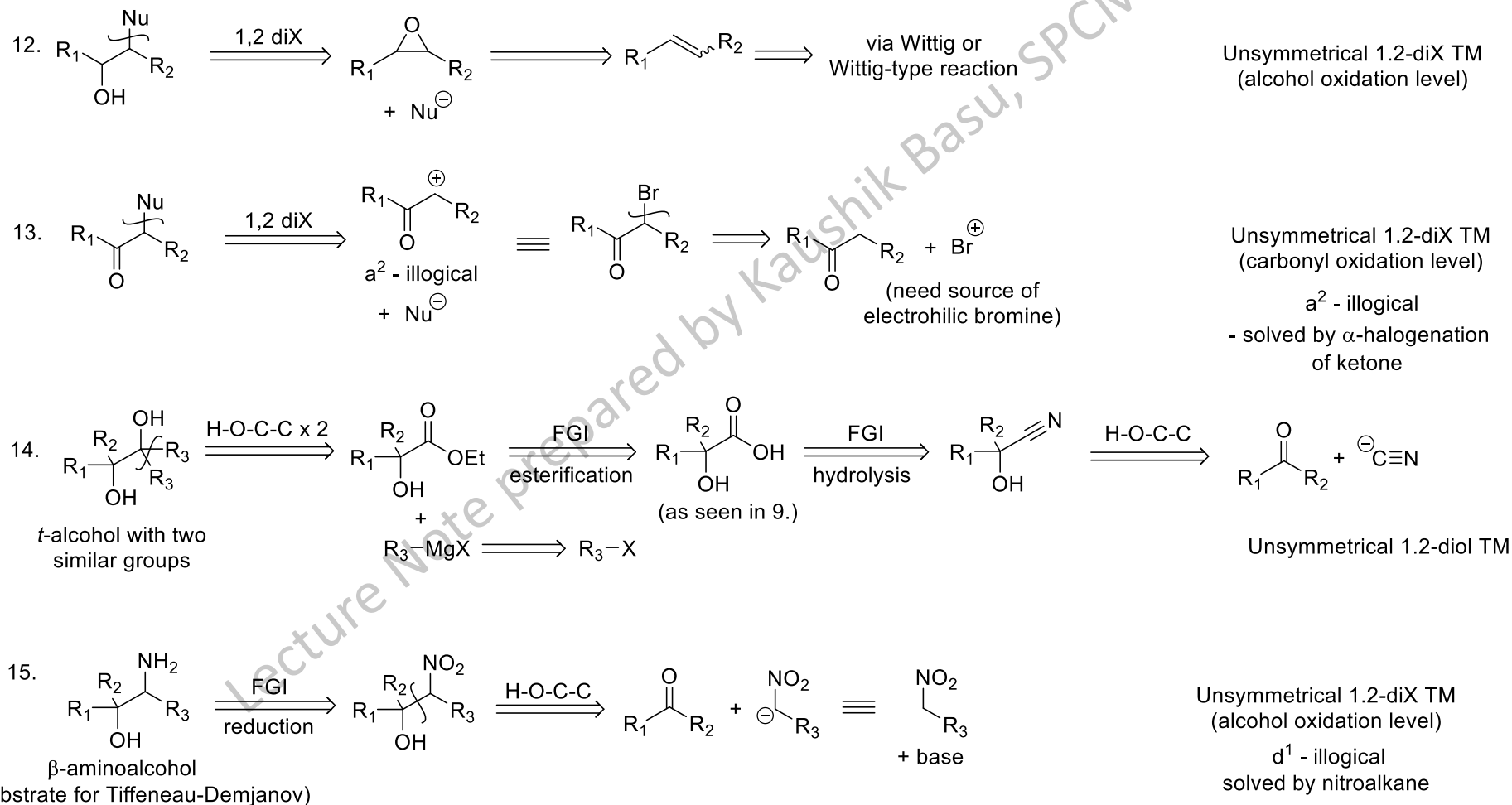


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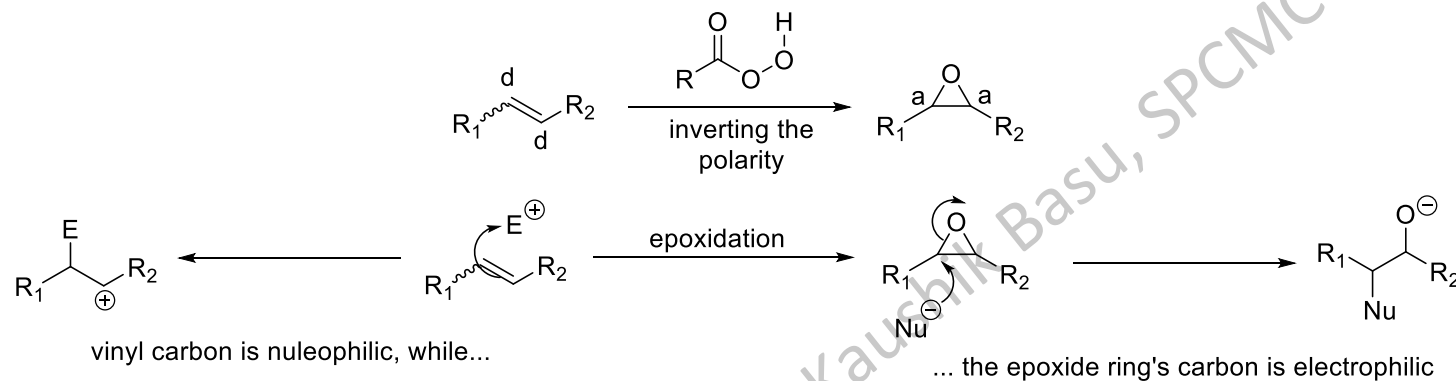


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