



MSP Mondal's  
Deogiri College Aurangabad

MSc Organic Chemistry SY Third Semester  
Organic Synthesis, CHEO-314

# 1. Oxidation

by

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# Content

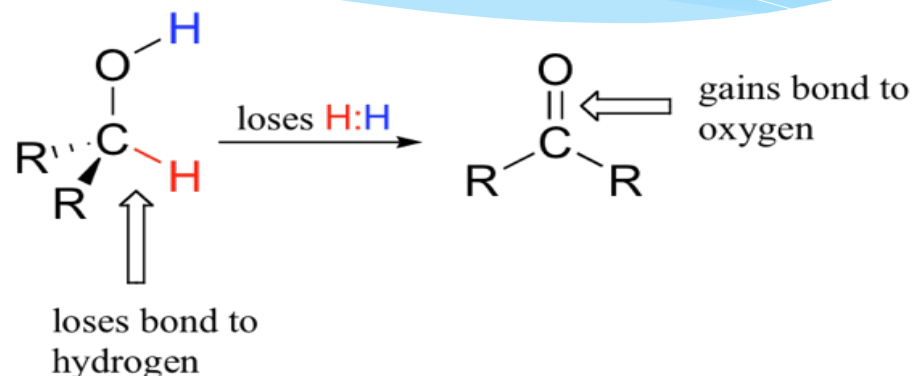
- \* (A) Oxidation of alcohol to aldehyde, ketone or acid: Jones reagent, Swern oxidation, Collins reagent, Fetizon's reagent, PCC, PDC, PFC, IBX, Activated  $\text{MnO}_2$ , Chromyl chloride (Etard reaction), TEMPO, CAN, NMO, Moffatt oxidation
- \* (b) Oxidative cleavage of Carbon-Carbon double bonds:  $\text{KMnO}_4$ , Ozonolysis.
- \* (c) Allylic Oxidation:  $\text{SeO}_2$ , PhSeBr.
- \* (d) Selective cleavages at functional groups: Cleavage of glycols,  $\text{IO}_4^-$ ,  $\text{Pb}(\text{OAc})_2$ .

# Introduction

- \* You are undoubtedly already familiar with the general idea of oxidation and reduction: you learned in general chemistry that when a compound or atom is oxidized it loses electrons, and when it is reduced it gains electrons. You also know that oxidation and reduction reactions occur in pairs: if one species is oxidized, another must be reduced at the same time - thus the term 'redox reaction'.
- \* In organic chemistry, redox reactions look a little different. Electrons in an organic redox reaction often are transferred in the form of a hydride ion - a proton and two electrons. Because they occur in conjunction with the transfer of a proton, these are commonly referred to as **hydrogenation** and **dehydrogenation** reactions:

- \* When a carbon atom in an organic compound loses a bond to hydrogen and gains a new bond to a heteroatom (or to another carbon), we say the compound has been dehydrogenated, or oxidized. A very common biochemical example is the oxidation of an alcohol to a ketone or aldehyde:

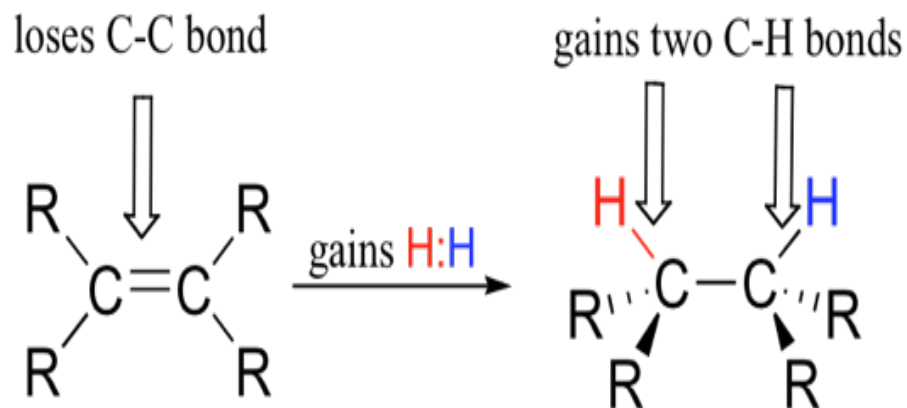
Dehydrogenation (oxidation) of an alcohol



- \* When a carbon atom loses a bond to hydrogen and gains a bond to a heteroatom (or to another carbon atom), it is considered to be an oxidative process because hydrogen, of all the elements, is the least electronegative. Thus, in the process of dehydrogenation the carbon atom undergoes an overall loss of electron density - and loss of electrons is oxidation.

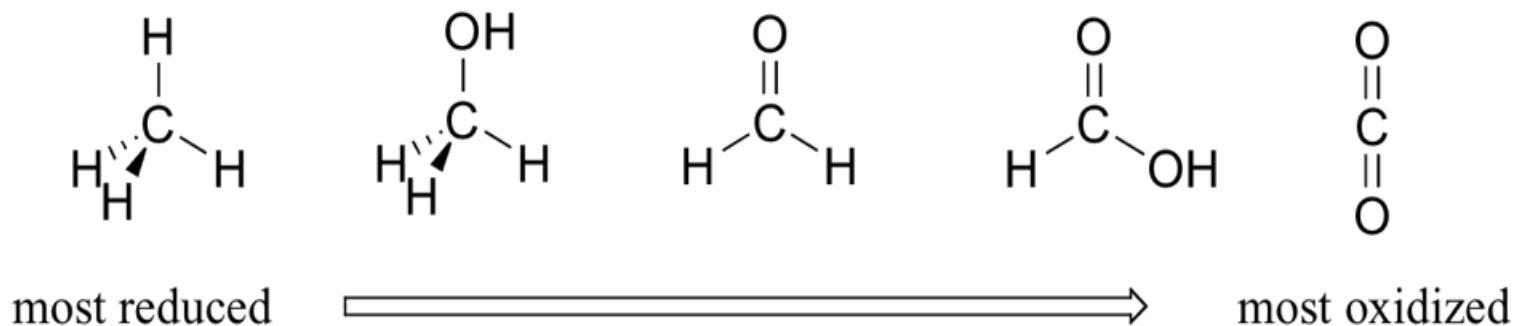
Conversely, when a carbon atom in an organic compound gains a bond to hydrogen and loses a bond to a heteroatom (or to another carbon atom), we say that the compound has been hydrogenated, or reduced. The hydrogenation of a ketone to an alcohol, for example, is overall the reverse of the alcohol dehydrogenation shown above. Illustrated below is another common possibility, the hydrogenation (reduction) of an alkene to an alkane.

Hydrogenation (reduction)  
of an alkene

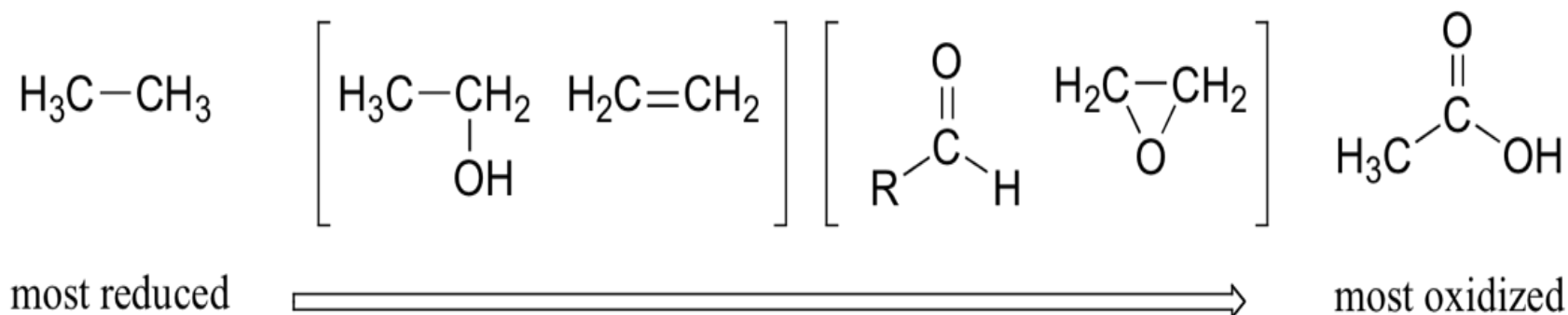


- \* Hydrogenation results in higher electron density on a carbon atom(s), and thus we consider process to be one of reduction of the organic molecule.
- \* Notice that neither hydrogenation nor dehydrogenation involves the gain or loss of an oxygen atom. Reactions which do involve gain or loss of one or more oxygen atoms are usually referred to as 'oxygenase' and 'reductase' reactions,
- \* For the most part, when talking about redox reactions in organic chemistry we are dealing with a small set of very recognizable functional group transformations. It is therefore very worthwhile to become familiar with the idea of 'oxidation states' as applied to organic functional groups.

By comparing the relative number of bonds to hydrogen atoms, we can order the familiar functional groups according to oxidation state. We'll take a series of single carbon compounds as an example. Methane, with four carbon-hydrogen bonds, is highly reduced. Next in the series is methanol (one less carbon-hydrogen bond, one more carbon-oxygen bond), followed by formaldehyde, formate, and finally carbon dioxide at the highly oxidized end of the group.



- \* This pattern holds true for the relevant functional groups on organic molecules with two or more carbon atoms:

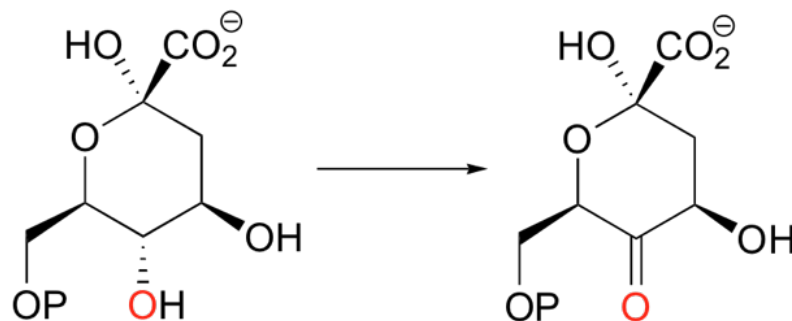


- \* Alkanes are highly reduced, while alcohols - as well as alkenes, ethers, amines, sulfides, and phosphate esters - are one step up on the oxidation scale, followed by aldehydes/ketones/imines and epoxides, and finally by carboxylic acid derivatives.

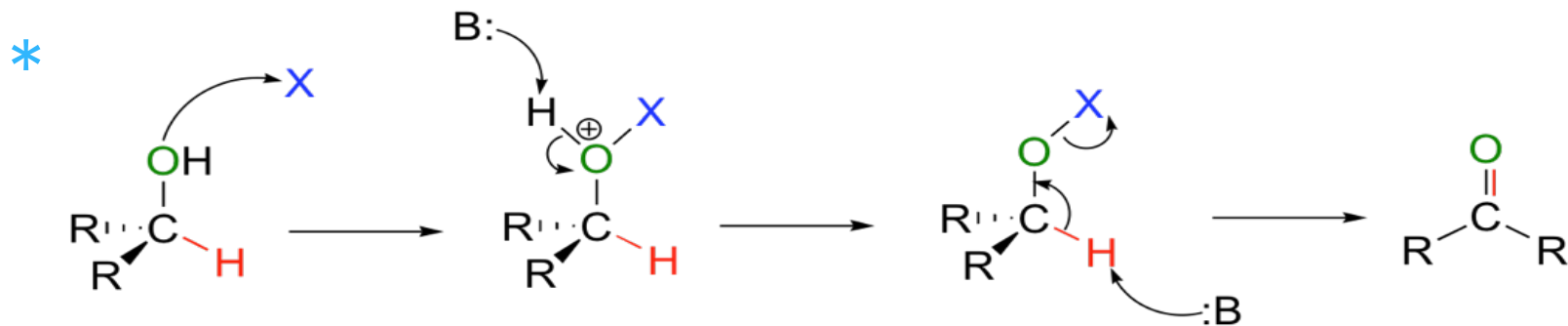


\* Ethanol and ethene are considered to be in the same oxidation state. You know already that alcohols and alkenes are interconverted by way of addition or elimination of water. When an alcohol is dehydrated to form an alkene, one of the two carbons loses a C-H bond and gains a C-C bond, and thus is oxidized. However, the other carbon loses a C-O bond and gains a C-C bond, and thus is considered to be reduced. Overall, therefore, there is no change to the oxidation state of the molecule.

\* You should learn to recognize when a reaction involves a change in oxidation state in an organic reactant : an alcohol functional group is converted to a ketone, which is one step up on the oxidation ladder.

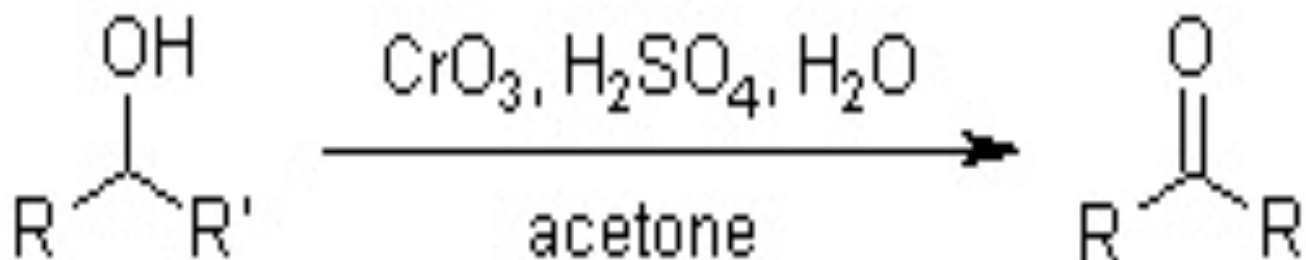


- \* The oxidation of an alcohol to form an aldehyde or ketone is very important in synthesis. In this process, the hydroxy hydrogen of the alcohol is replaced by a leaving group (X in the figure below).
- \* Then, a base can abstract the proton bound to the alcohol carbon, which results in elimination of the X leaving group and formation of a new carbon-oxygen double bond. As you can see by looking closely at this general mechanism, *tertiary alcohols cannot be oxidized in this way* – there is no hydrogen to abstract in the final step!



# Jones Reagent

- \* The Jones Oxidation allows a relatively inexpensive conversion of secondary alcohols to ketones. The Jones reagent is an excellent reagent for the oxidation of secondary alcohols that do not contain acid-sensitive group such as acetals.

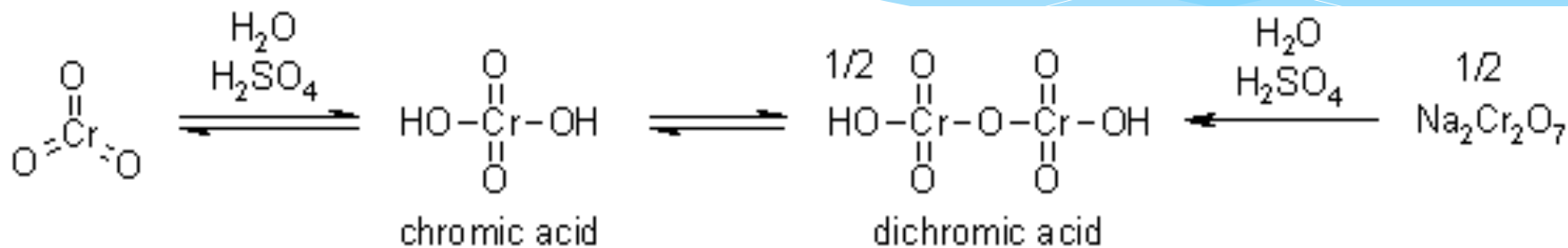


- \* Jones described for the first time a conveniently and safe procedure for a chromium (VI)-based oxidation,

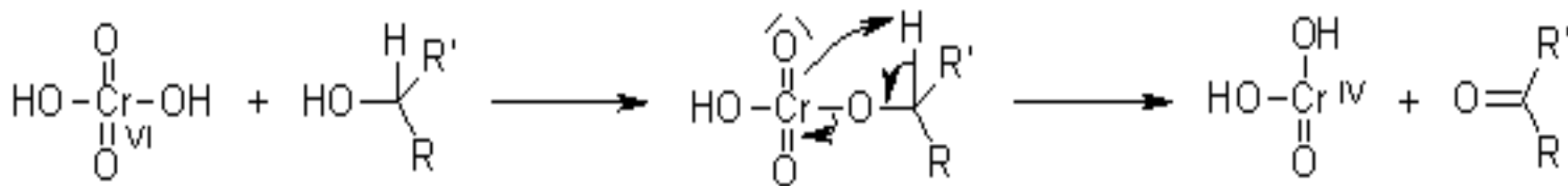


## \* Mechanism of the Jones Oxidation

- \* The Jones Reagent is a mixture of chromic trioxide or sodium dichromate in diluted sulfuric acid, which forms chromic acid in situ.

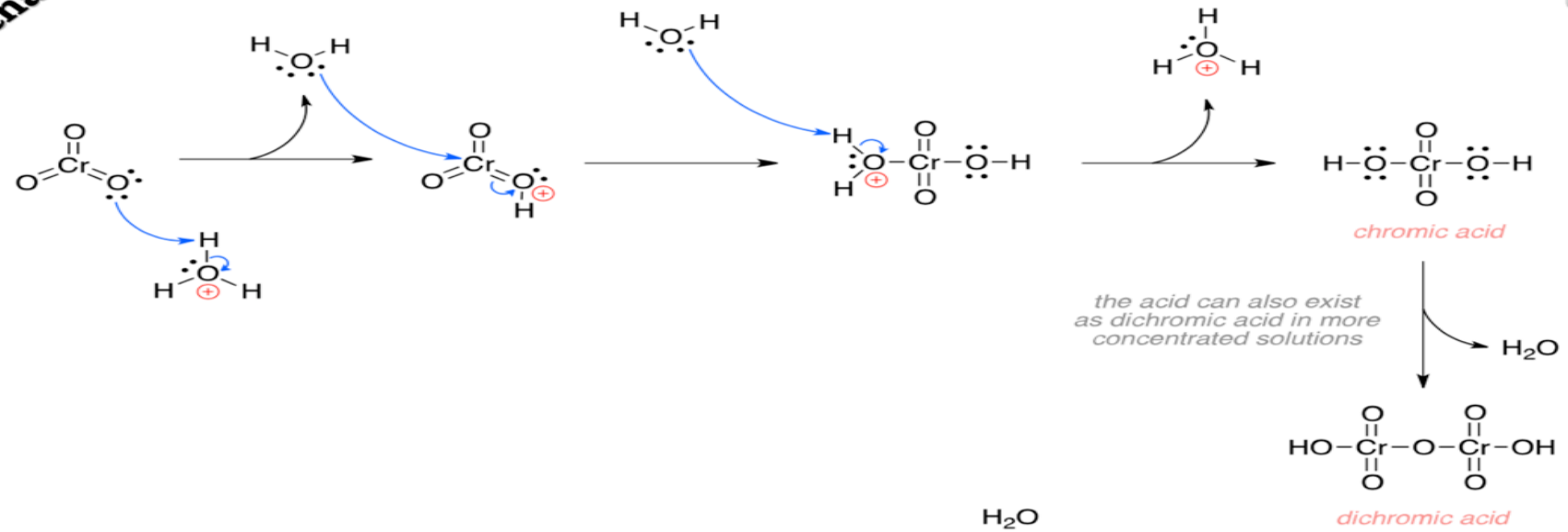


- \* The alcohol and chromic acid form a chromate ester that either reacts intramolecularly or intermolecularly in the presence of a base (water) to yield the corresponding carbonyl compound:

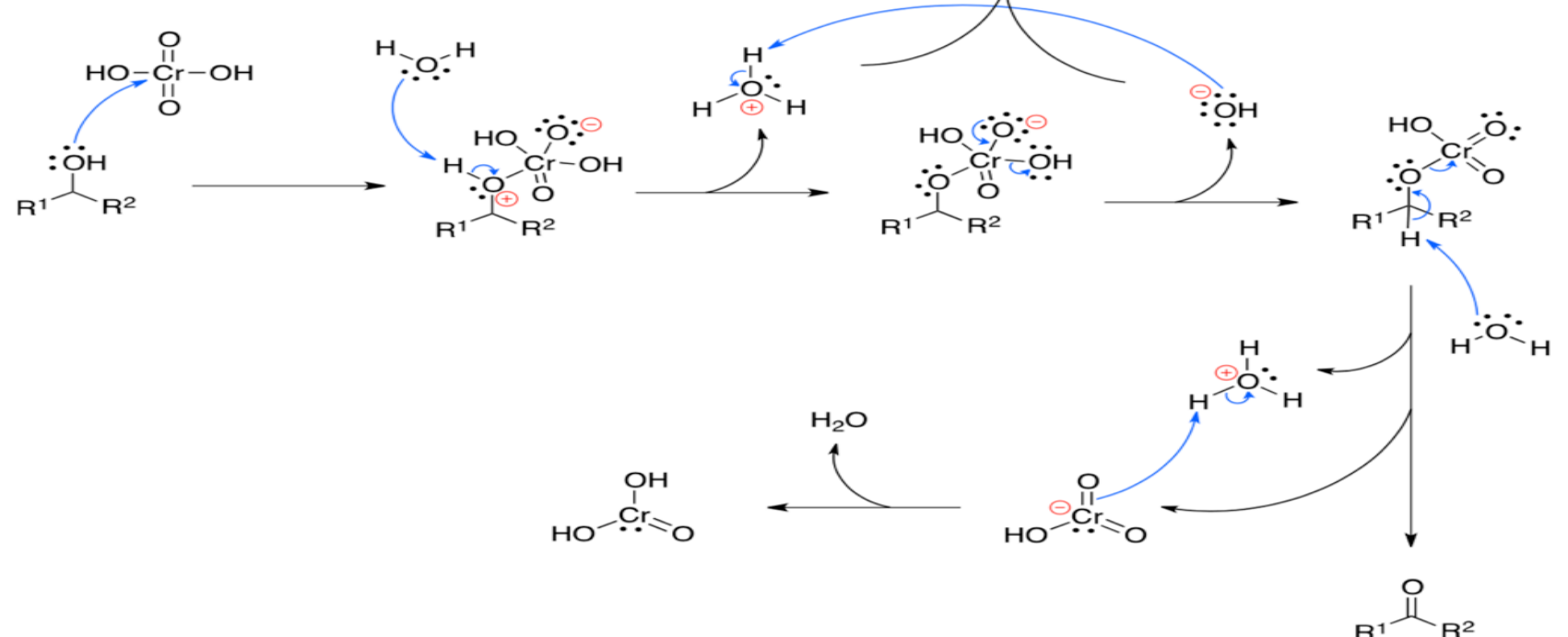


# Mechanism

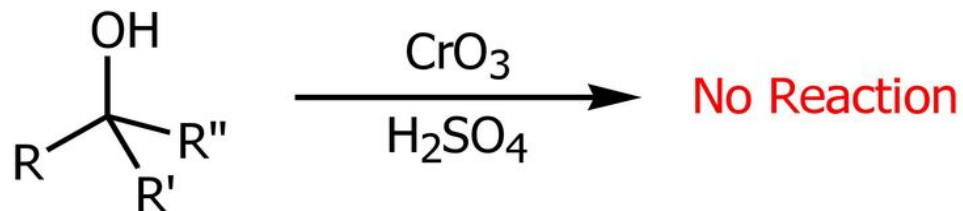
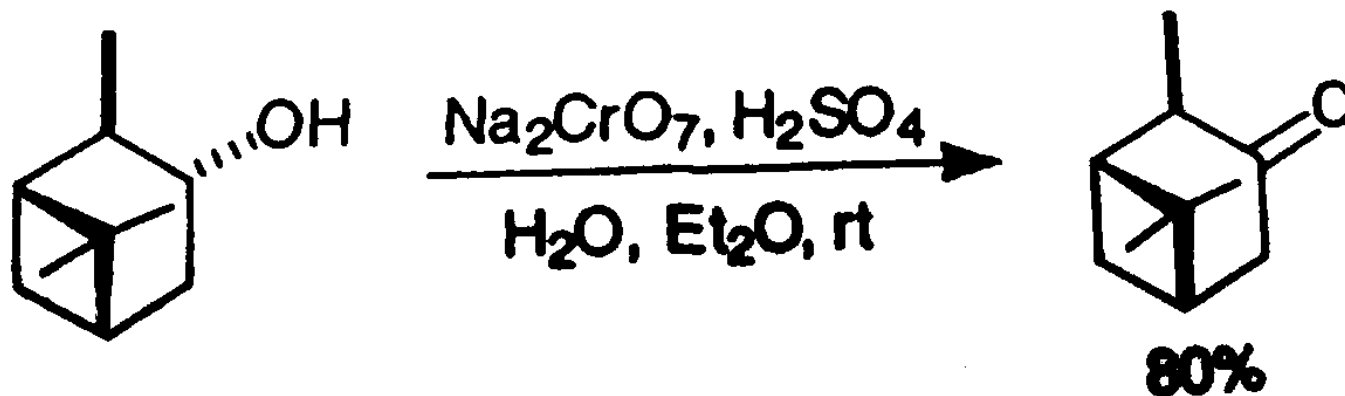
## Formation of Chromic Acid



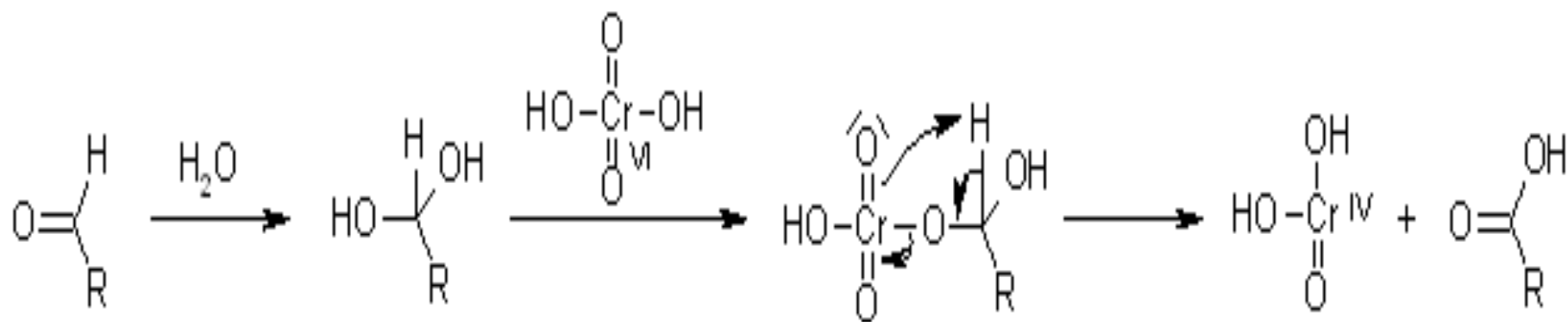
## Alcohol Oxidation with Chromic Acid



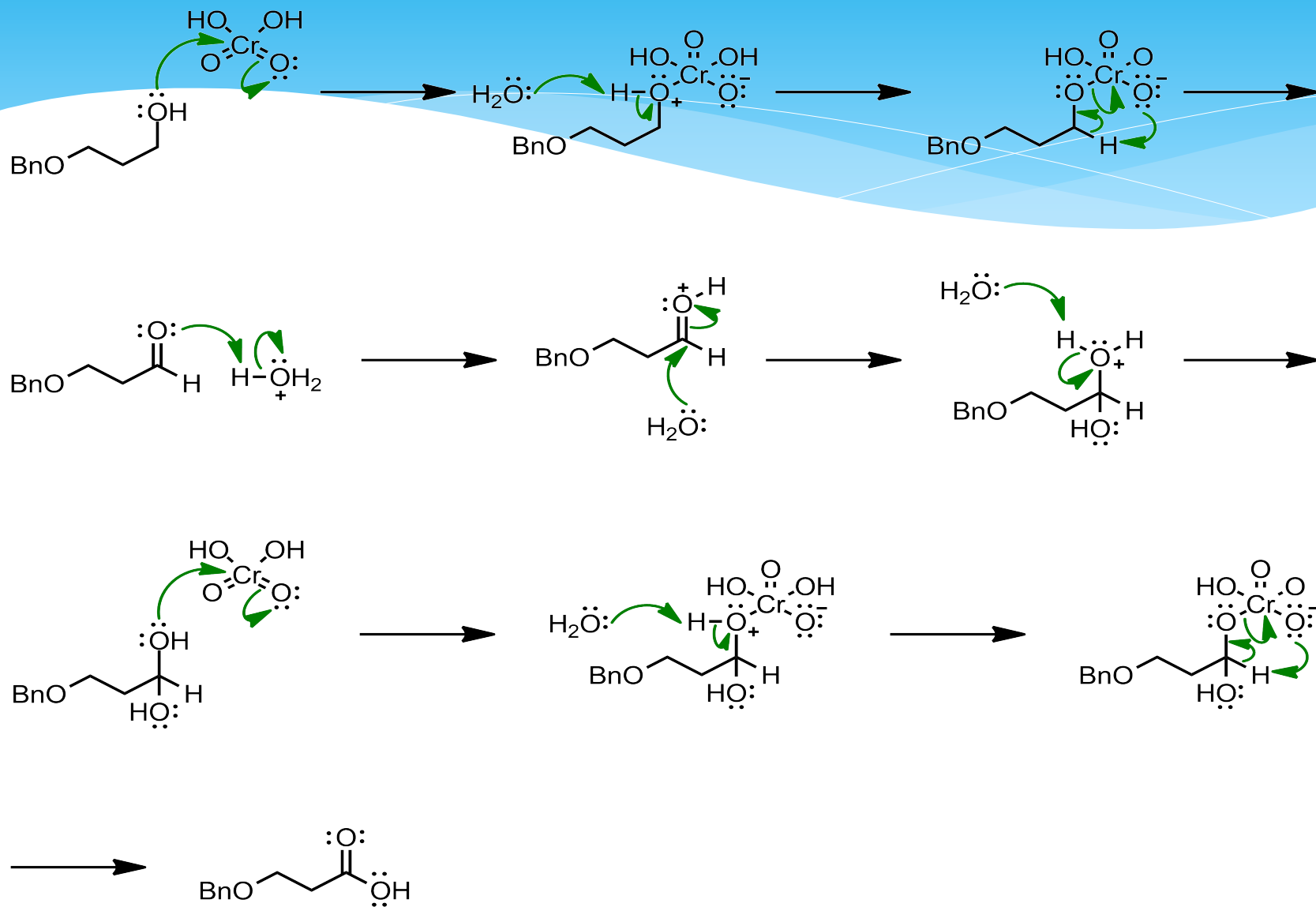
## \* Examples



- \* Oxidation of primary alcohols to carboxylic acids.. Aldehydes that can form hydrates in the presence of water are further oxidized to carboxylic acids:
- \* Oxidation of primary alcohols with Jones reagent may result in the conversion of the aldehydes initially formed to the corresponding carboxylic acids. The reagent is added to the alcohol contained in acetone at 0-25 °C,

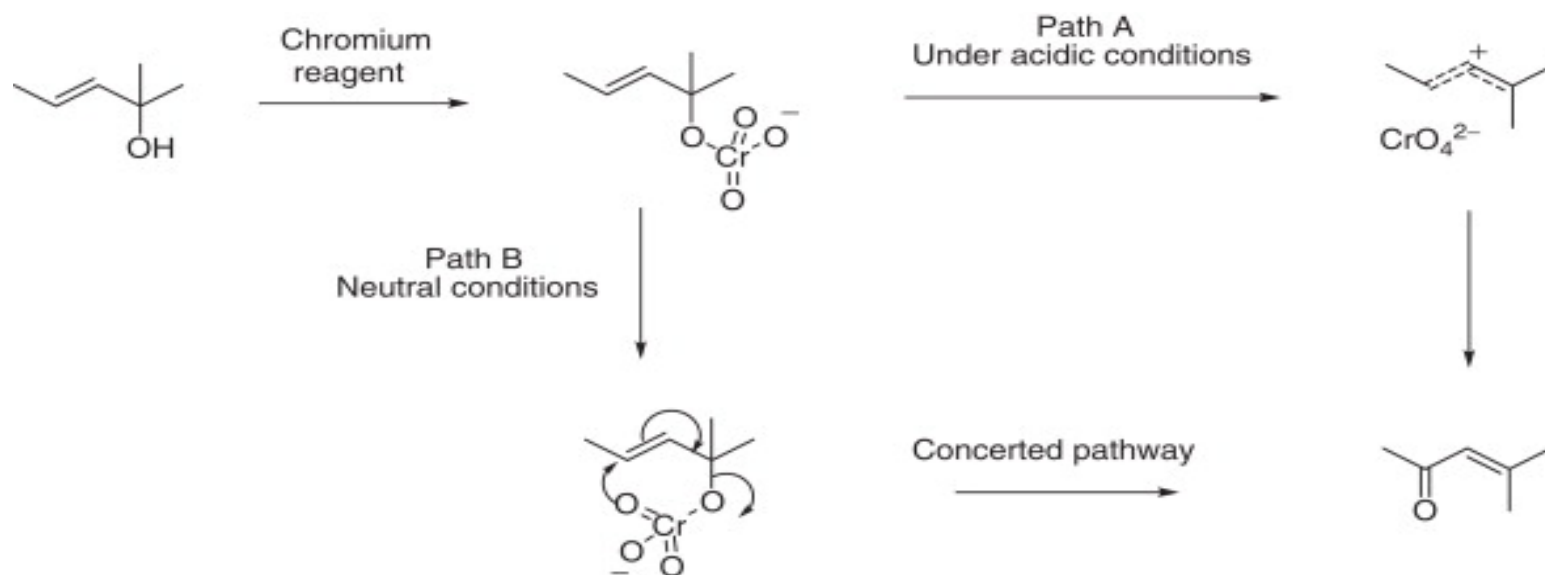


# Mechanism of Oxidation of Primary alcohol to carboxylic Acid by Jones reagent.

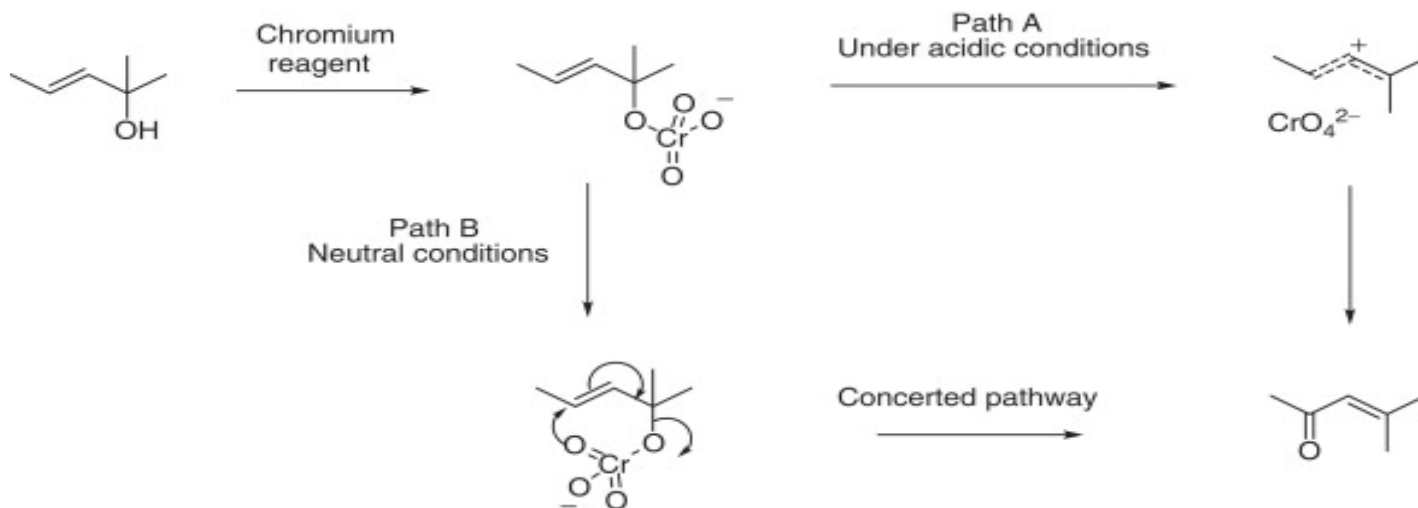
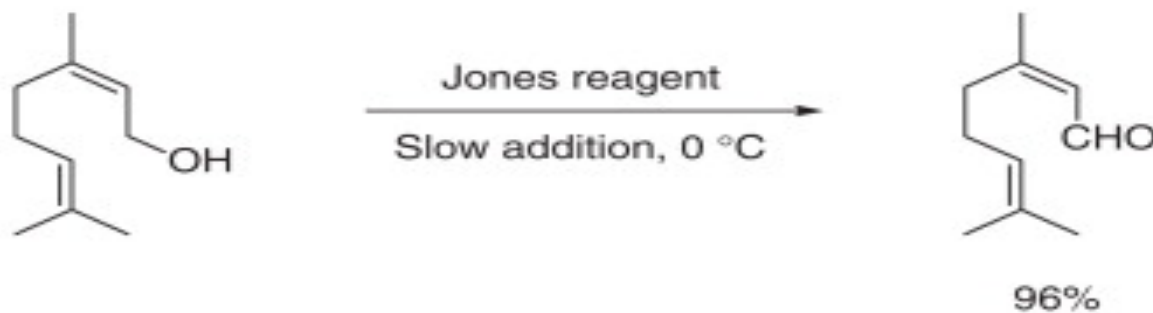
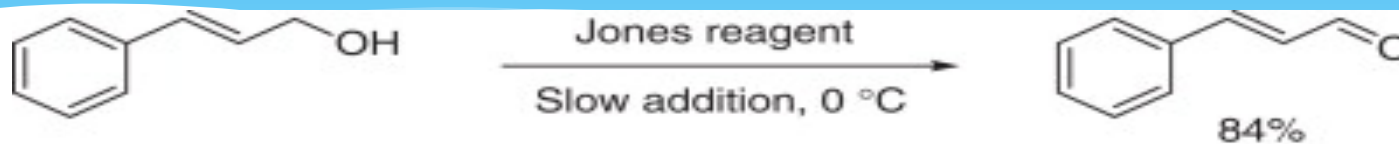




- \* The oxidation of primary allylic and benzylic alcohols gives aldehydes.
- \* Chromium can oxidize allylic alcohols to  $\alpha,\beta$ -unsaturated ketones on the opposite side of the unsaturated bond from the alcohol. This is via a concerted hetero-Claisen reaction, although there are mechanistic differences since the chromium atom has access to d-orbitals which allow the reaction under a less constrained set of geometries.

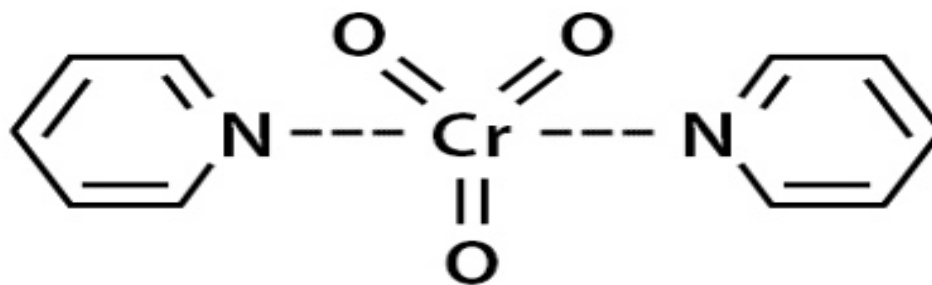


## \* Examples



# Collins Reagent

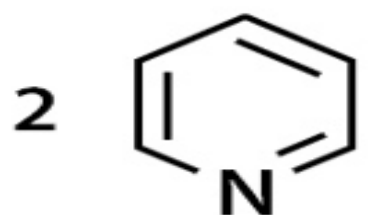
- \* A solution of  $\text{CrO}_3 \cdot 2 \text{Py}$  (Sarett Reagent) in methylene chloride is called the "Collins Reagent". One advantage over the Sarett Reagent is that the addition of one equivalent chromium trioxide to a stirred solution of two equivalents of pyridine in methylene chloride allows the convenient and safe preparation of the oxidant. Thus, most acid and base-sensitive substrates can be oxidized with Collins Reagent, unlike Jones Reagent.



Dipyridine chromium(VI) oxide

\* *Preparation of Collins Reagent*

\* The reagent is prepared by adding  $\text{CrO}_3$  to a mixture of pyridine- $\text{CH}_2\text{Cl}_2$ .