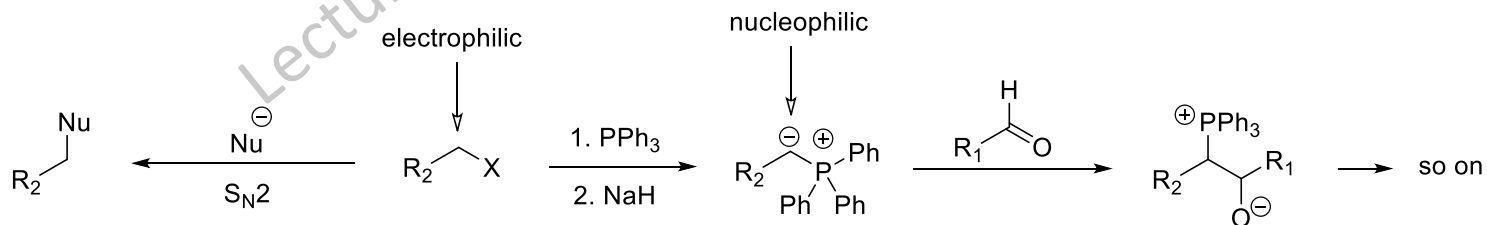
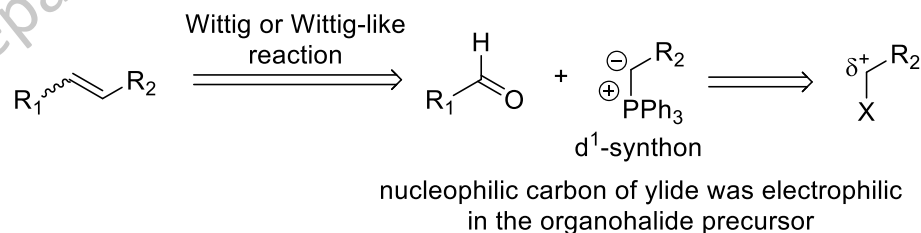
We have seen the use of alkenes in many of the preceding examples.