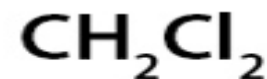


Pyridine

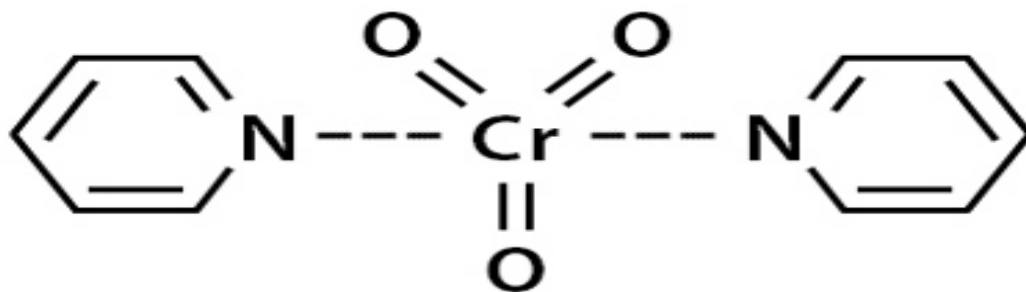
+



Chromium trioxide

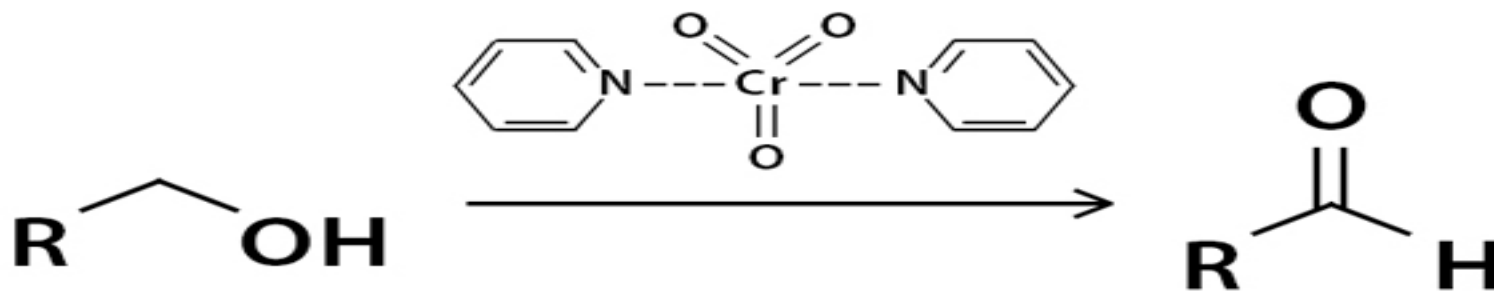


25 °C

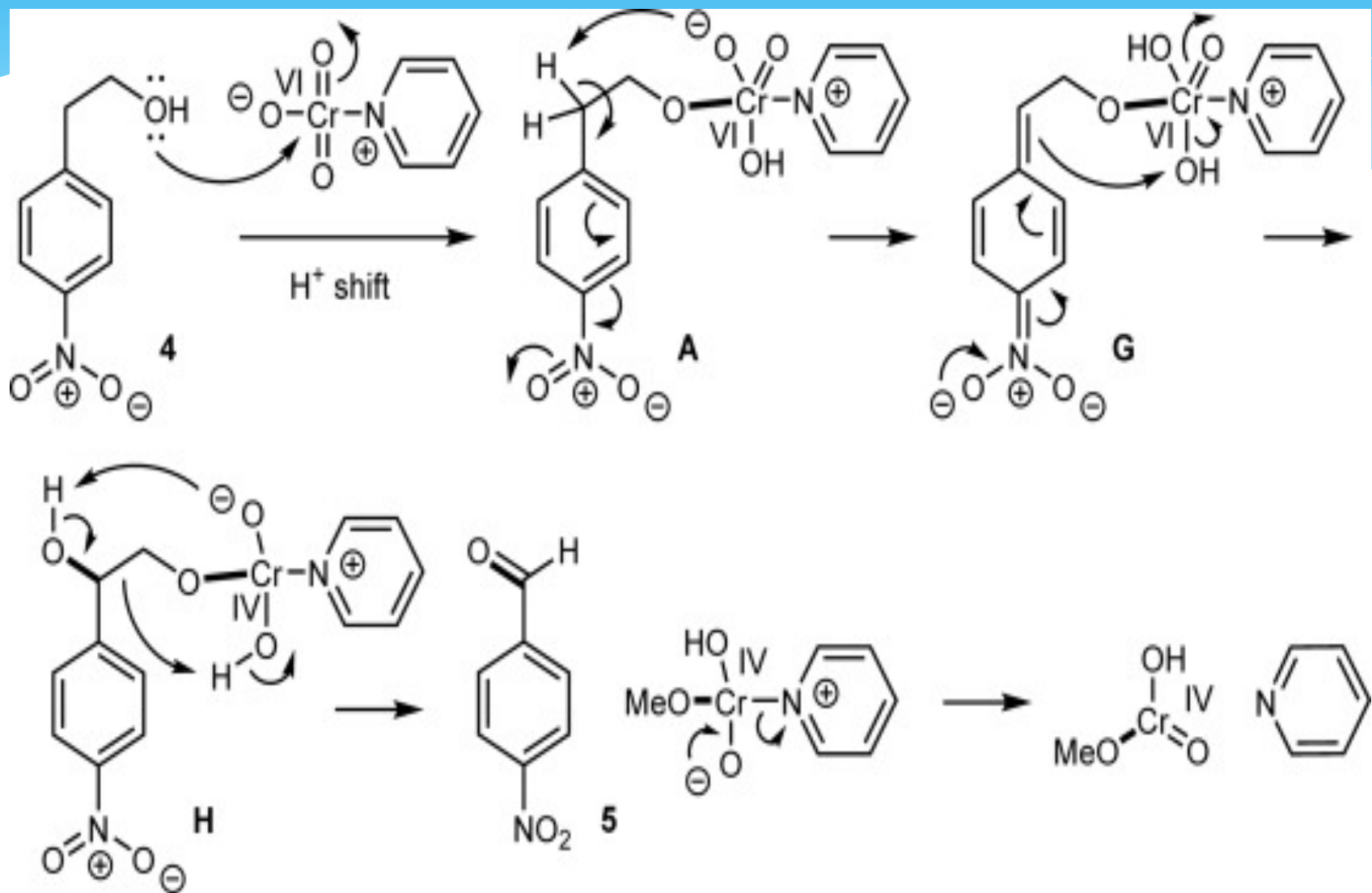


Dipyridine chromium(VI) oxide

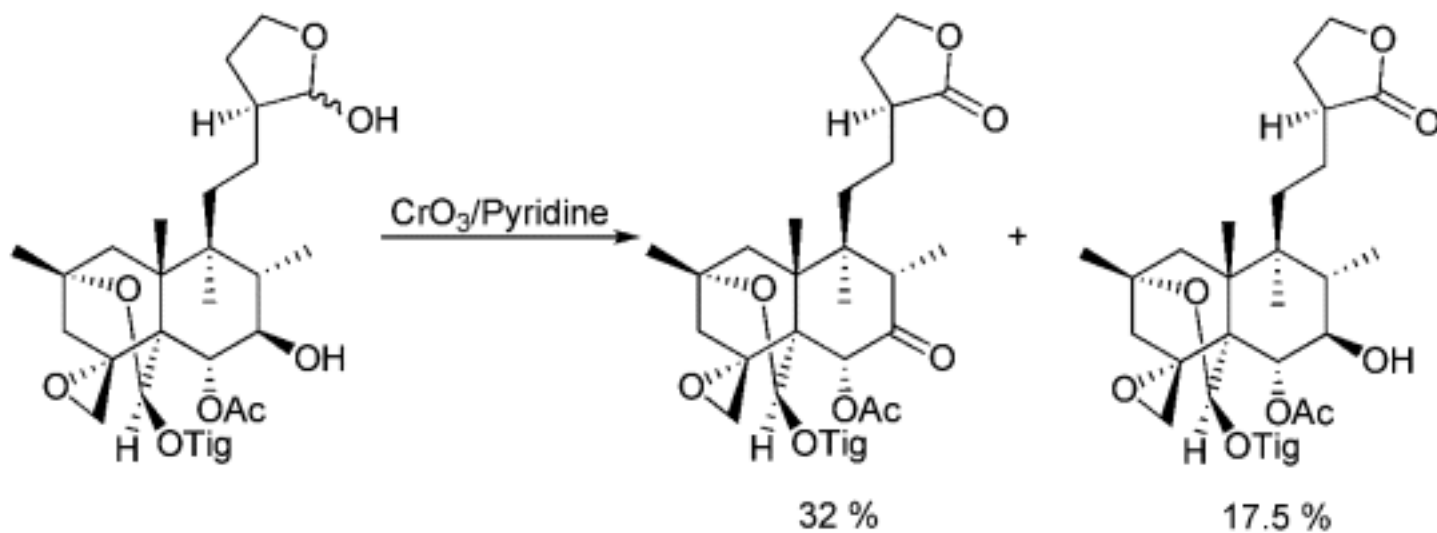
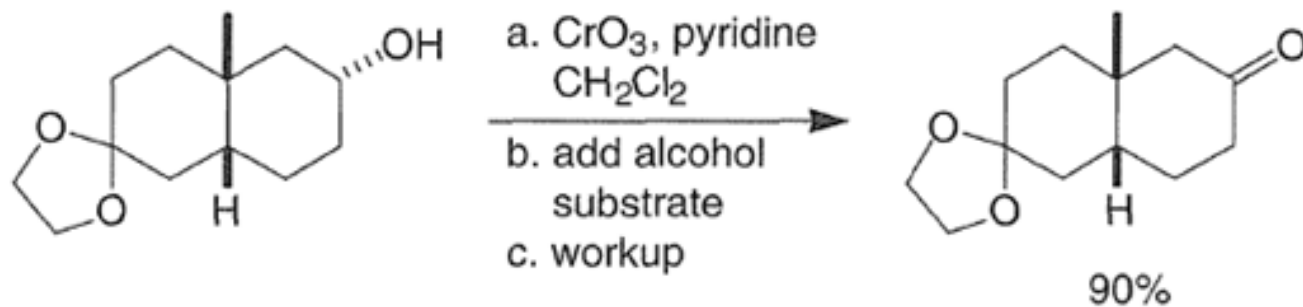
\* As the Collins Reagent does not contain water (compared to the Jones Reagent) and is not as hygroscopic as is the Sarett Reagent, the oxidant is especially useful for the oxidation of primary alcohols to aldehydes where traces of water can lead to over oxidation.



# \* Mechanism of oxidation by collins reagent



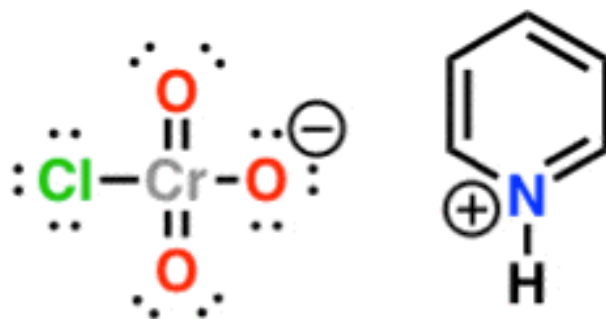
## Examples



# PCC (Pyridinium Chloro Chromate)

## PFC (Pyridinium Fluoro Chromate)

- \* PCC/PFC is a milder version of chromic acid. Essentially, what it does is oxidize alcohols one rung up the oxidation ladder, from primary alcohols to aldehydes and from secondary alcohols to ketones. Unlike chromic acid, PCC will not oxidize aldehydes to carboxylic acids.

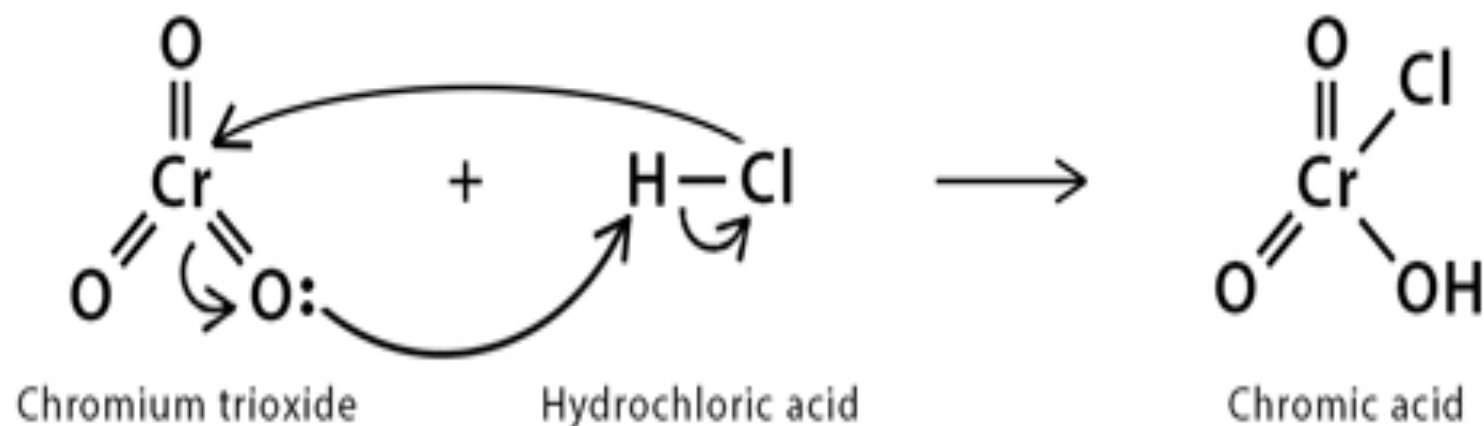


**PCC**  
**(Pyridinium chlorochromate)**

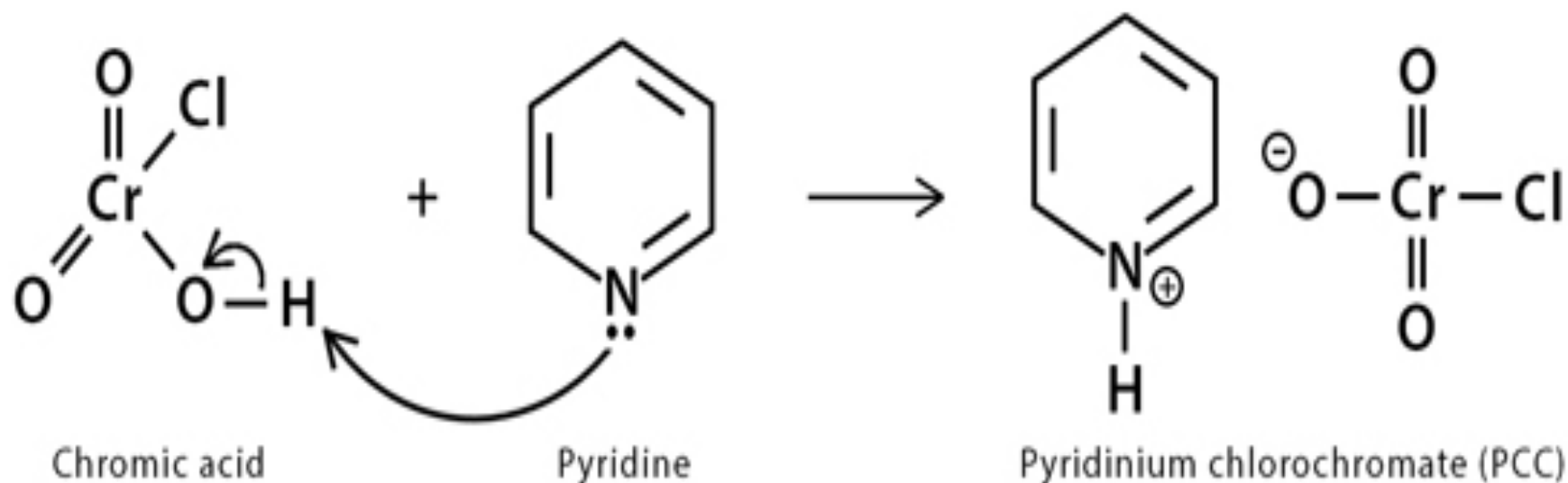


# Preparation of PCC Reagent

**Step 1:** Chromium trioxide dissolves in hydrochloric acid to form chlorochromic acid

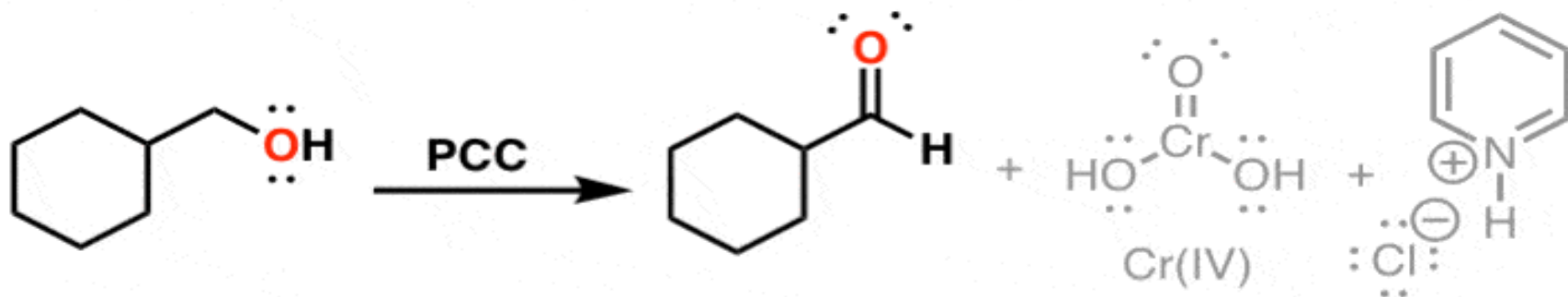


**Step 2:** Addition of pyridine to chlorochromic acid gives PCC reagent

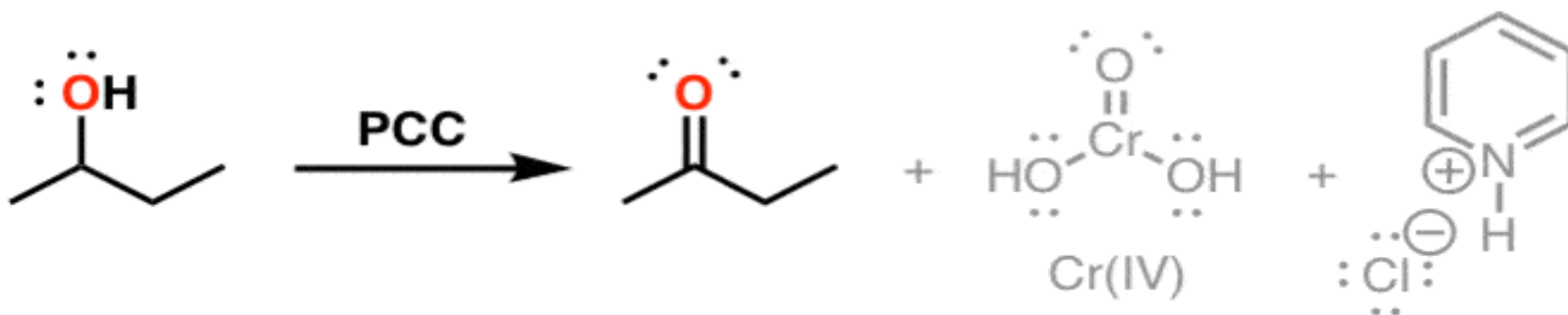


- PCC is used as an oxidant. In particular, it has proven to be highly effective in oxidizing primary and secondary alcohols to aldehydes and ketones, respectively. The reagent is more selective than the related Jones reagent.

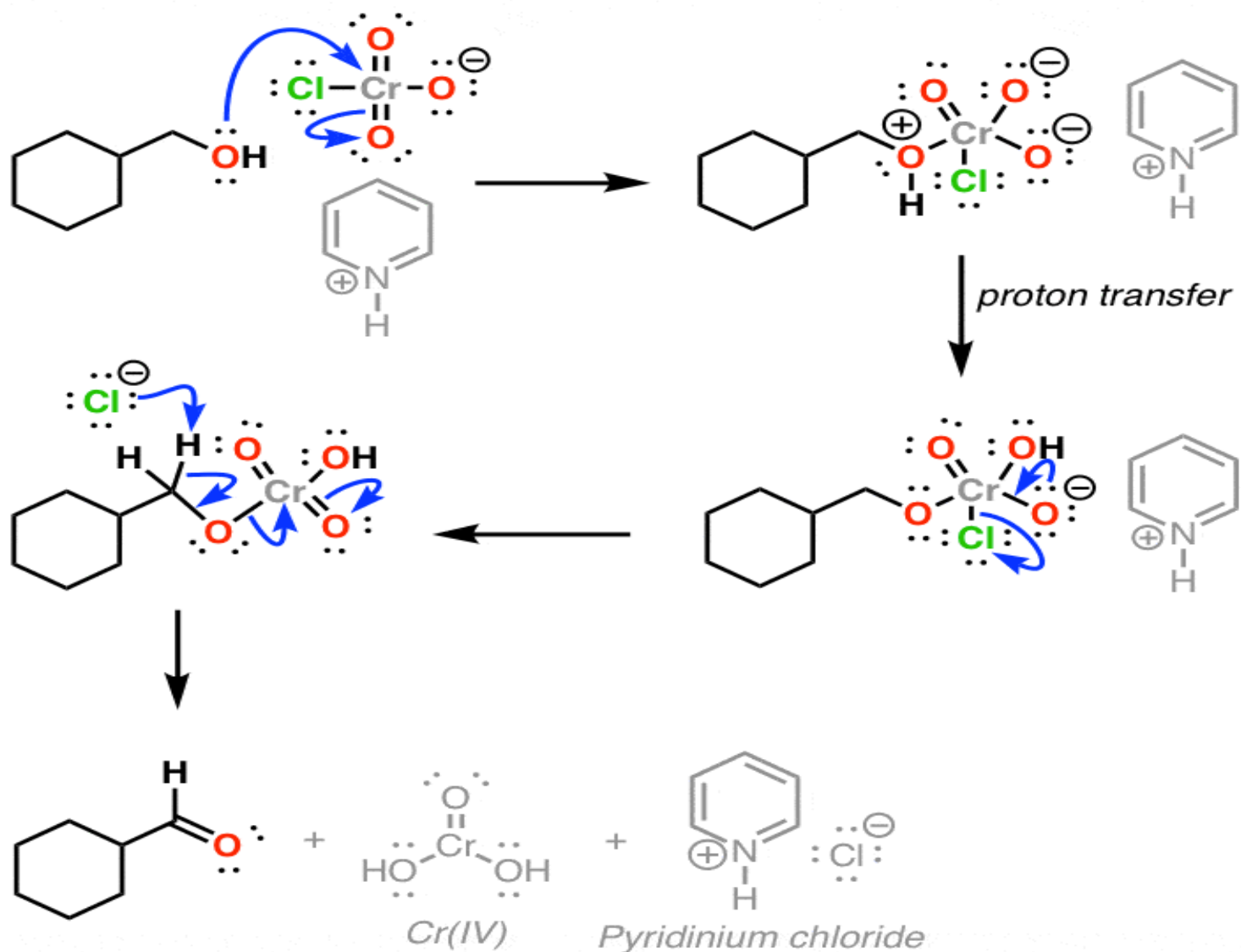
### Example 1: Oxidation of primary alcohols to aldehydes



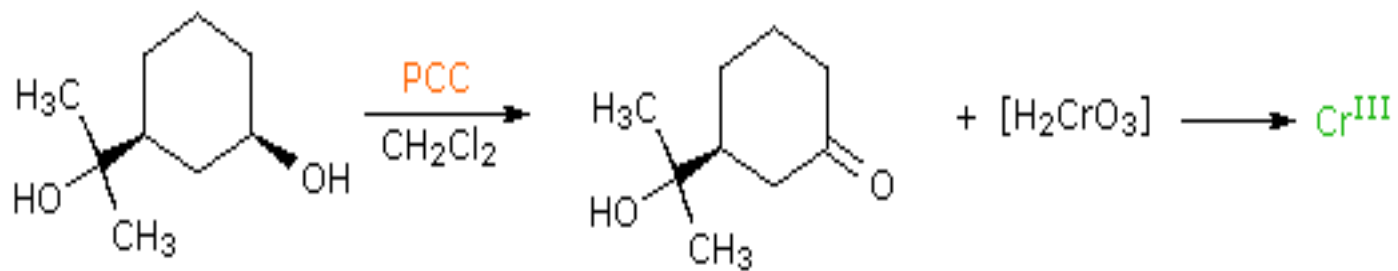
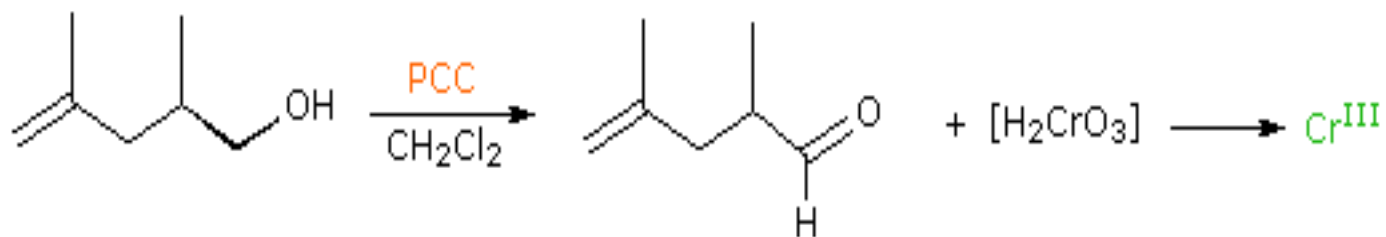
### Example 2: Oxidation of secondary alcohols to ketones



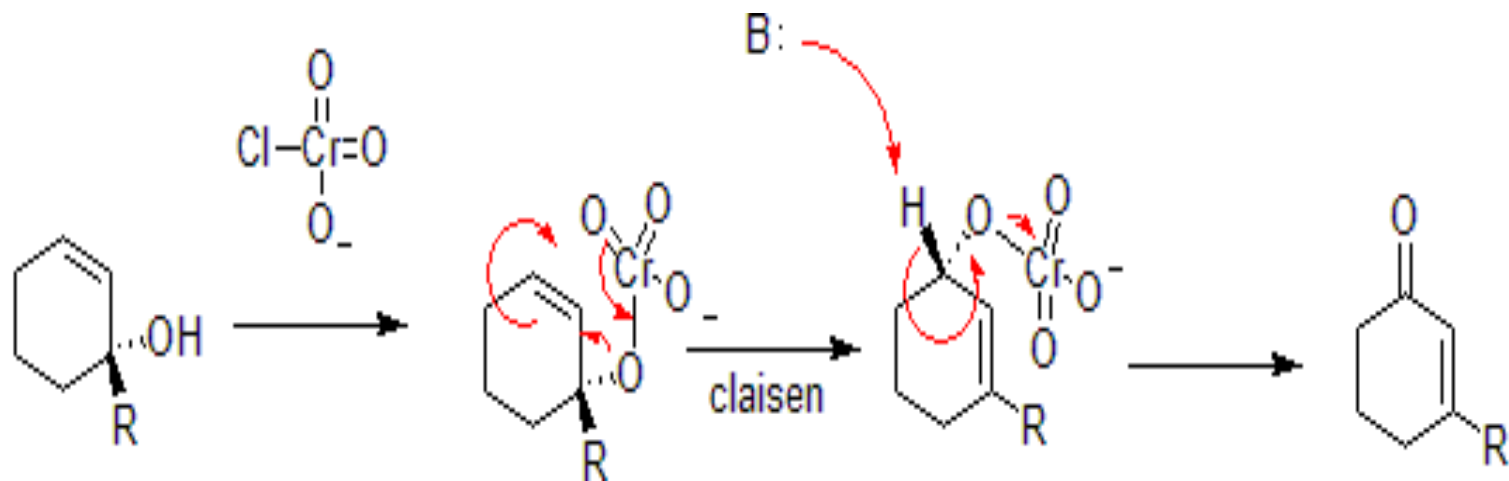
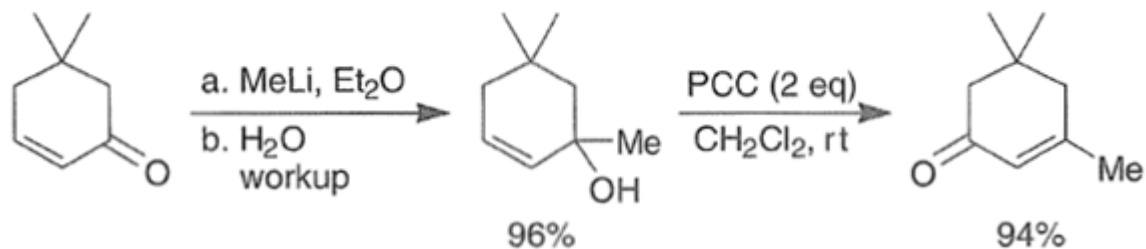
# Mechanism of Oxidation by PCC



\* Example

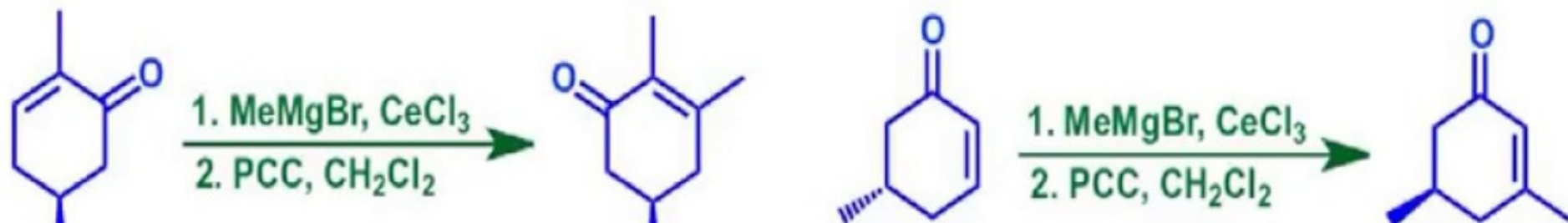
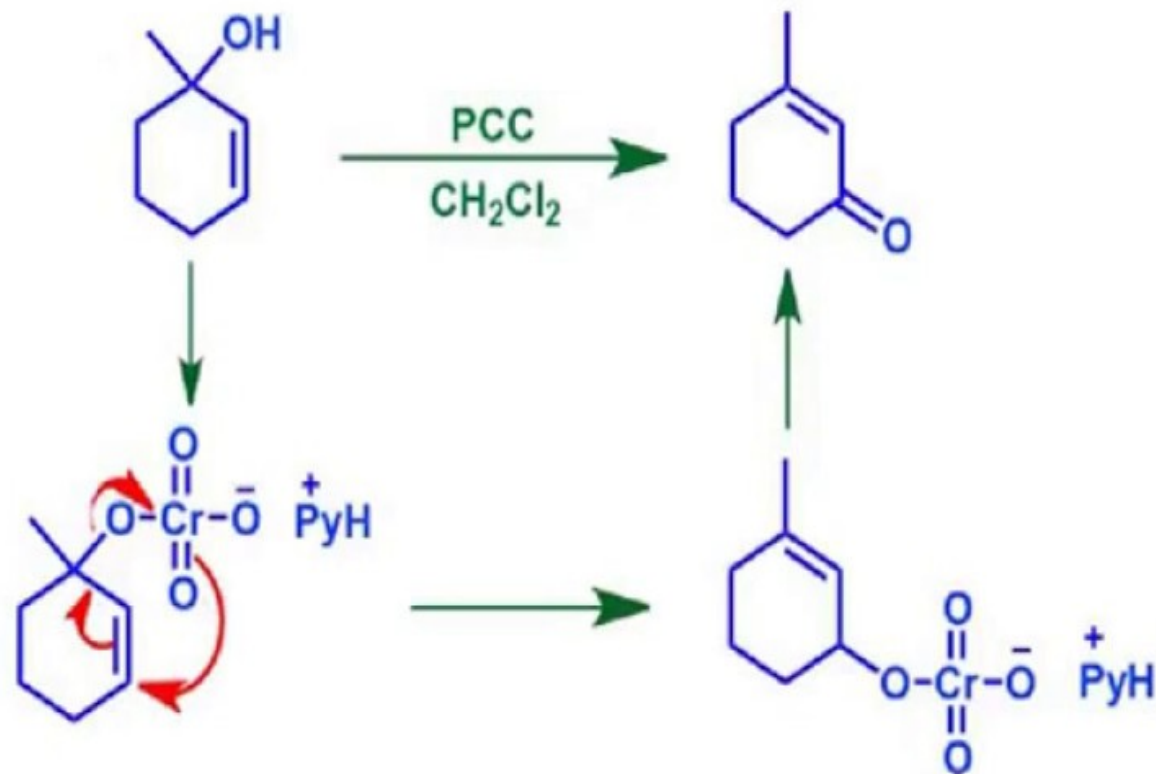


- Tertiary Allylic alcohol Oxidized by PCC to gives unsaturated ketone.



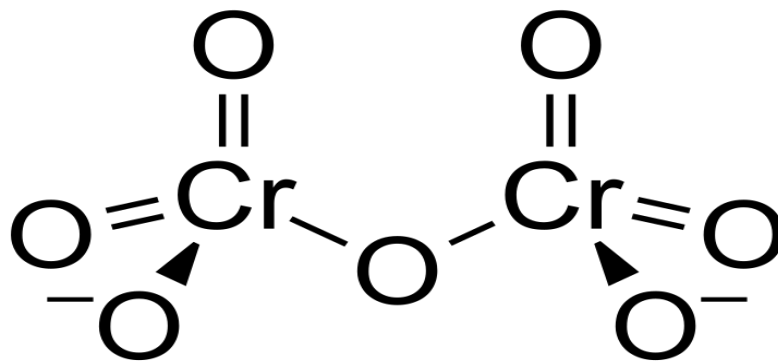
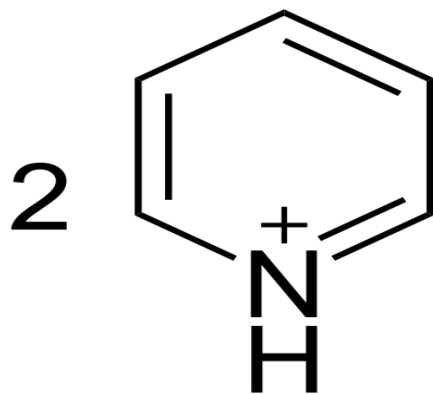
# Pyridinium Chlorochromate (PCC)

## Oxidation of Tertiary Allylic Alcohols:



# PDC (Pyridinium Dichromate)

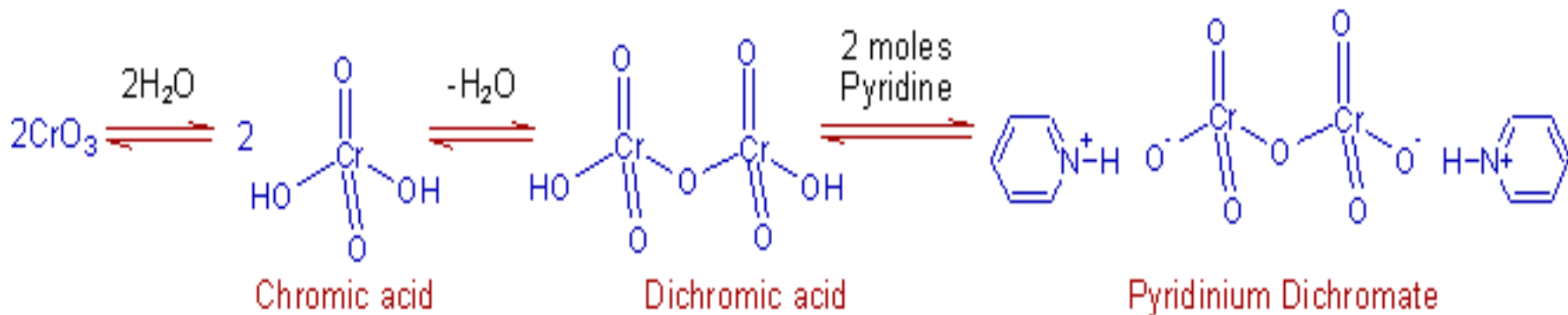
- \* Pyridinium dichromate is the pyridinium salt of dichromate that can be obtained by addition of pyridine to a solution of chromium trioxide in water.
- \* The oxidation of alcohols by **PDC (Pyridinium Dichromate)** works under mild conditions and can be used for compounds containing unstable functional groups. This method is useful to synthesize aldehydes.
- \* PDC is closer to neutral.



- Pyridinium dichromate (PDC)**,  $(C_5H_5NH)_2Cr_2O_7$  is an orange colored solid used as an oxidizing agent.
- \* PDC is less acidic than PCC ( Pyridinium Chloro Chromate) and hence is more suitable in the oxidation of acid sensitive compounds.

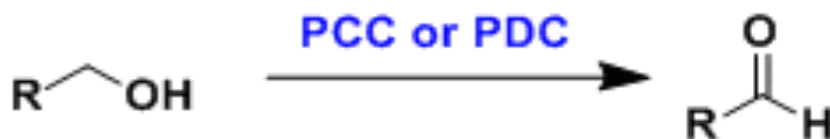
### *Preparation of PDC*

- \* Pyridinium dichromate, PDC can be obtained by gradual addition of a solution of chromic anhydride ( $CrO_3$ ) in water to pyridine in ice cold conditions.

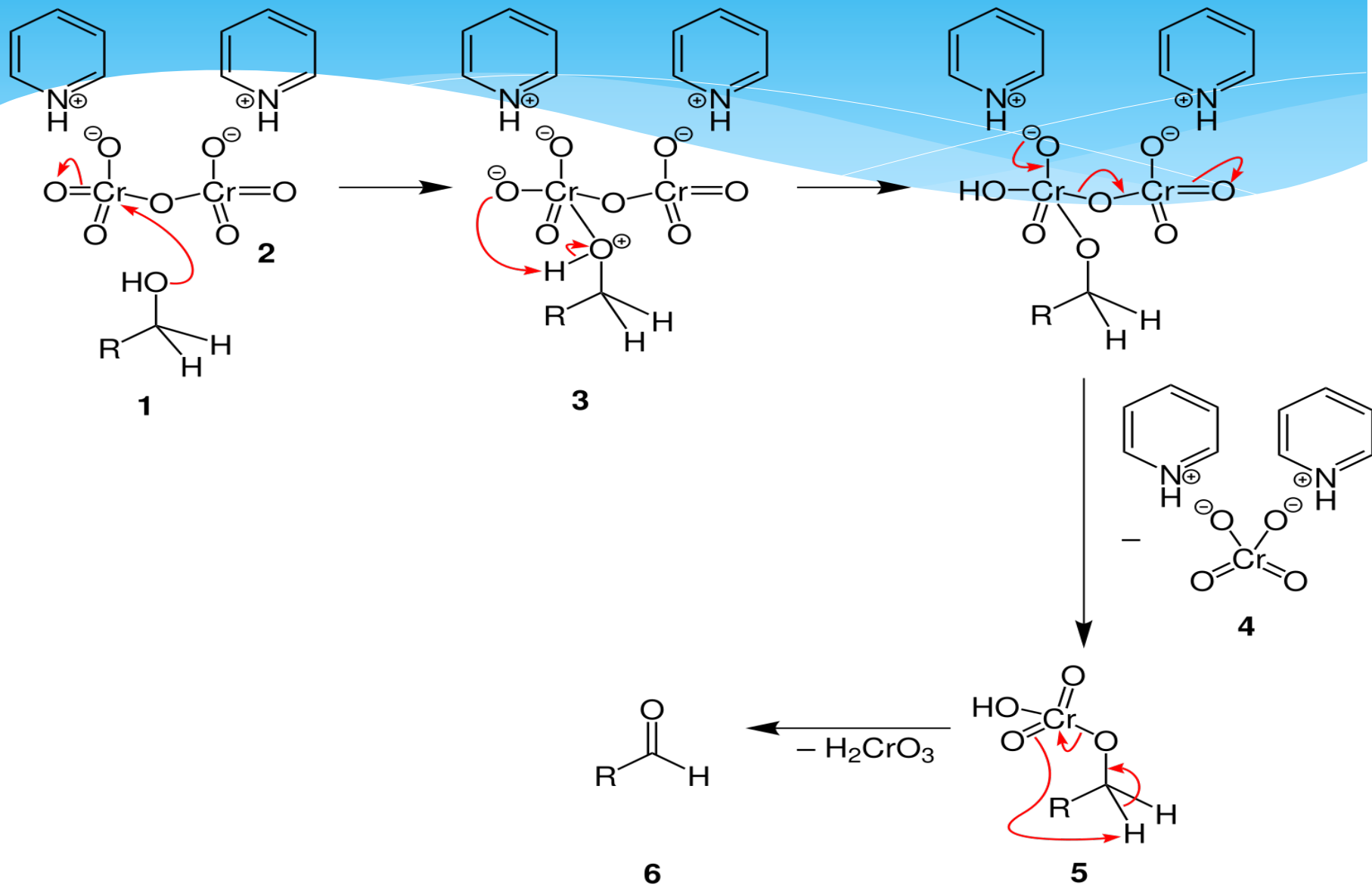




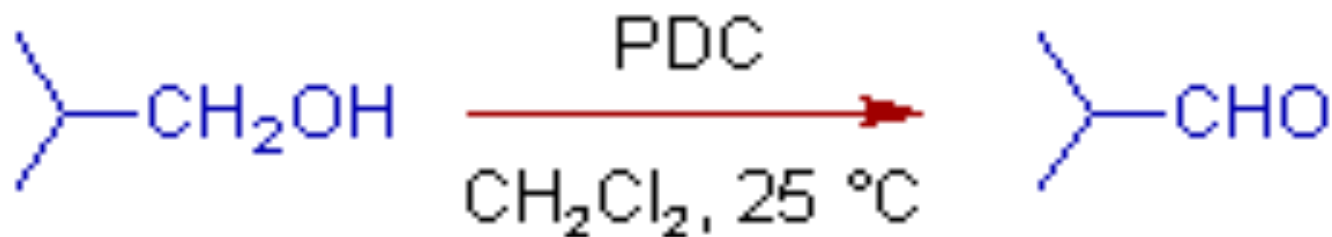
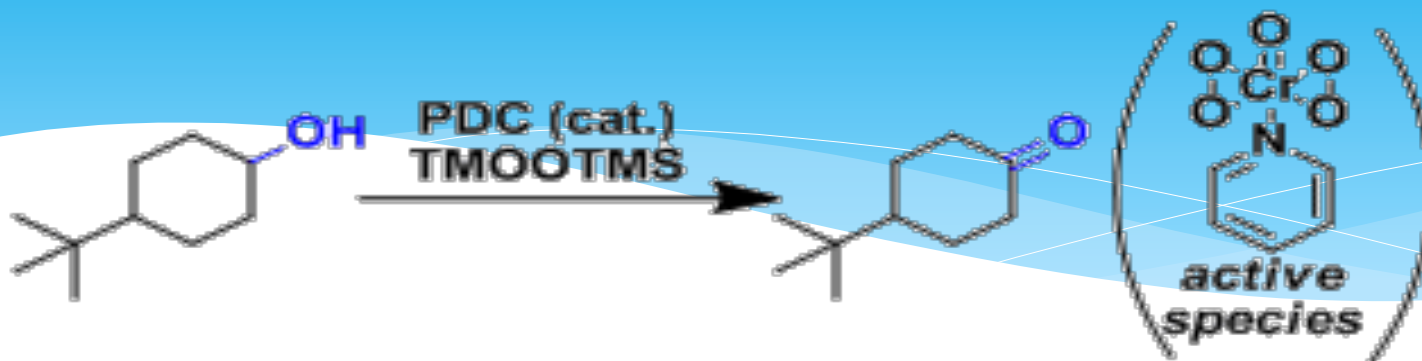
- \* It is soluble in water, DMF and DMSO. But sparingly soluble in  $\text{CH}_2\text{Cl}_2$  or  $\text{CH}_3\text{Cl}$ .
- \* The reaction conditions are mild and neutral. It can be employed to oxidize compounds containing acid sensitive functional groups.
- \* PDC is less acidic than PCC ( Pyridinium Chloro Chromate) and hence is more suitable in the oxidation of acid sensitive compounds.