Note that alkenes are nucleophilic in general. When you make epoxides out of them, you invert the polarity of the vinylic carbons:



So, we have done an umpolung operation.

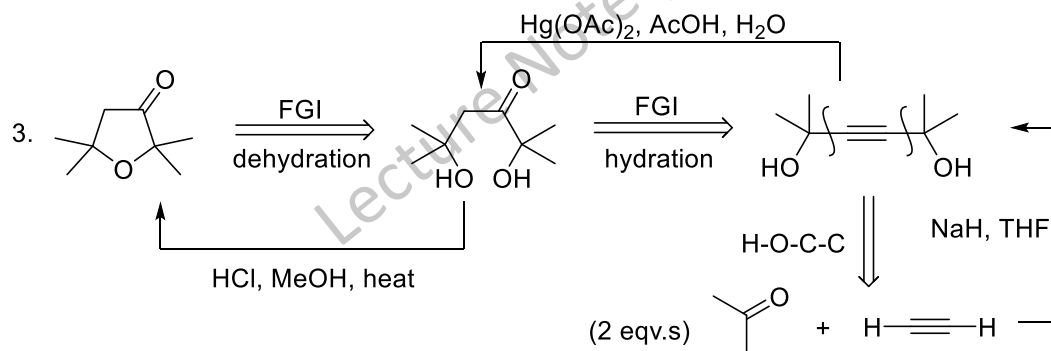
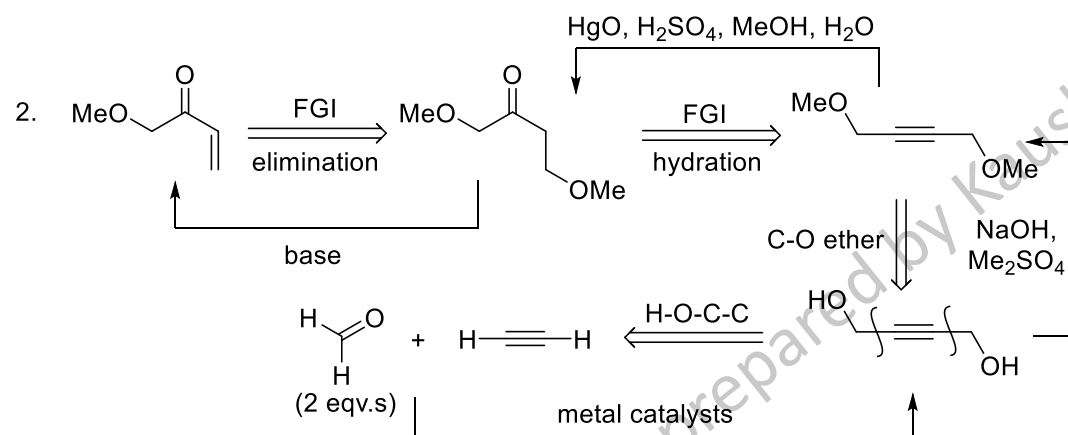
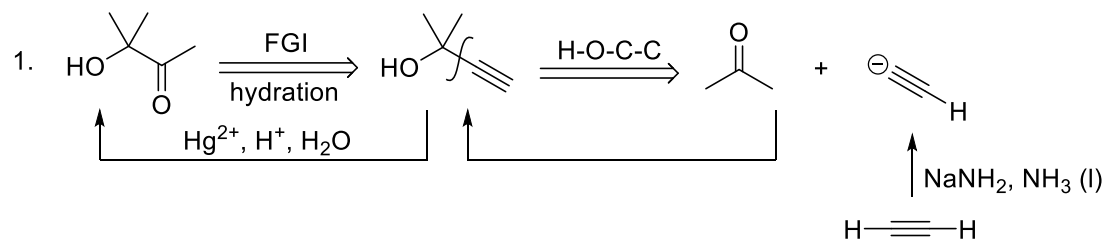
Same is the case with Wittig methodology, that also involves a polarity inversion:



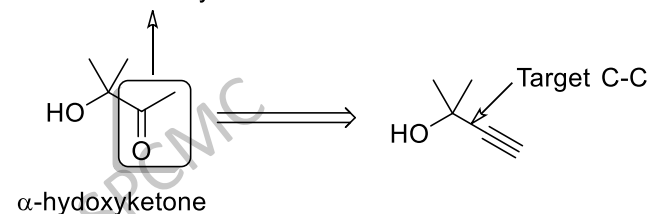
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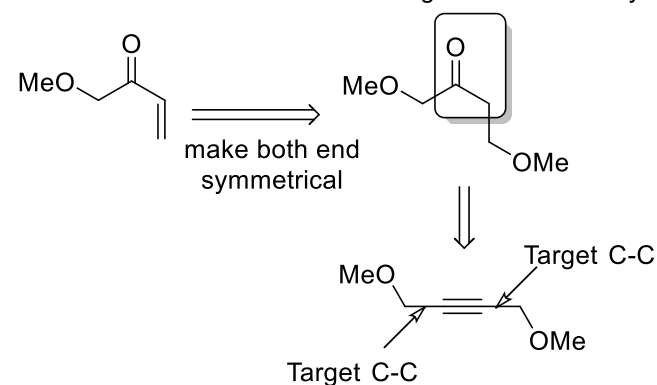
Let us now consider a few examples:



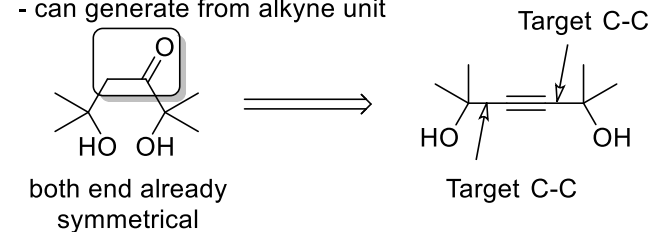
Target ketomethyl first, can be derived from acetylene unit