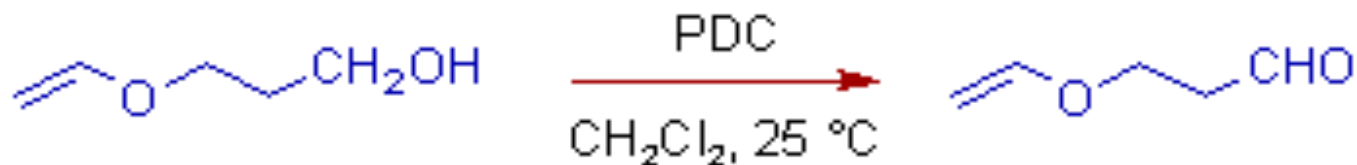
\* Mechanism of oxidation by PDC



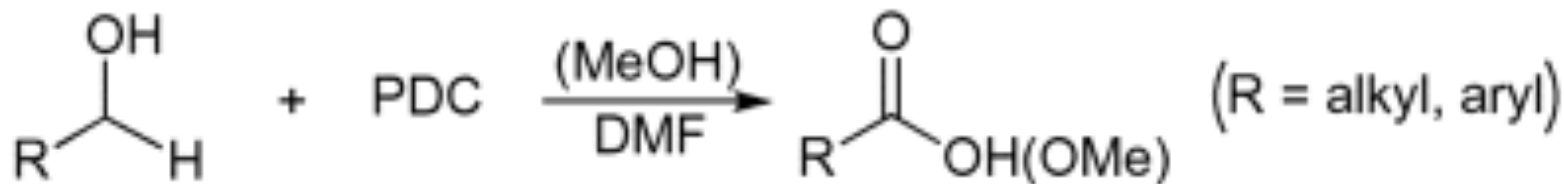
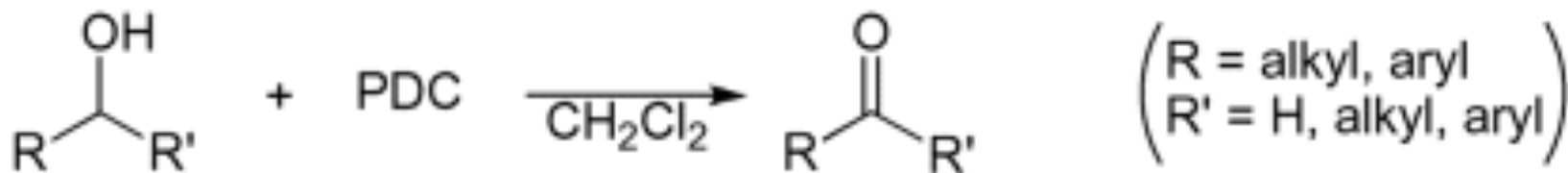
\* *Examples of PDC oxidation*



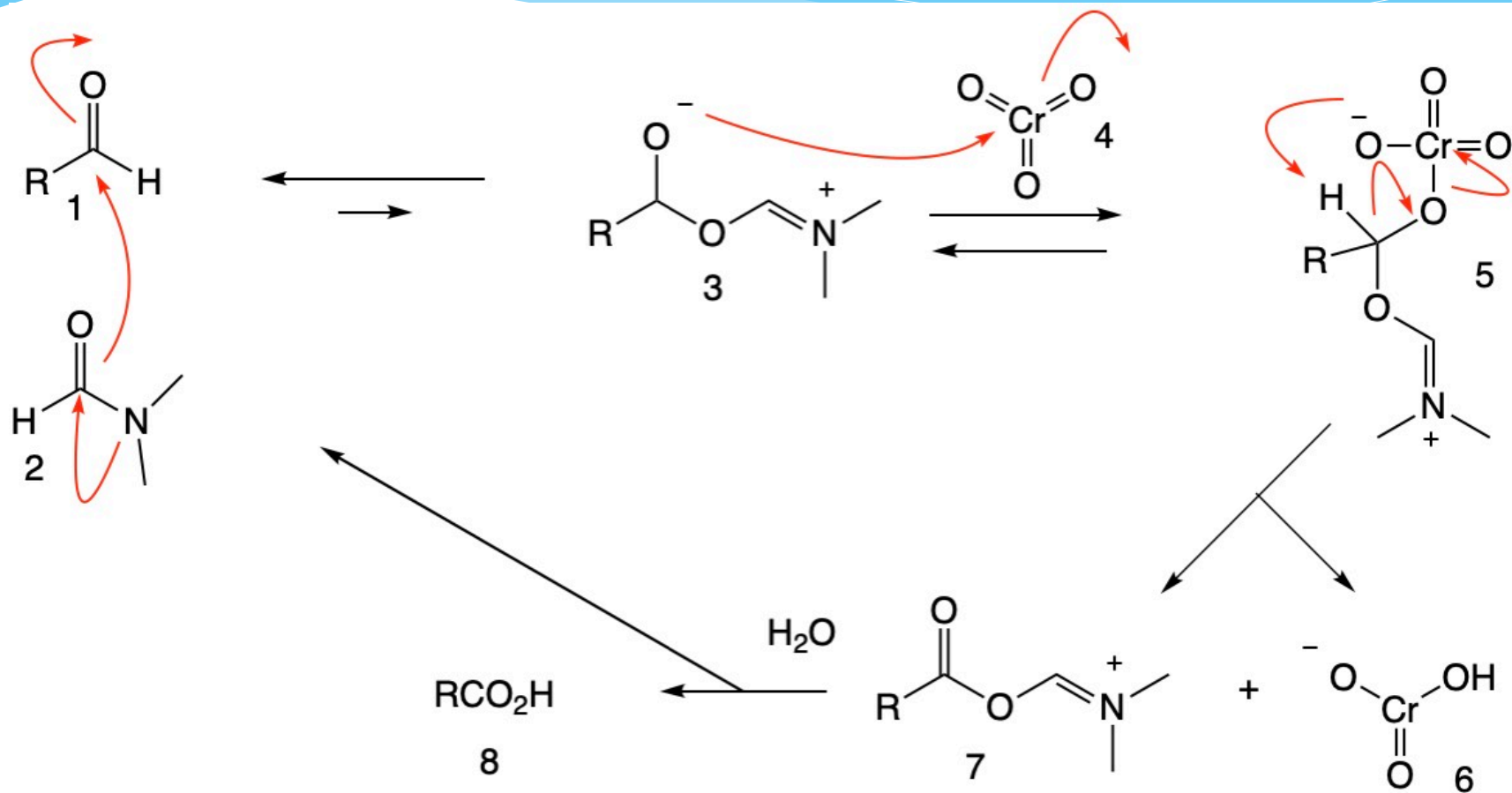
\* Acid sensitive groups, such as enol ethers, are not affected during the oxidation with PDC.



- \* In DMF, the reaction of primary alcohols with PDC (except for ally alcohols) leads to complete oxidation to carboxylic acids. But in DCM reaction is stop at the aldehyde as product only.
- \* PDC in  $\text{CH}_2\text{Cl}_2$  or DMF is also called as **Corey-Schmidt reagent**. In this case, PDC is maintained in anhydrous conditions.

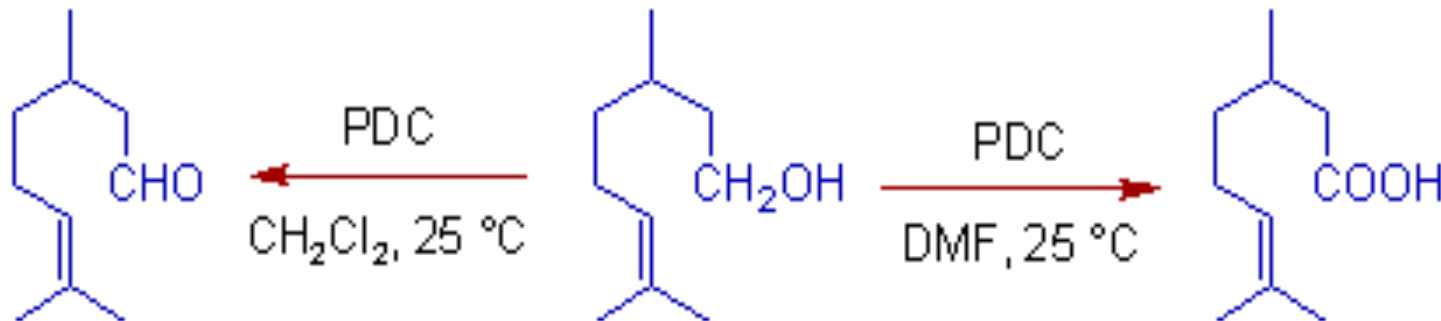


# \* Over oxidation mechanism of primary alcohol to carboxylic acid by PDC In DMF as solvent



- \* Examples

- \* Non-conjugated primary alcohols are oxidized to carboxylic acids with excess of PDC in moist DMF. But in Dichloromethane, the oxidation stops at aldehyde level only.

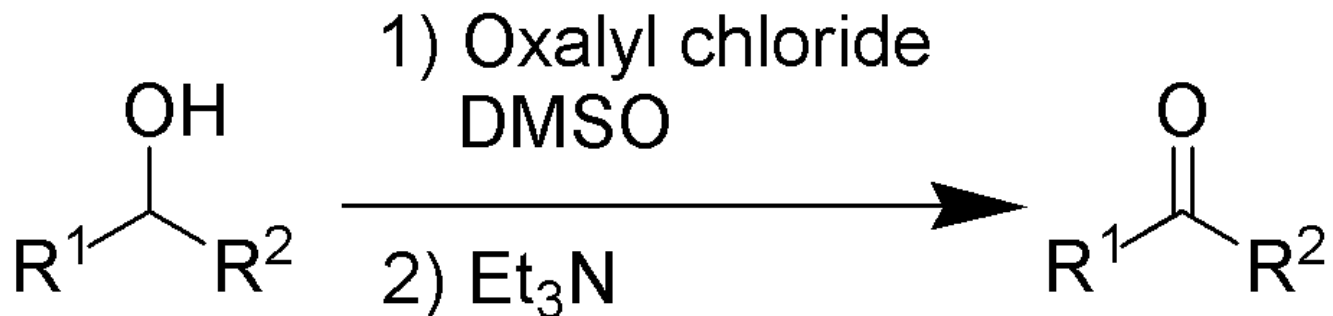


- \* However the conjugated primary alcohols are only oxidized to aldehydes even in DMF.



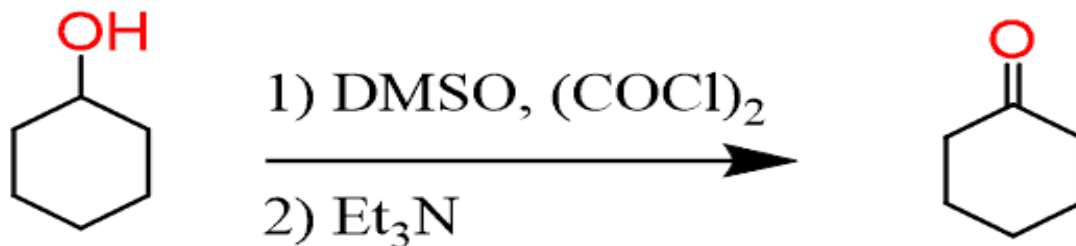
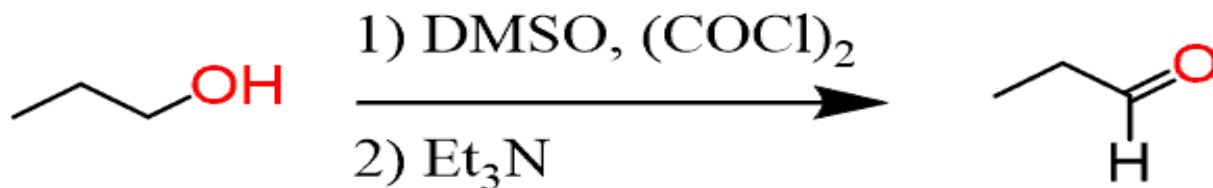
# Swern Oxidation

\* The **Swern oxidation**, named after [Daniel Swern](#), is a chemical reaction whereby a primary or secondary alcohol is oxidized to an aldehyde or ketone using oxalyl chloride, dimethyl sulfoxide (DMSO) and an organic base, such as triethylamine. It is one of the many oxidation reactions commonly referred to as 'activated DMSO' oxidations. The reaction is known for its mild character and wide tolerance of functional groups.



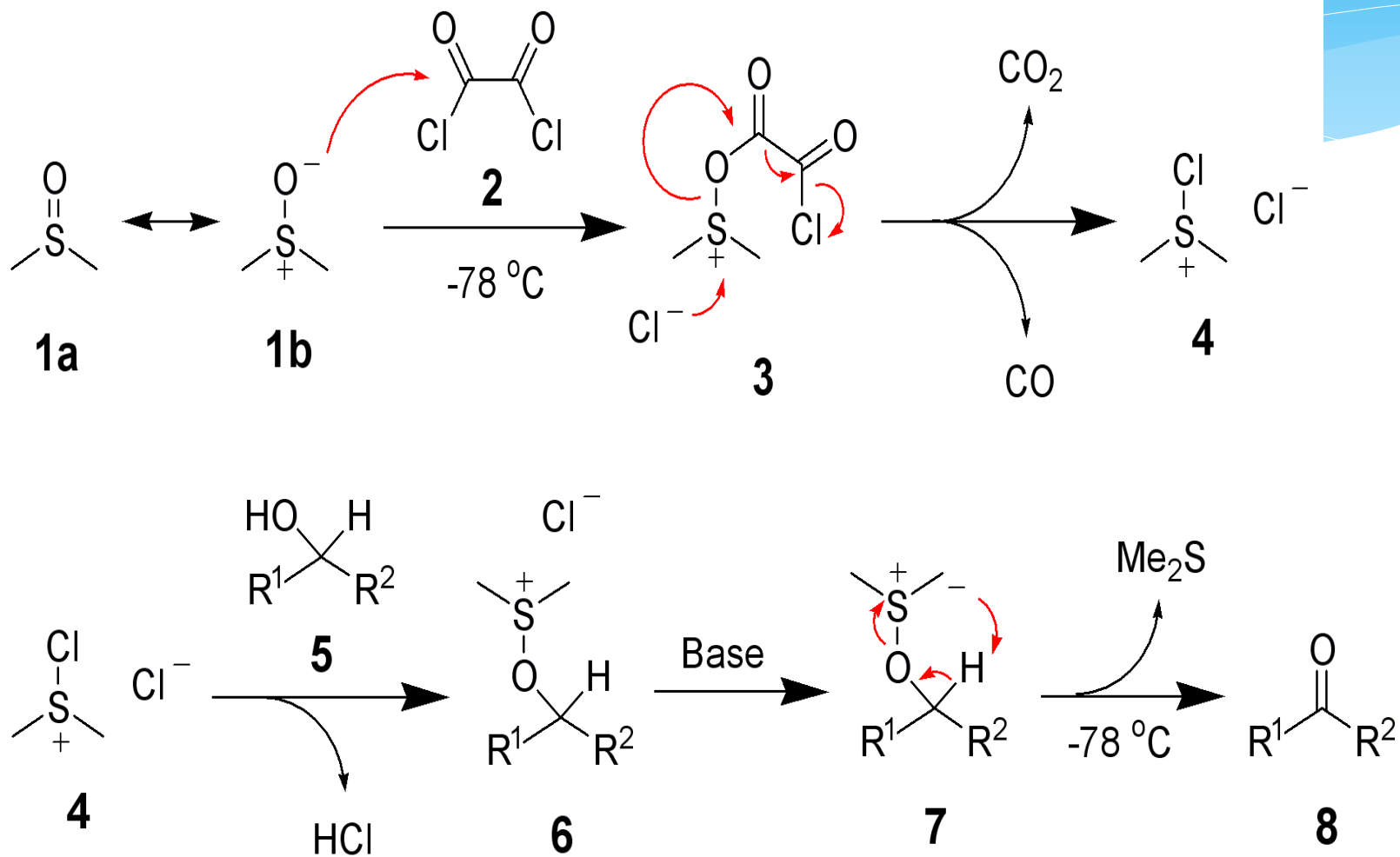
- \* Dichloromethane is usually the solvent of choice for this reaction, but Et<sub>2</sub>O or THF may also be used.
- \* For secondary alcohols, warming the reaction to -40 °C after the addition of the alcohol for 20 min may help.
- \* Base is must for the oxidation.

**Swern Oxidation: 1° Alcohols - Aldehyde, 2° - Ketone**





## Mechanism of Swern oxidation

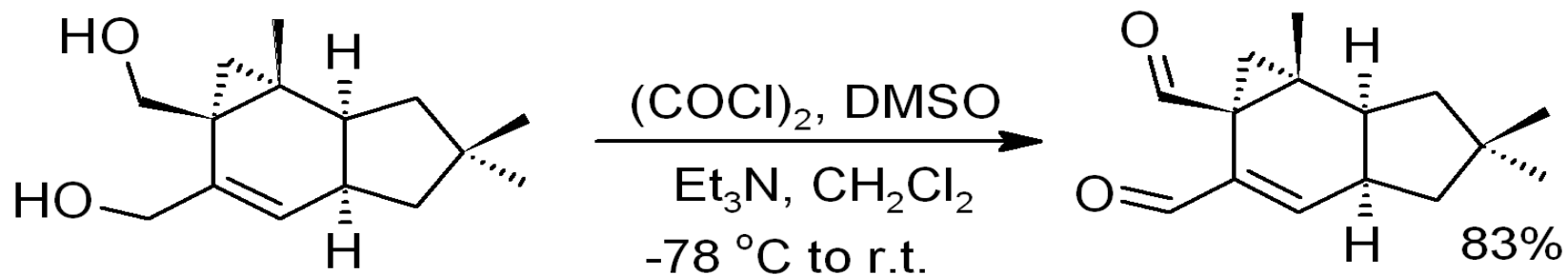
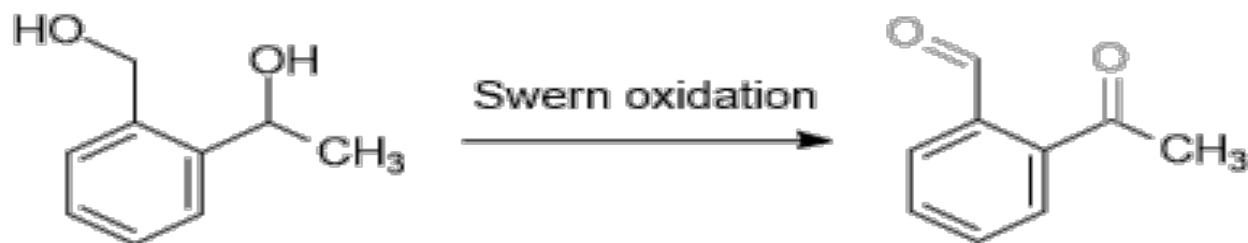


## \* Examples

### Selected Example 1<sup>1)</sup>

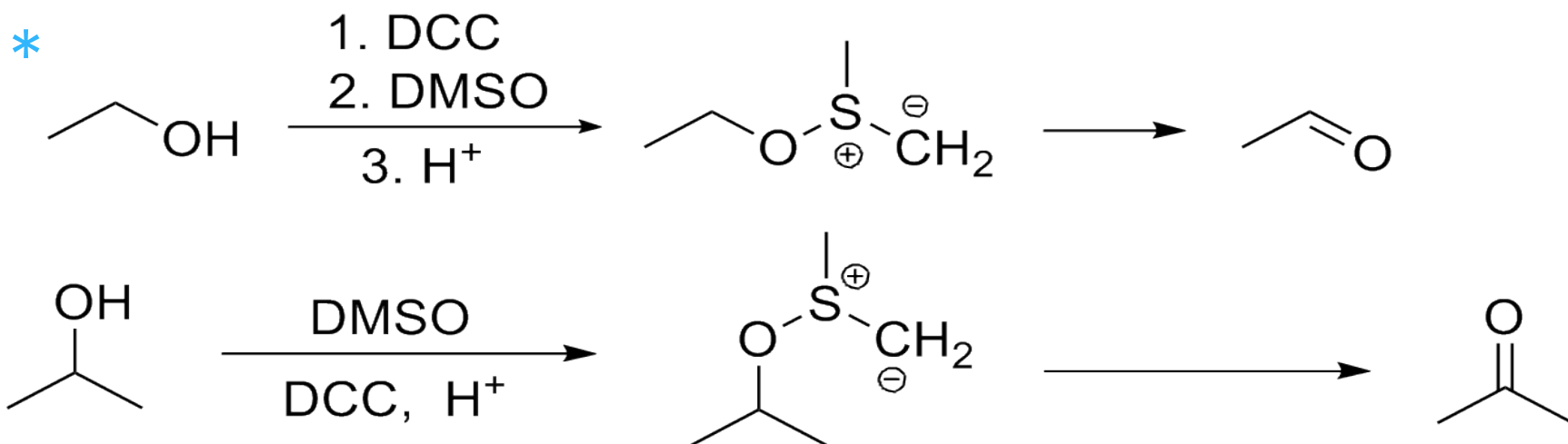


### Selected Example 2<sup>2)</sup>

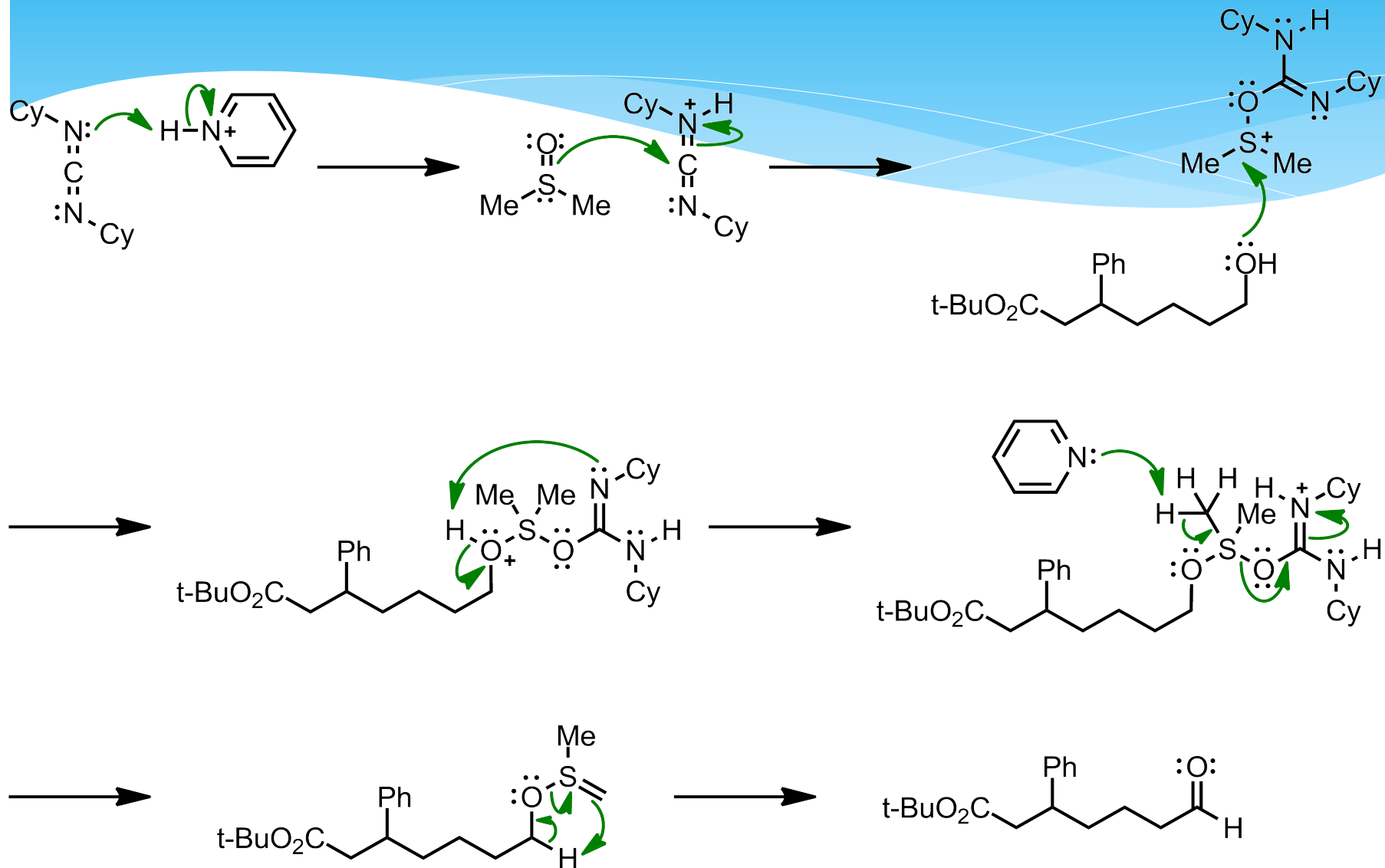


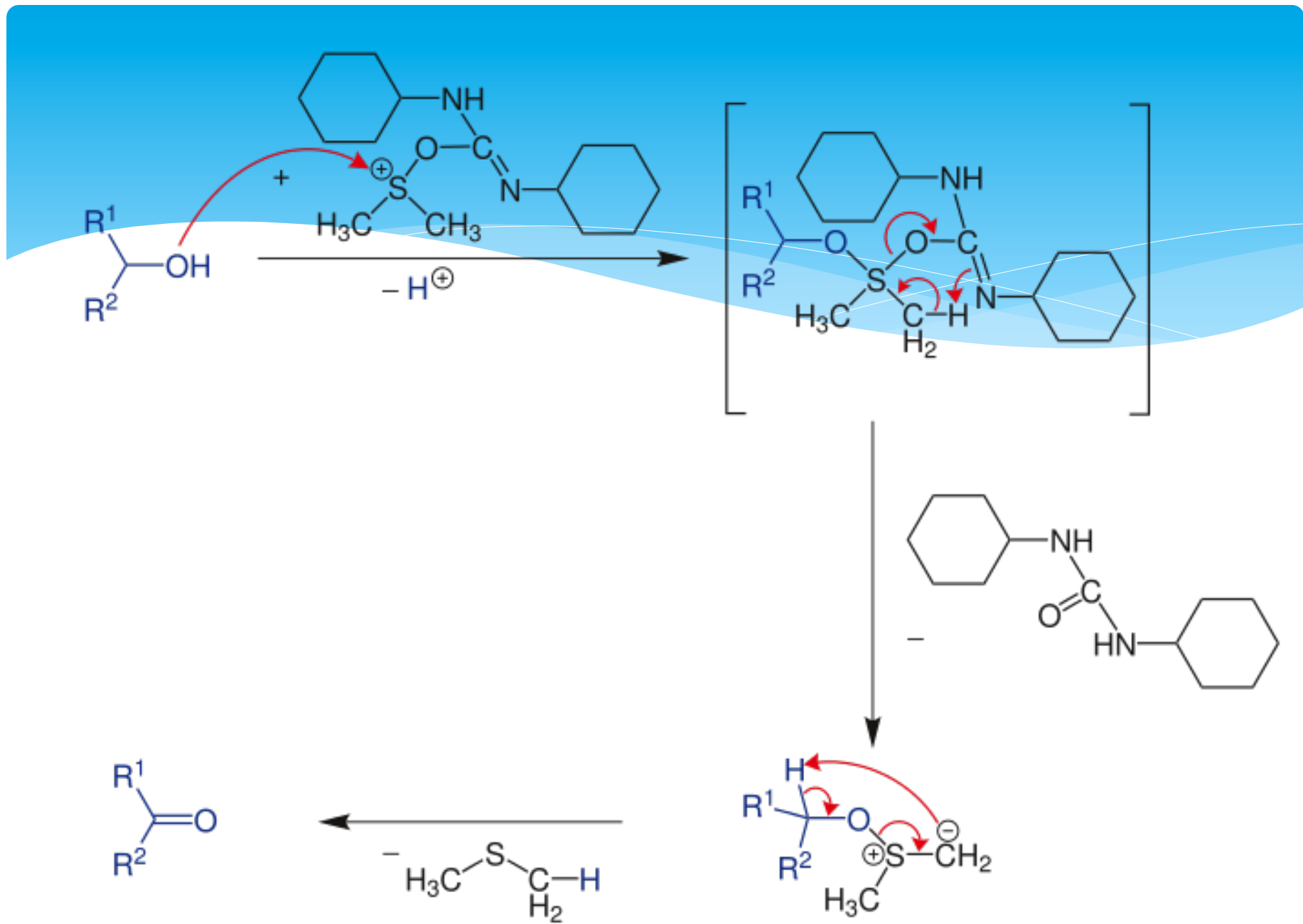
# Moffatt Oxidation

\* The **Pfitzner–Moffatt oxidation**, sometimes referred to as simply the **Moffatt oxidation**, is a chemical reaction for the oxidation of primary and secondary alcohols to aldehydes and ketones, respectively. The oxidant is a combination of dimethyl sulfoxide (DMSO) and dicyclohexylcarbodiimide (DCC).



# \* Mechanism of Moffatt Oxidation

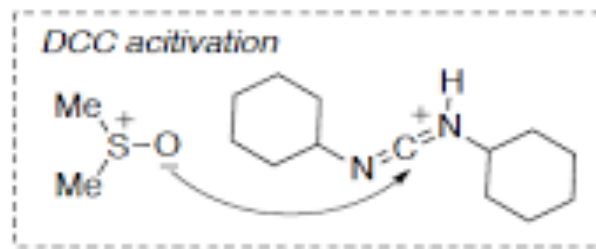
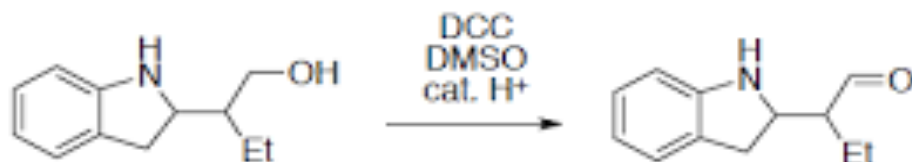




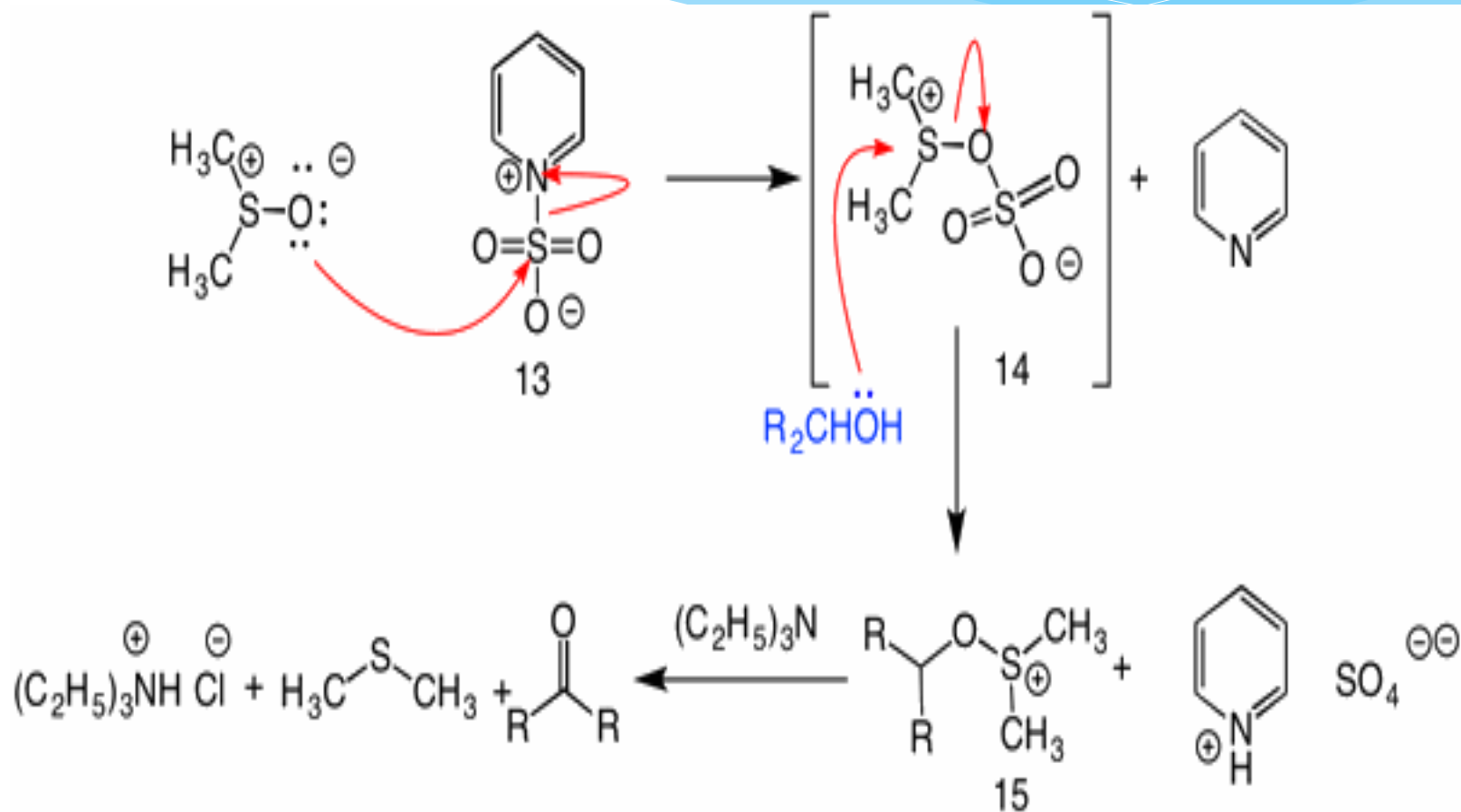
# Examples



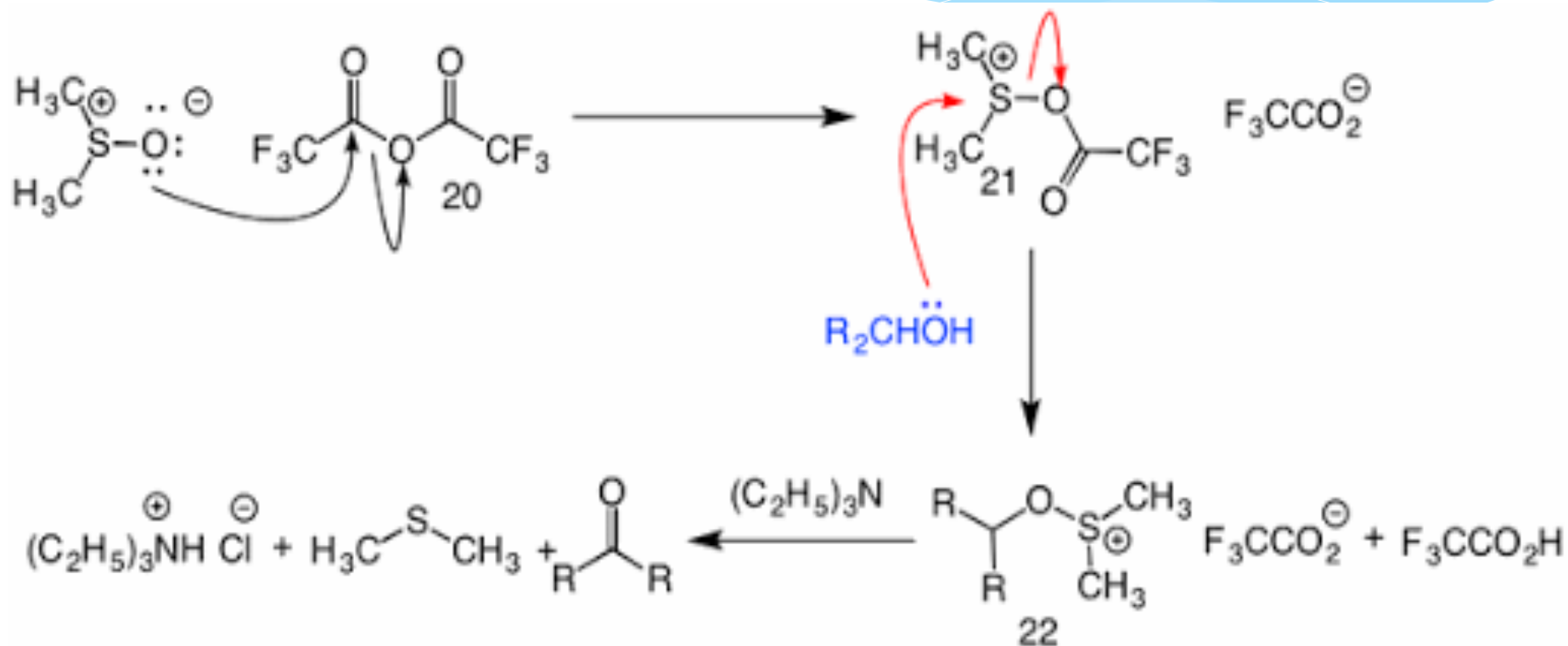
Moffatt oxidation:



*Parikh – Doering Oxidation reaction* : Modified reaction of Moffatt oxidation. DMSO – SO<sub>3</sub> mediated reaction.

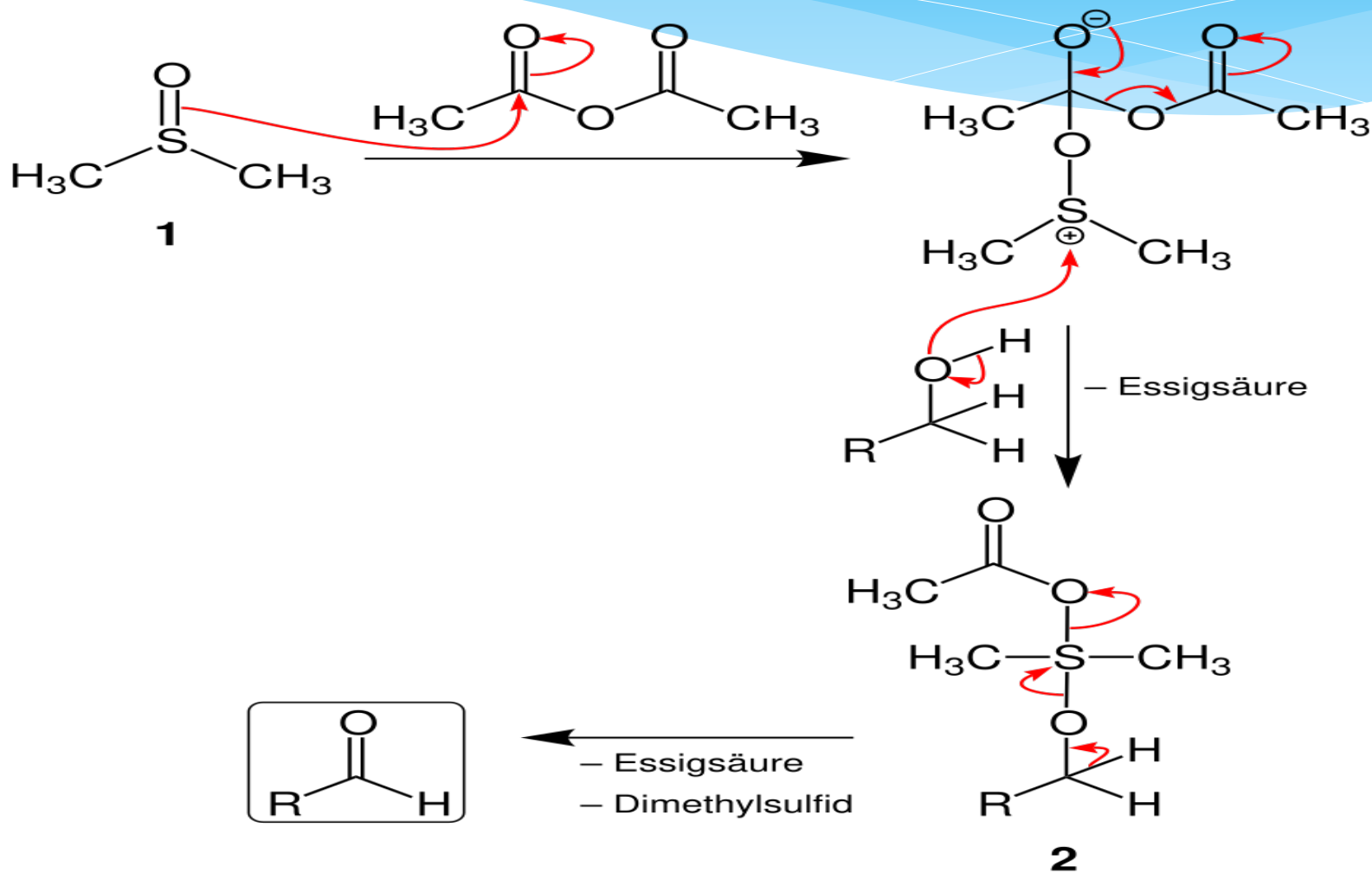


\* Omura- Sharma- Swern Oxidation reaction : Modified reaction of Moffatt oxidation. DMSO –TFAA mediated reaction.





\* *Albright-Goldman Oxidation* reaction : Modified reaction of Moffatt oxidation. DMSO –Aceticunhydride mediated reaction.