Target CH<sub>2</sub>CO fragment - can generate from alkyne unit



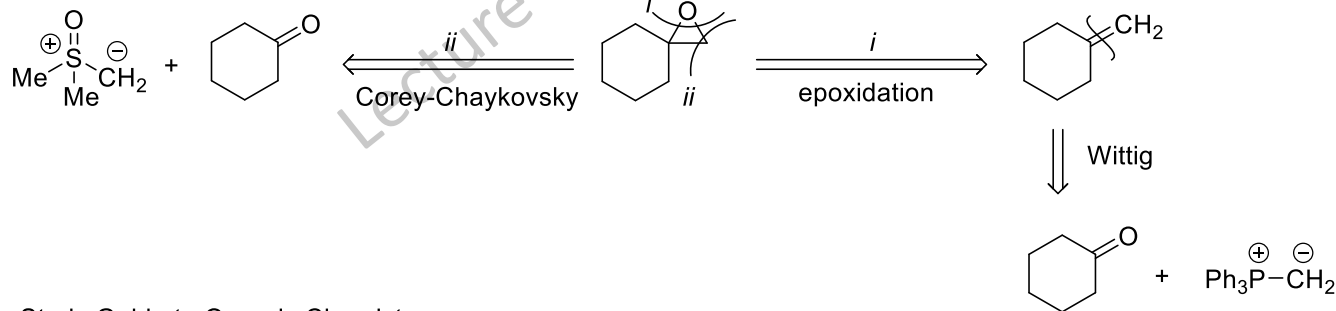
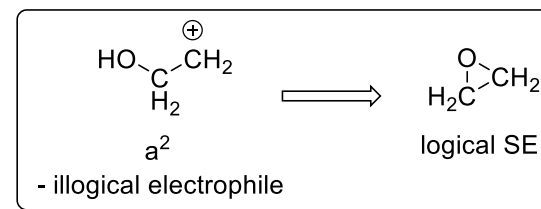
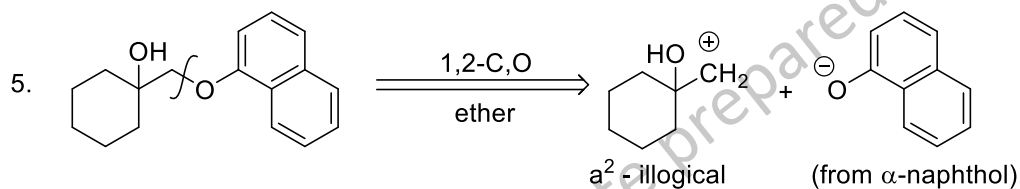
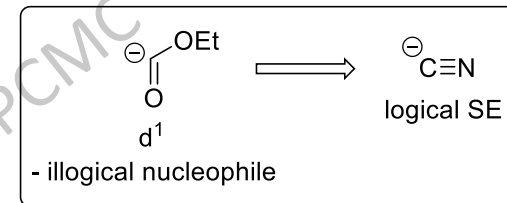
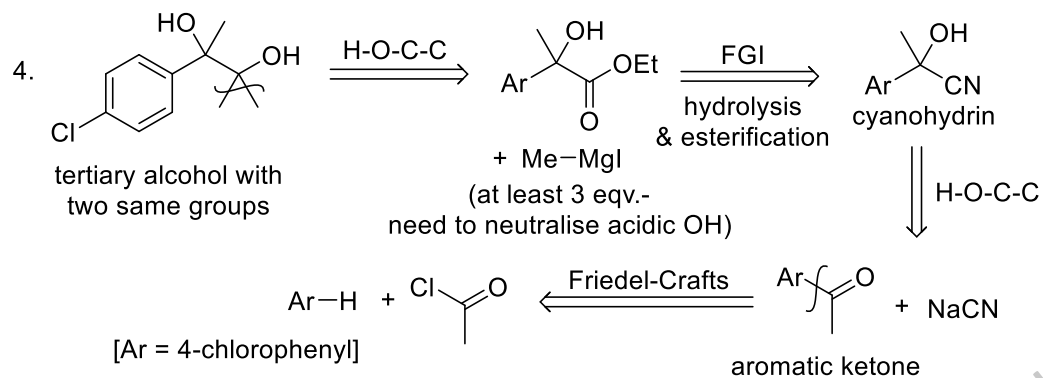
Target CH<sub>2</sub>CO fragment - can generate from alkyne unit



### The Logic of Organic Synthesis: Analysis of bifunctional target molecules:

#### A] 1,2-bifunctional (1,2-diX) compounds (contd.):

Let us now consider a few examples:

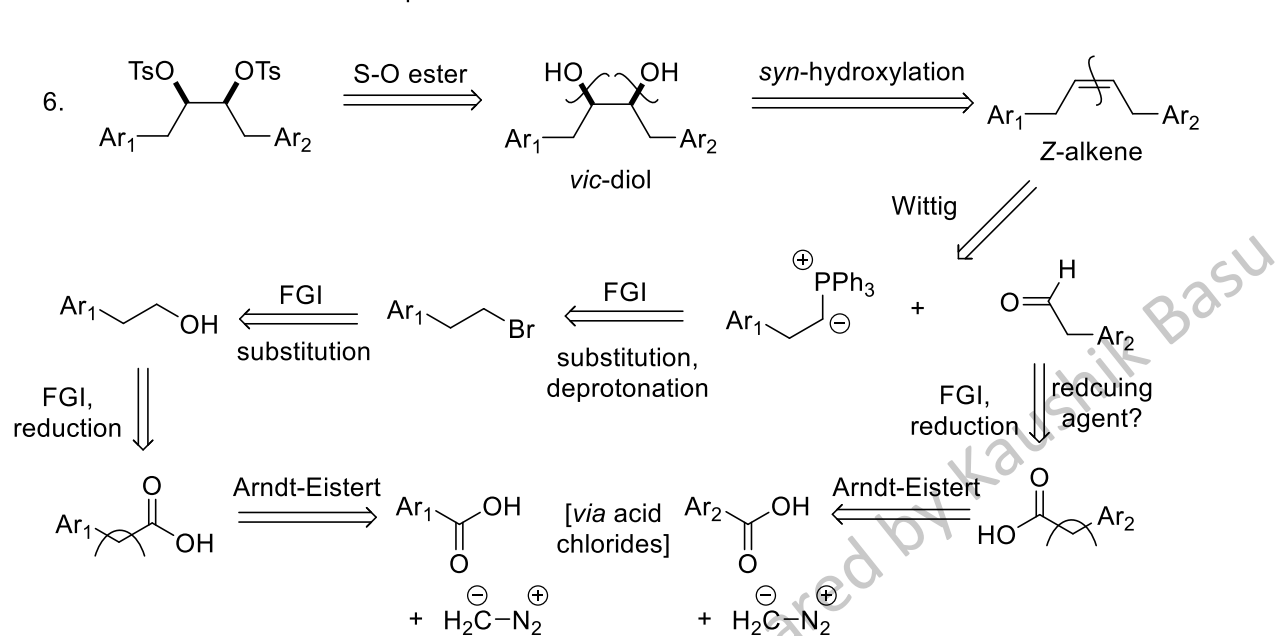




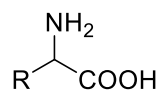
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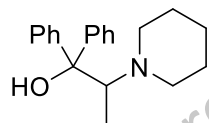
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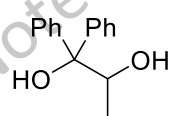
Try the retrosynthetic analysis of the following 1,2-bifunctional TMs:



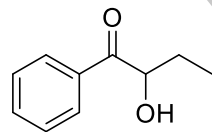
[A.1]



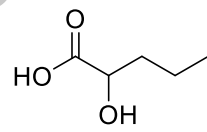
[A.2]



[A.3]

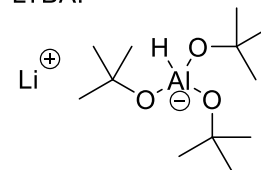


[A.4]

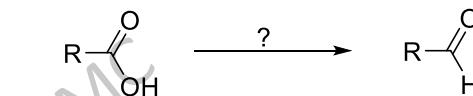
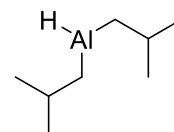


[A.5]

LTBA:

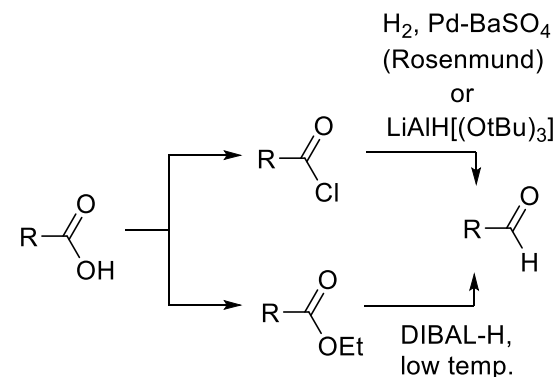


DIBAL-H:



Aldehyde is more reactive than acid, so it is difficult to stop the reduction at the aldehyde stage, there is a strong tendency to undergo further reduction to alcohol.

Commonly done in the following way:



is a much more selective, and less reactive hydride transfer agent than  $\text{LiAlH}_4$ .

is a reducing agent that operates in a fundamentally different manner than  $\text{LiAlH}_4$

LAH are  $\text{NaBH}_4$  are nucleophilic hydride transfer agents while DIBAL-H is electrophilic in nature.