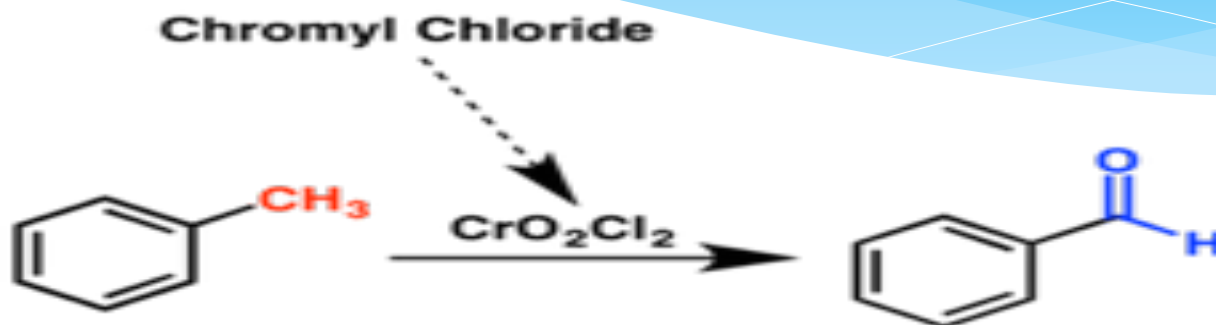


# Etard Oxidation

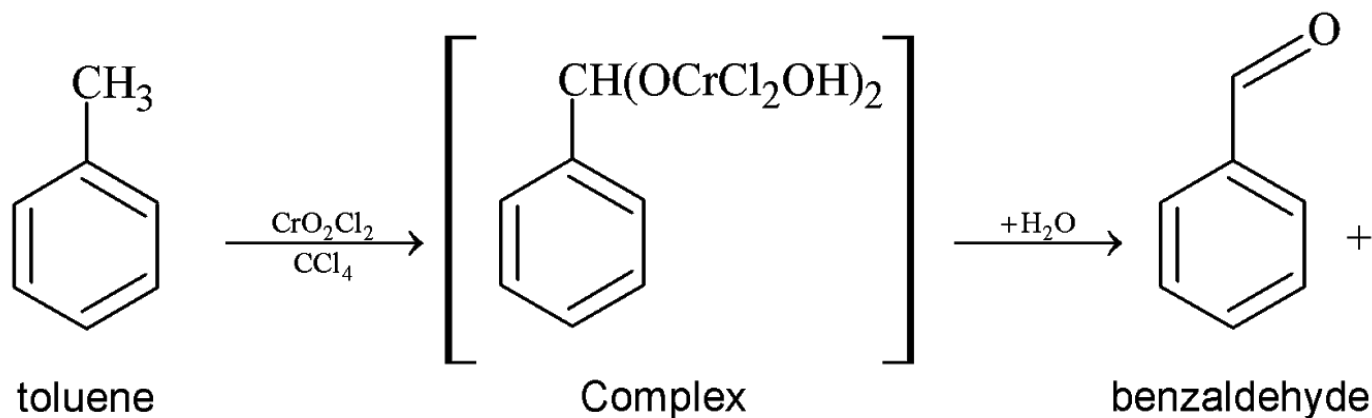
- \* The **Etard reaction** is an organic transformation in which a methyl group (-CH<sub>3</sub>) bonded to an aromatic (benzene) ring undergoes an oxidation reaction and becomes an aldehyde functional group. Consider as an example the oxidation of toluene to produce benzaldehyde. The general reaction looks like:



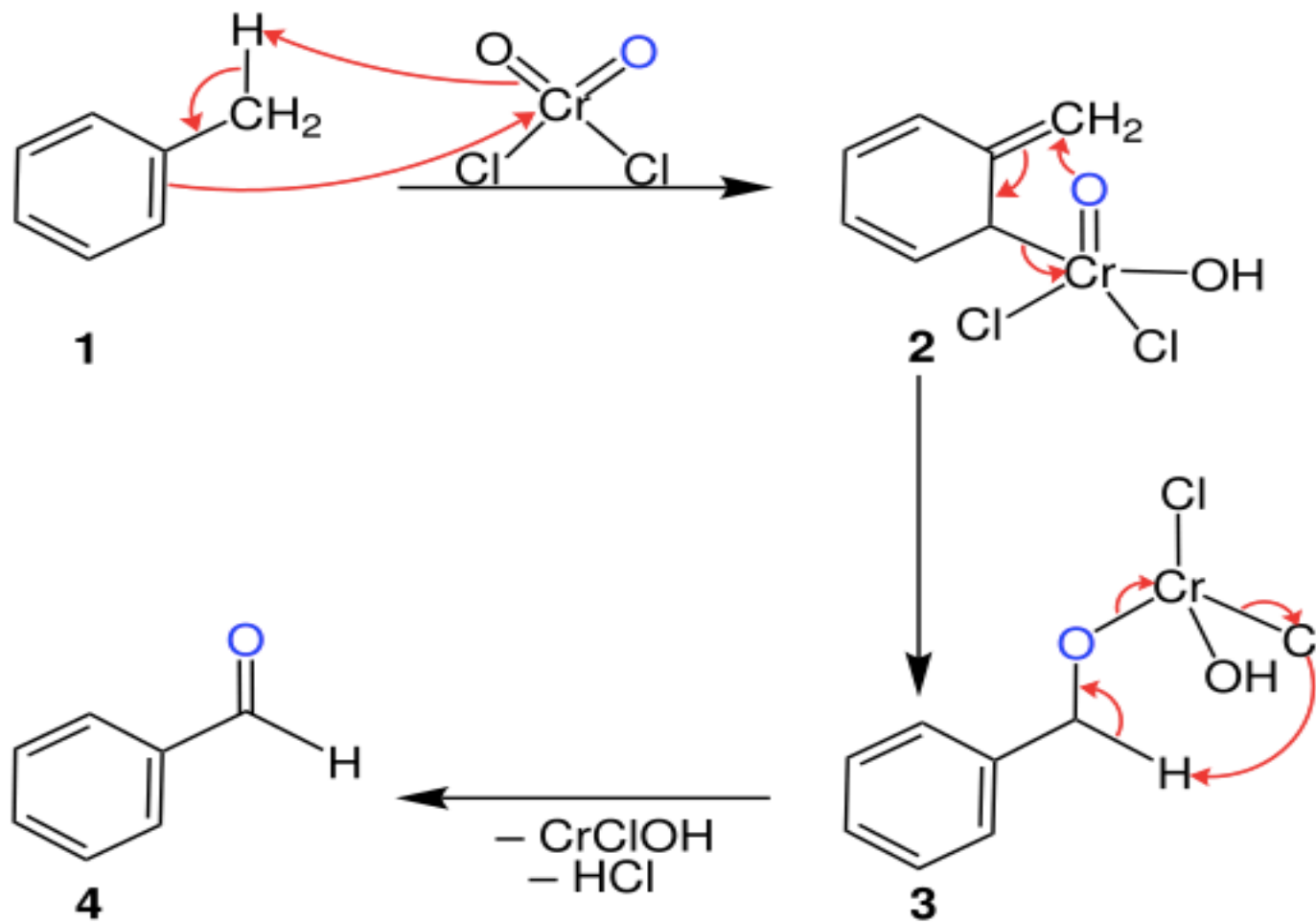
- \* The specific oxidizing agent the Etard reaction employs is chromyl chloride. Chromyl chloride is a chromium-based, mild oxidizing agent that is excellent at making aldehydes.



- \* Reaction:

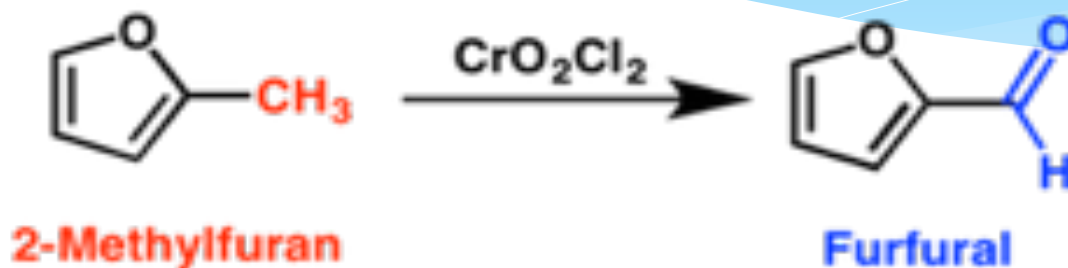


## Mechanism of Etard Oxidation Reaction

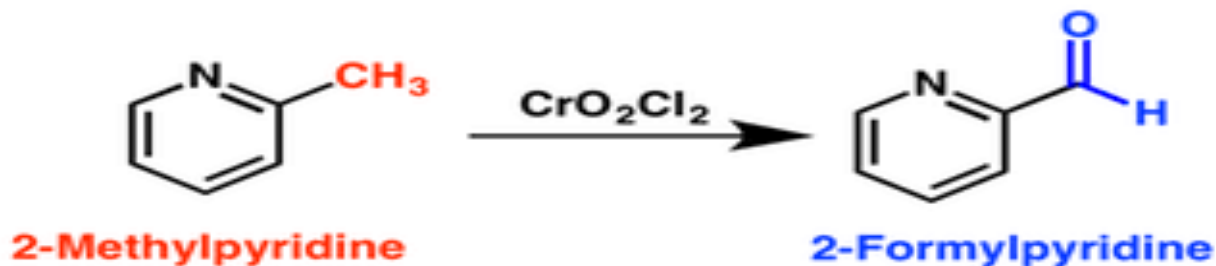


\* *Examples of Etard Oxidation*

- \* 2-Methylfuran can also participate in the Etard reaction, and the product is furfural, which itself is an industrially and synthetically useful organic building block.

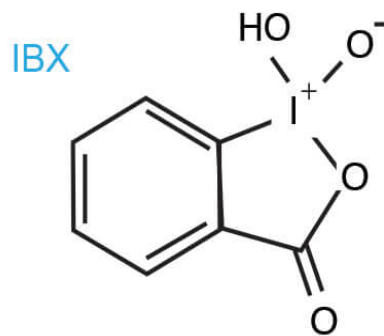


- \* Organic compounds that contain nitrogen atoms can also undergo an Etard reaction. For example, 2-methylpyridine can be taken and transformed into 2-formylpyridine easily by virtue of the Etard reaction



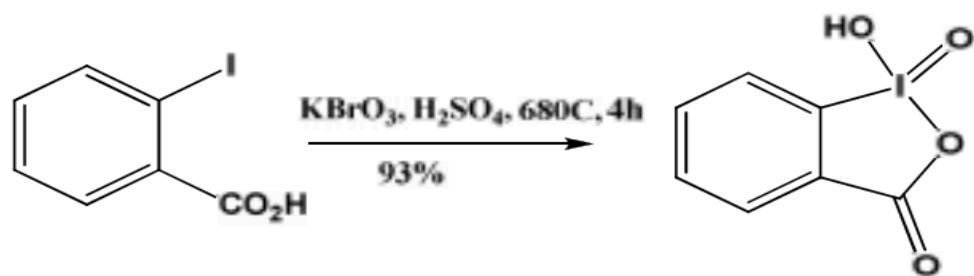
# Iodoxybenzoic Acid (IBX)

- \* A mild and efficient oxidation of alcohols with *o*-iodoxybenzoic acid (IBX) is catalyzed by  $\beta$ -cyclodextrin in a water/acetone mixture (86:14). Various alcohols were oxidized at room temperature in excellent yields.

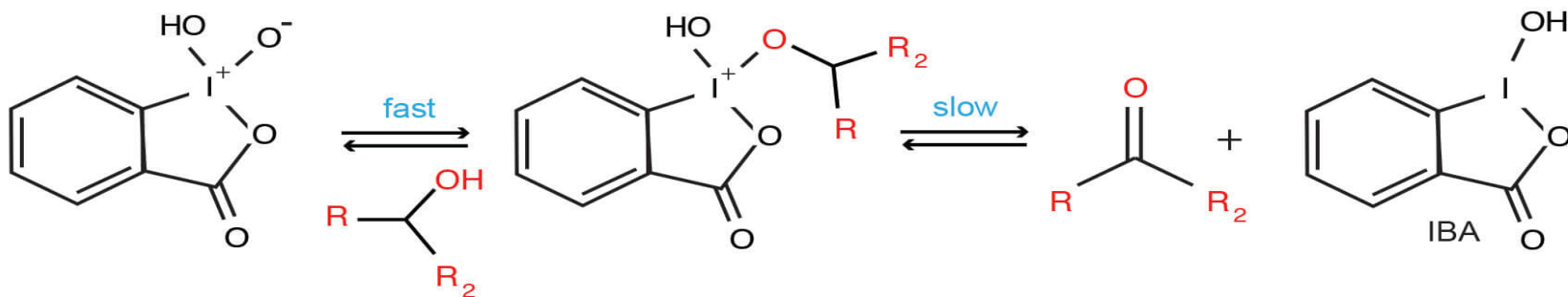


\* Preparation of IBX

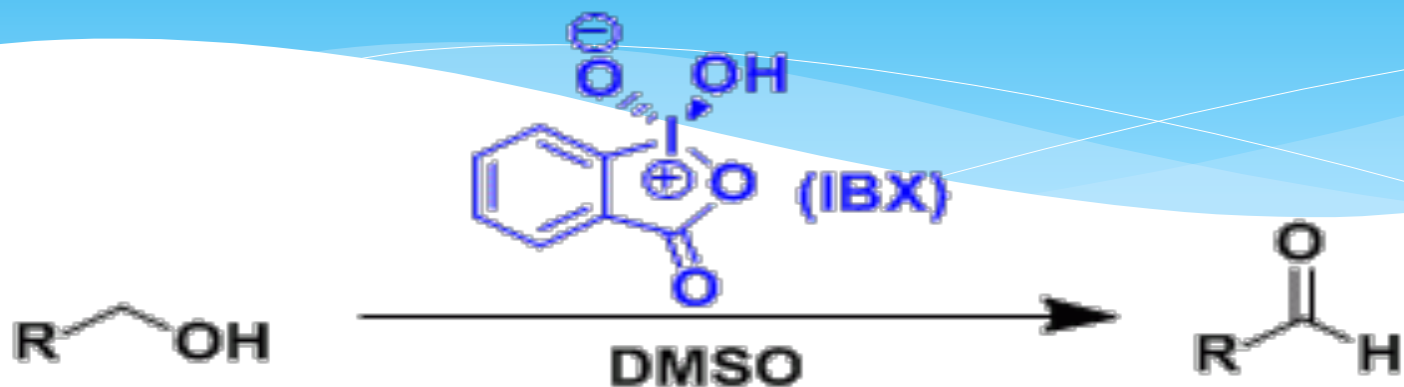
\* IBX is prepared from 2-iodobenzoic acid, potassium bromate, and sulfuric acid.



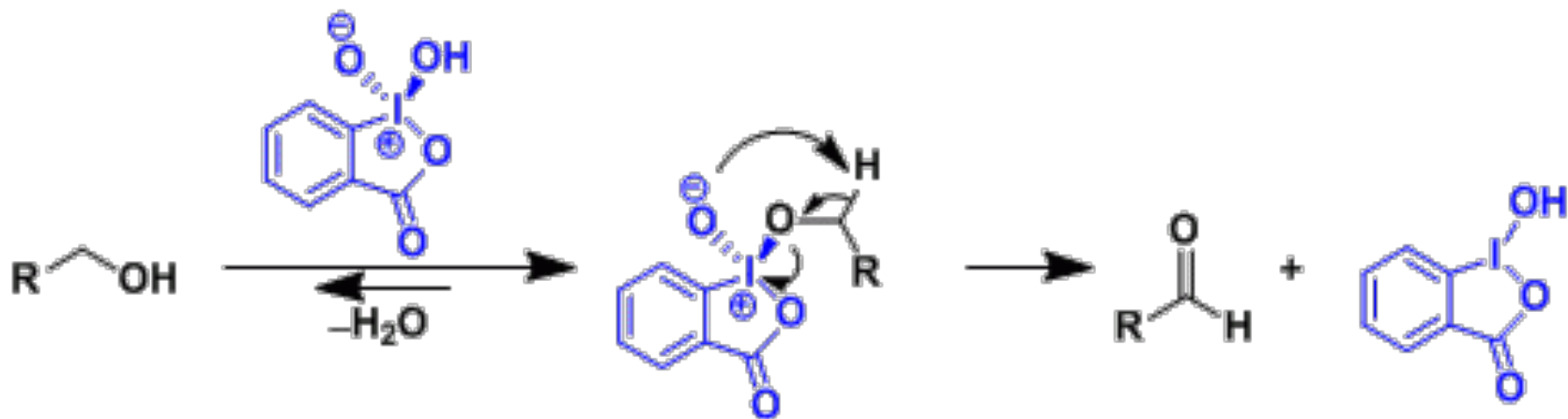
\* IBX oxidized secondary alcohol to Ketone.



## *IBX Oxidized Primary alcohol to aldehyde*

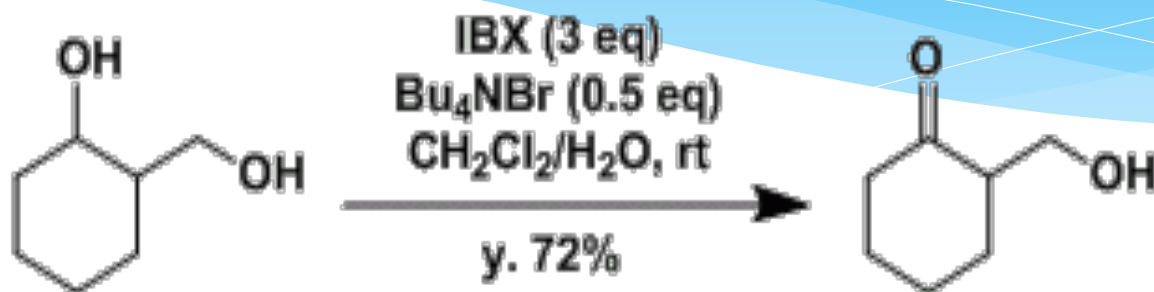


## *Mechanism of IBX Oxidation*

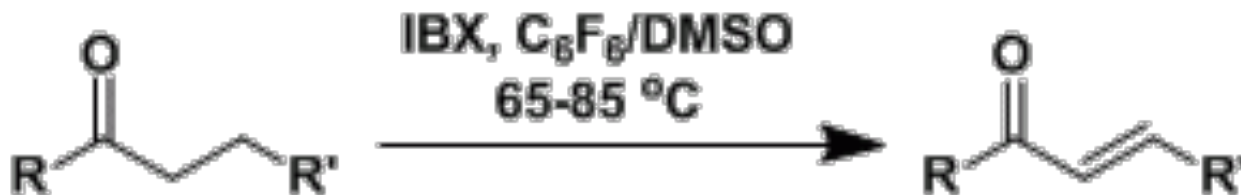




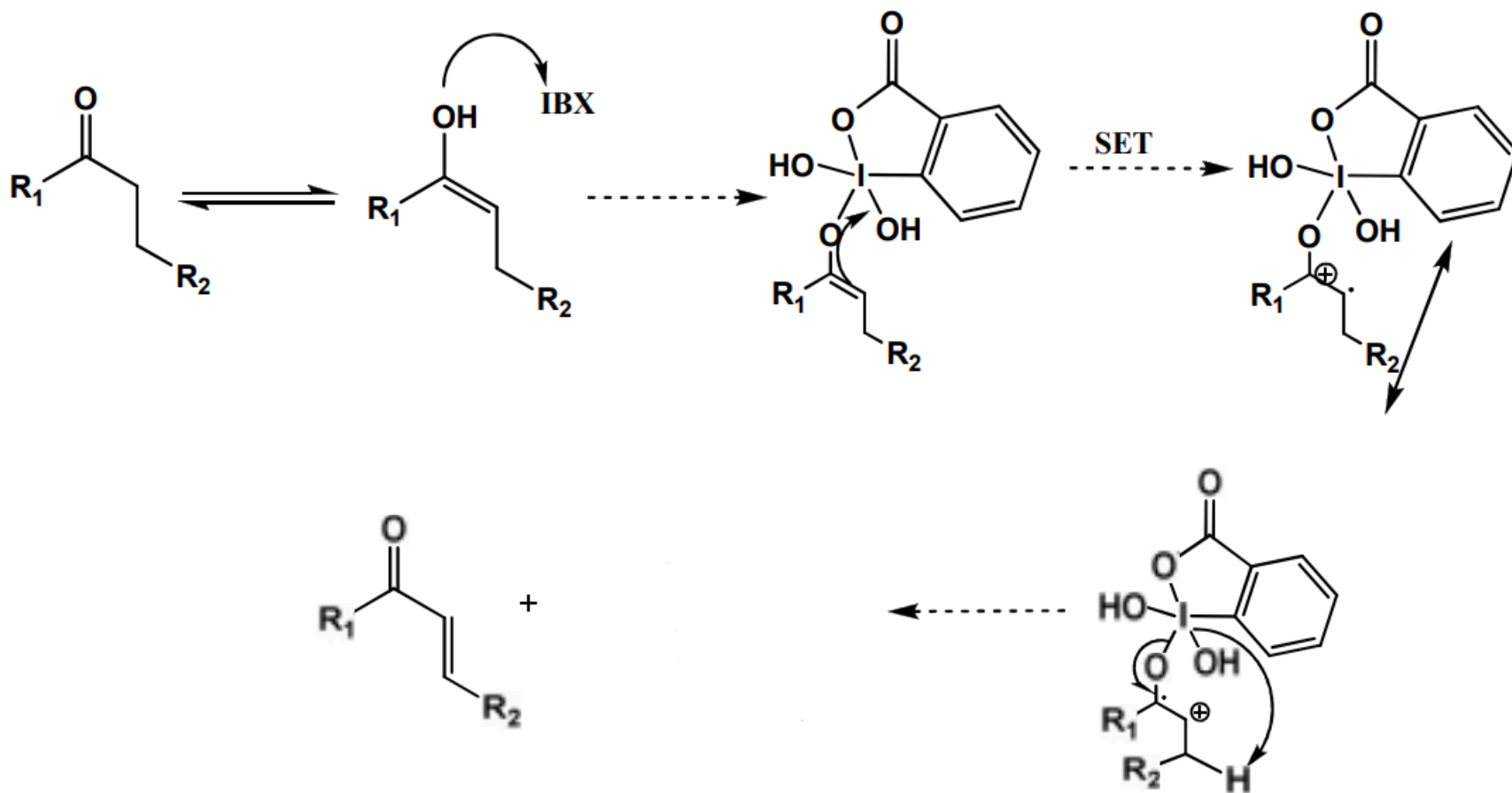
- \* Selective oxidation of secondary hydroxyl groups in the presence of primary hydroxyl groups is possible.



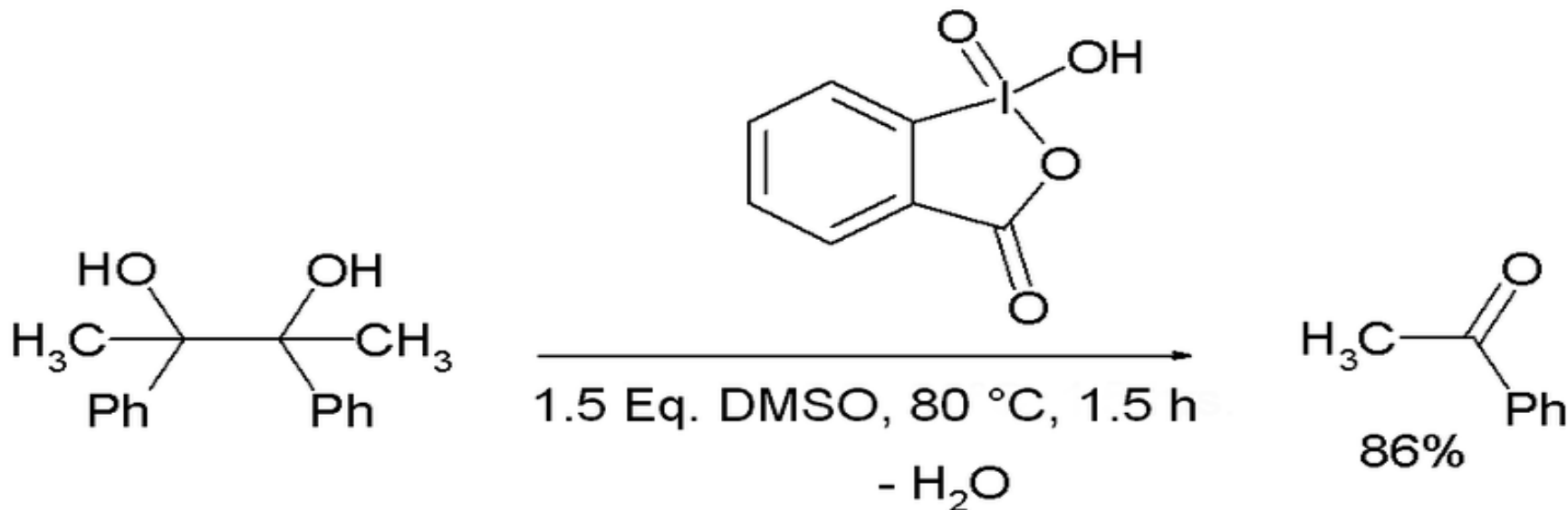
- \* IBX also oxidized ketone into the  $\alpha$ - $\beta$  unsaturated ketone while using more equivalent of IBX.



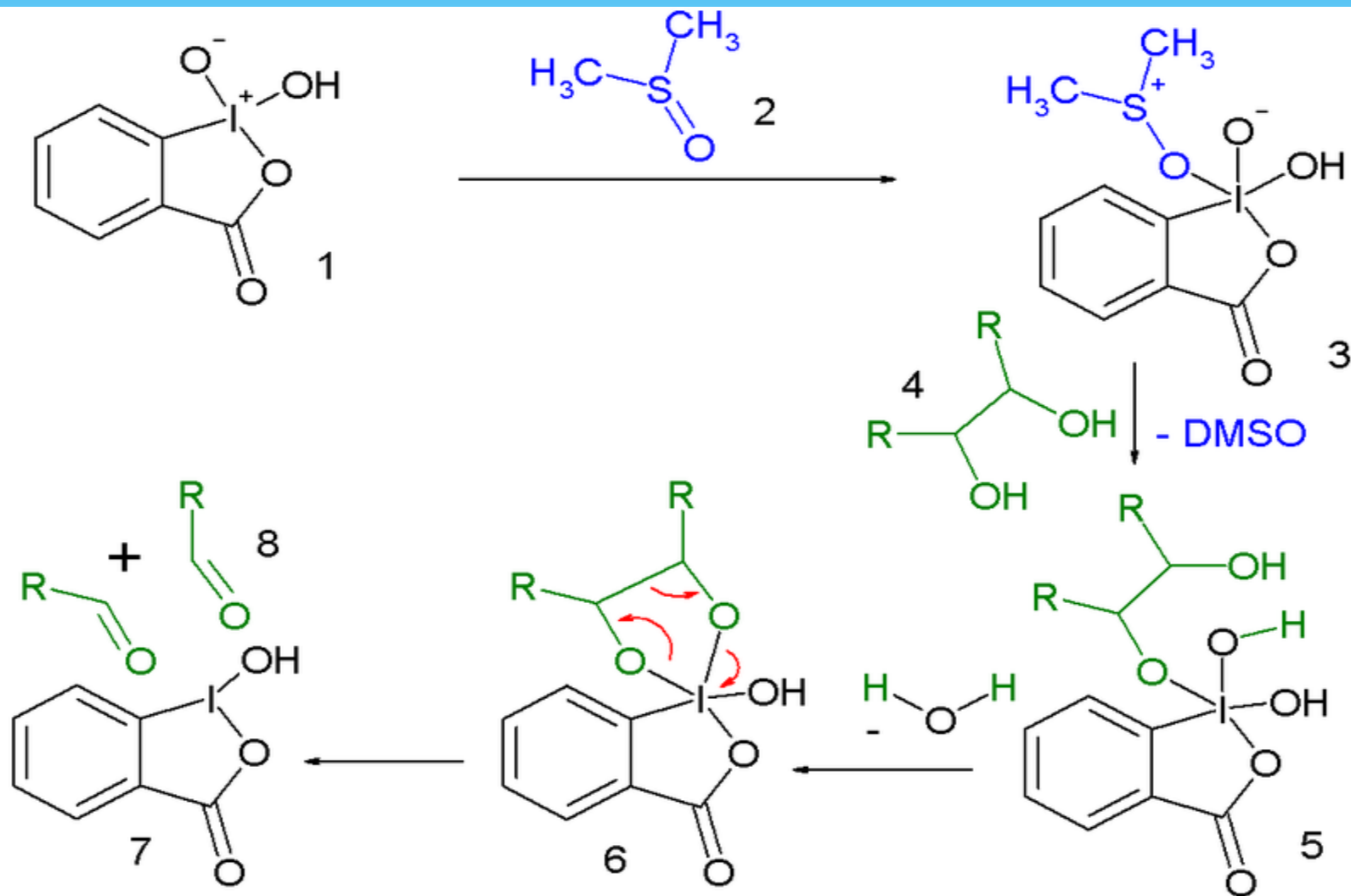
# \* Mechanism



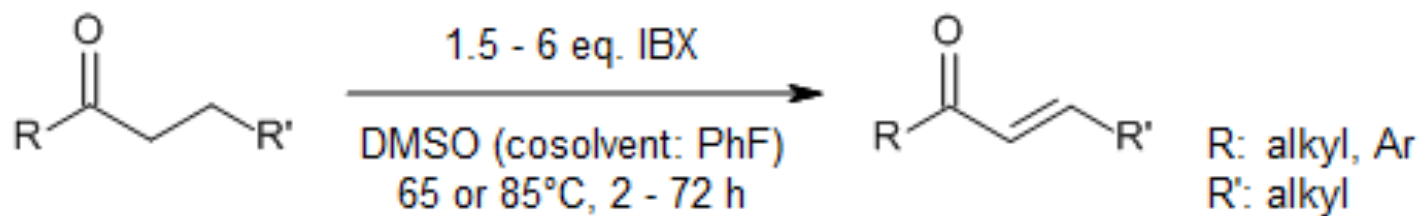
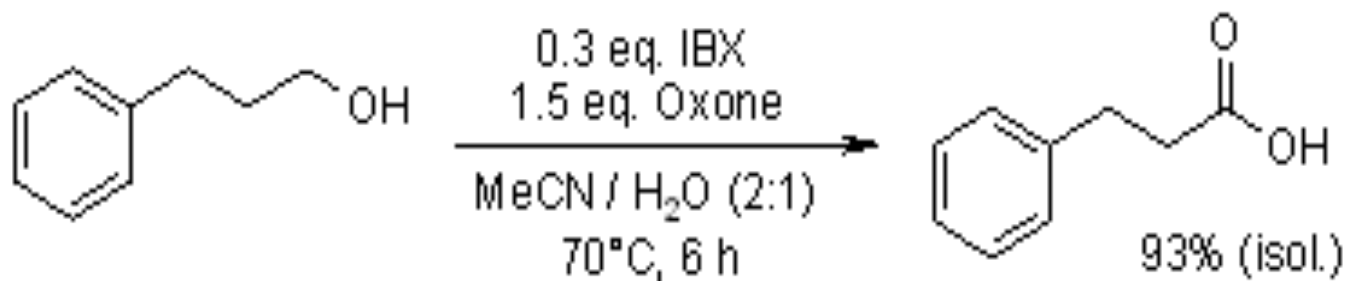
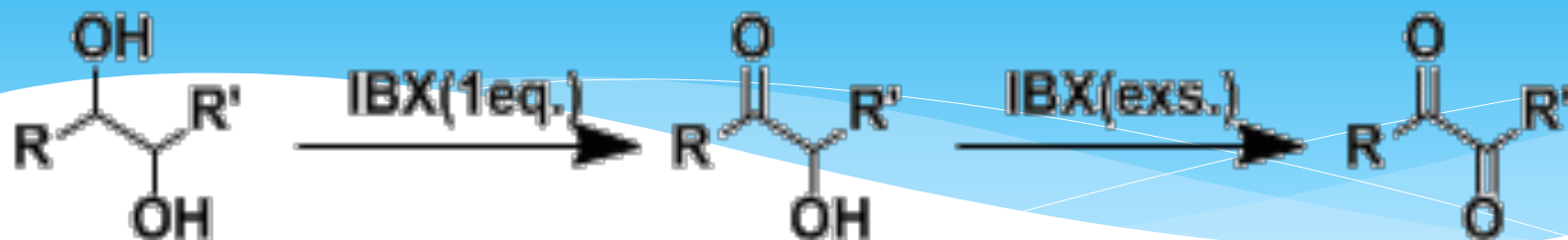
- \* *Oxidative cleavage of diols by IBX*
- \* IBX is notable for oxidizing vicinal diols (or glycols) to diketones without cleavage of the carbon-carbon bond, but oxidative cleavage of glycols to two aldehydes or ketones can occur when modified conditions are used (elevated temperatures or trifluoroacetic acid solvent)



## Mechanism of oxidative cleavage of diols by IBX

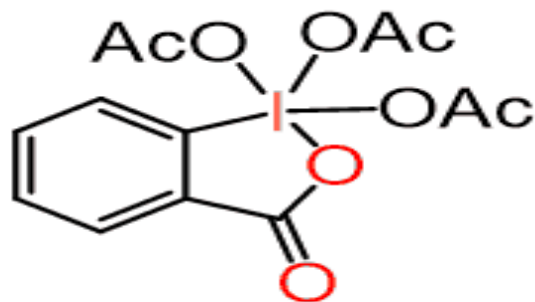


\* *Examples*



# Dess Martine Periodinate (DMP)

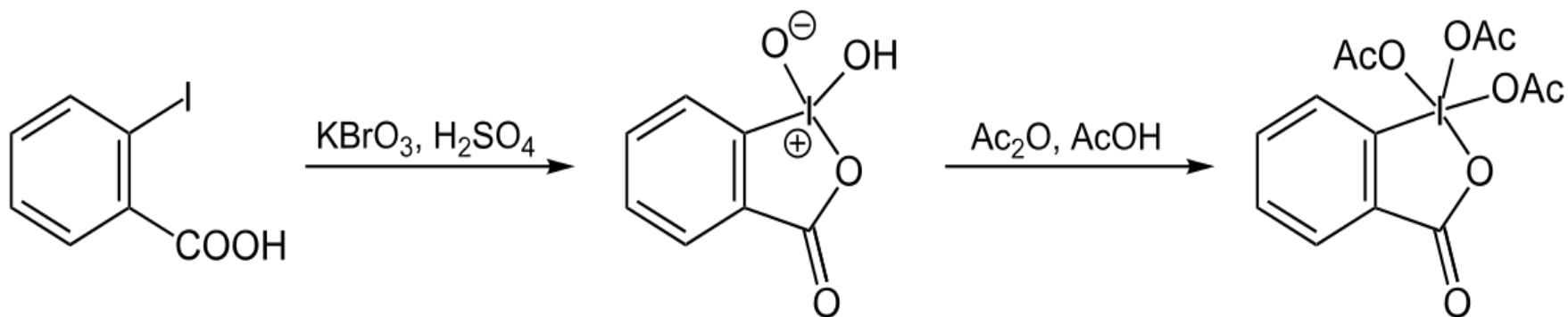
- \* Alcohols can be oxidized to aldehydes, ketones, and carboxylic acids depending on their structure and the type of oxidizing agent. In general, we can classify oxidizing agents as strong and mild. Soluble with organic solvent than IBX.
- \* Mild oxidizing reagents stop the oxidation of the alcohol once the carbonyl group is formed. And if the alcohol is a primary, the product is an aldehyde while the oxidation of a secondary alcohol results in a ketone.



**Dess-Martin**

- \* This periodinane has several advantages over chromium- and DMSO-based oxidants that include milder conditions (room temperature, neutral pH), shorter reaction times, higher yields, simplified workups, high chemoselectivity, tolerance of sensitive functional groups, and a long shelf life. However, use on an industrial scale is made difficult by its cost and its potentially explosive nature.

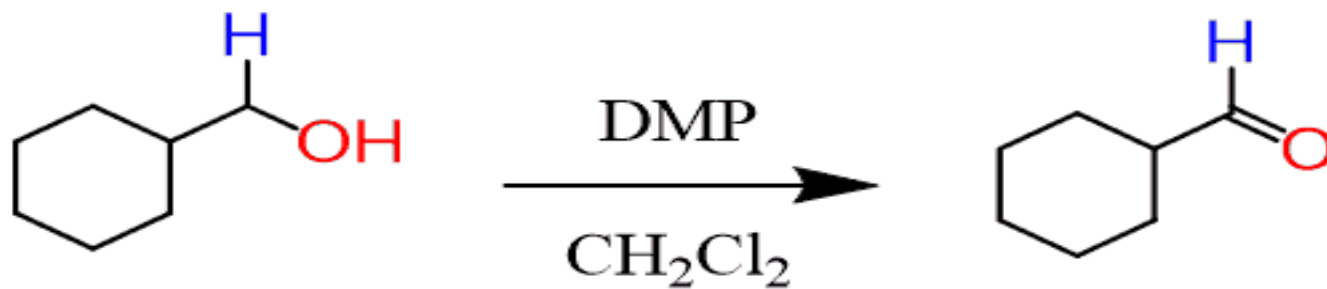
\* Preparation of DMP.



\*

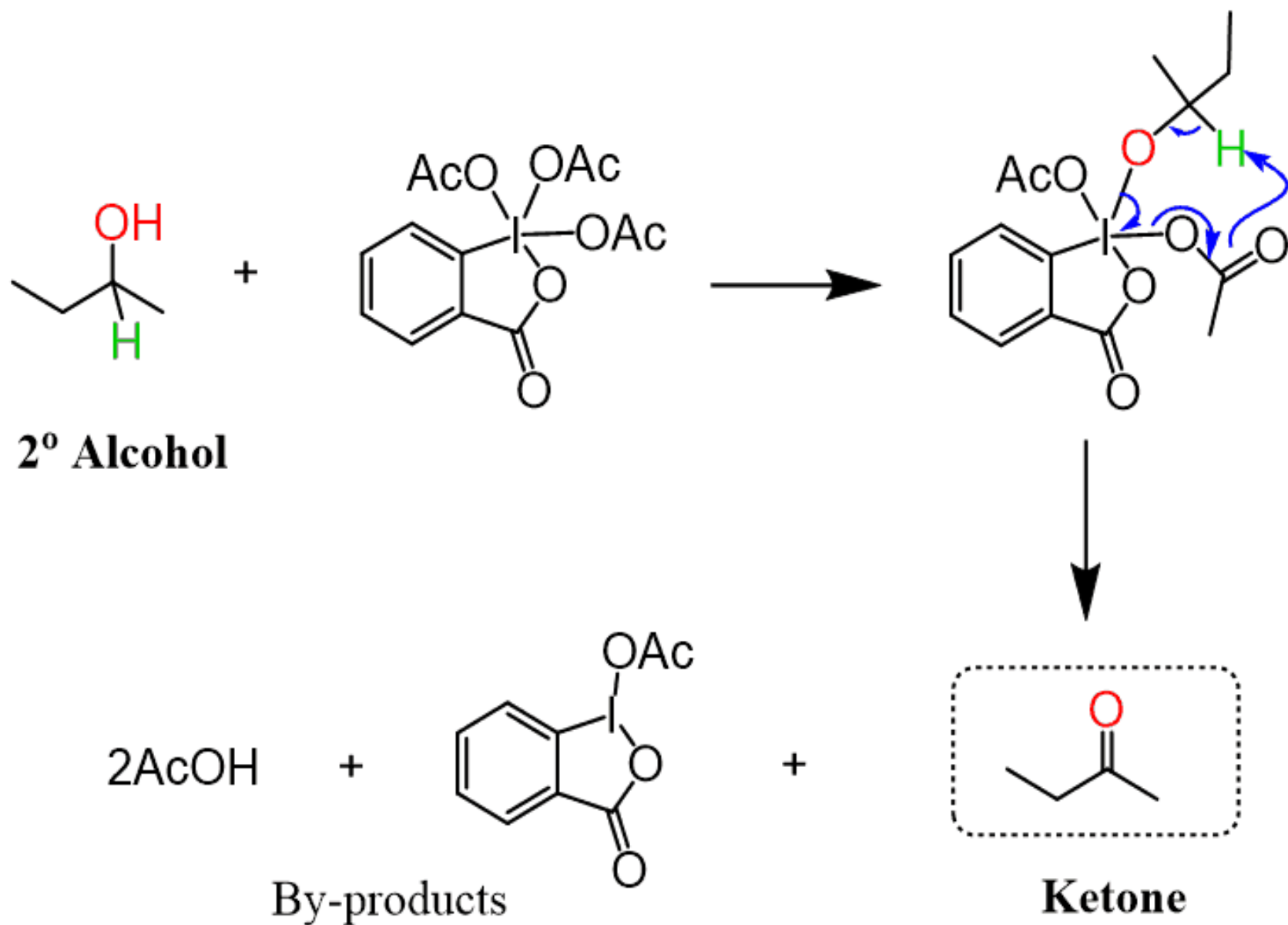
- \* Dess–Martin periodinane (DMP oxidation) is a selective method for oxidizing primary alcohols to aldehydes. Secondary alcohol to ketone.

## Dess–Martin Oxidation

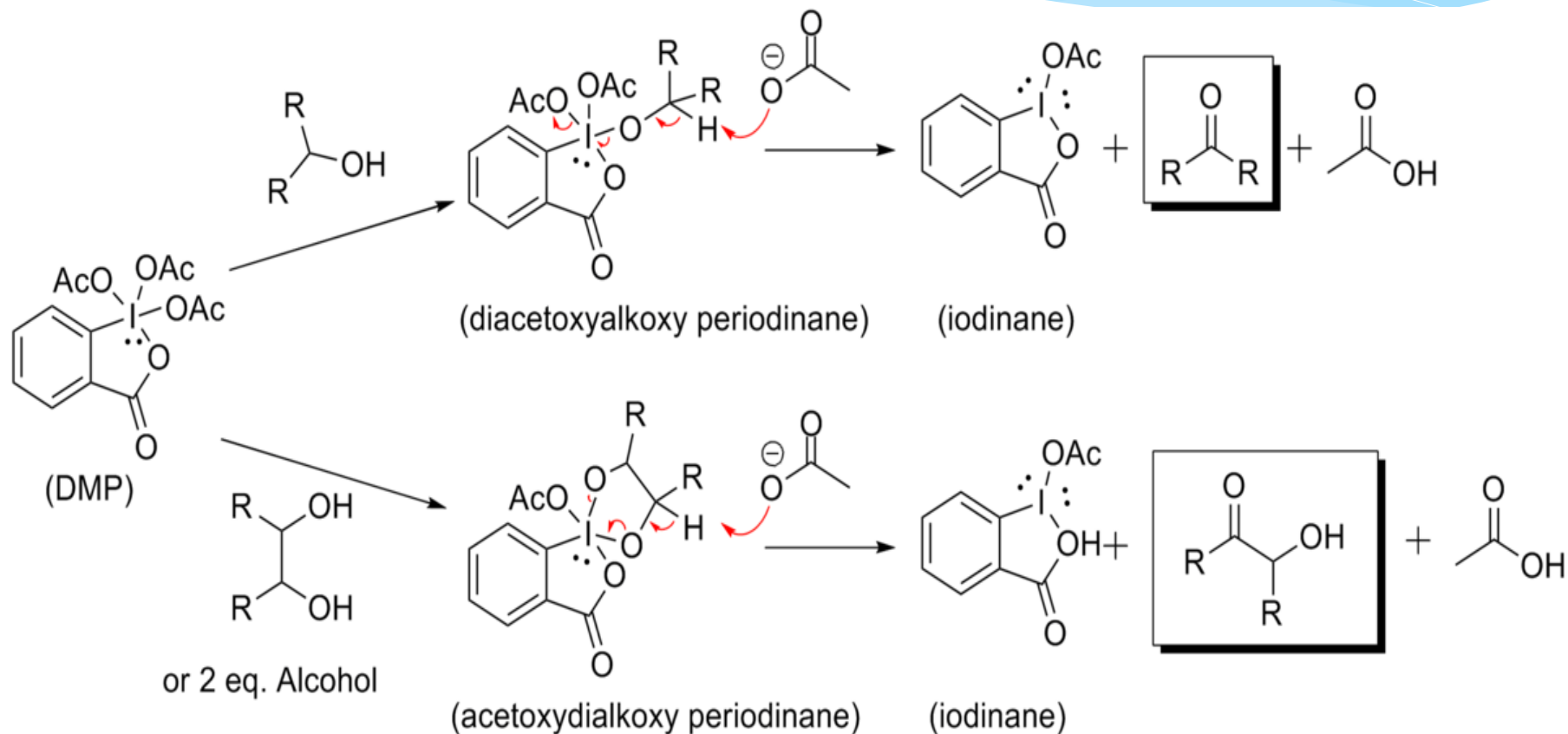




## Dess-Martin Oxidation Mechanism



- When a diol or more than one equivalent of alcohol is used, acetoxydialkoxyperiodinane is formed instead. Due to the labile nature of this particular periodinane, oxidation occurs much faster.



## \* Examples of DMP Oxidation

