BHARATHIDASAN UNIVERSITY

Tiruchirappalli-620024

Tamil Nadu, India

Programme: M.Sc. Chemistry

Course title: Organic Reactions, Spectroscopy and Asymmetric Synthesis

Course Code: CHE631CC

UNIT-III

Reagents in Organic Synthesis: Oxidation

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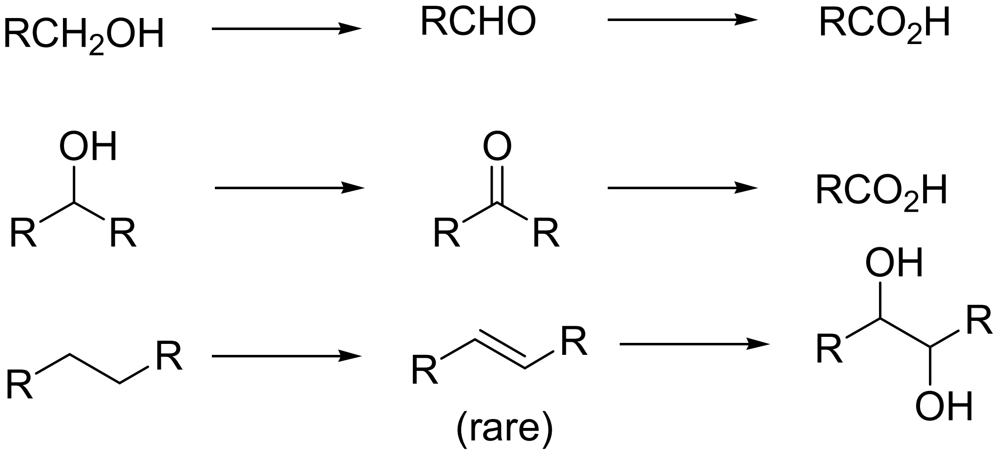
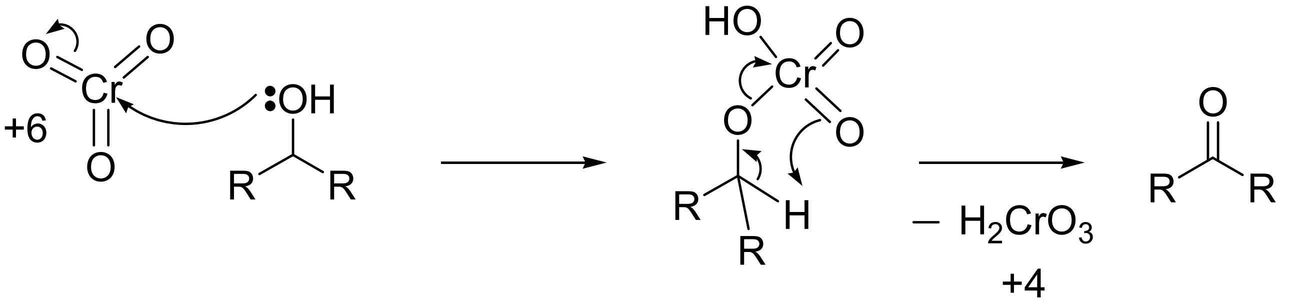
Introduction

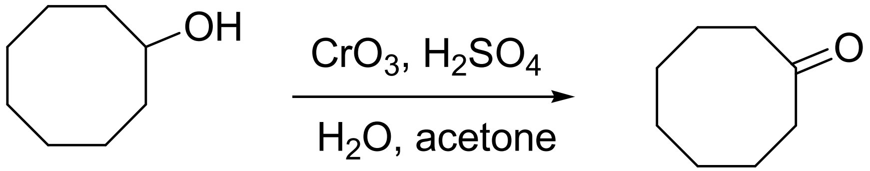
Oxidation: addition of oxygen or removal of hydrogen.

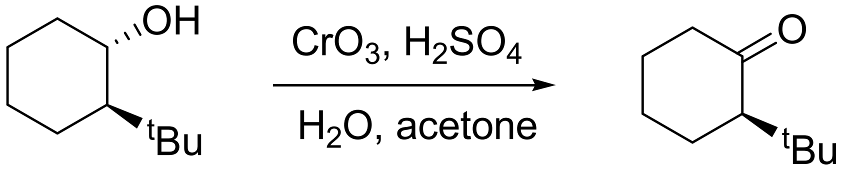


- **Cr(VI) Reagents (CrO_3):** Toxic and hence rarely used nowadays.
- Typical mechanism:

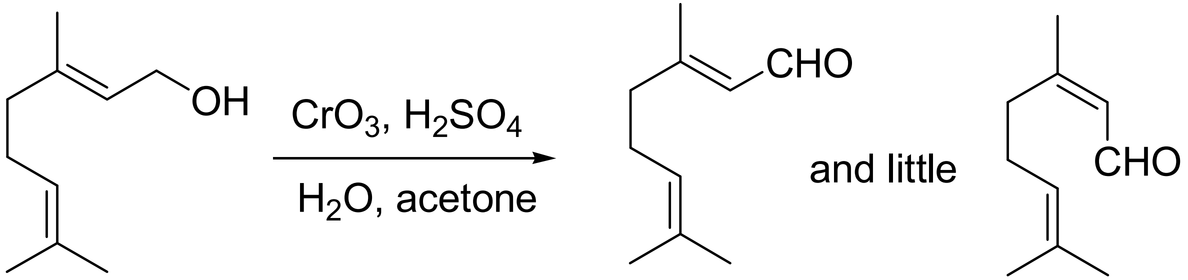


- **Jones reagent:** A solution of CrO_3 and H_2SO_4 in water.
- Useful for the oxidation of secondary alcohols to ketones and certain primary alcohols (such as allylic and benzylic alcohols) to aldehydes. With other primary alcohols, over oxidation to acid is always a problem.
- Examples:





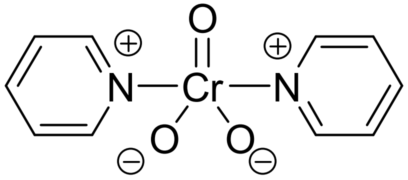
- Stereochemistry at the chiral centeris not affected



- Double bond is not oxidized (triple bond, if present is also not affected)
- Little isomersation of allyic double bond is possible

With primary alcohols, over oxidation to acid is always problem.

- Many milder CrO_3-based oxidizing agents have been developed (by including pyridine) for the oxidation of secondary alcohols to ketones and primary alcohols to aldehydes (no over-oxidation). They include:
- **Collins reagents:** CrO_3-Py complex

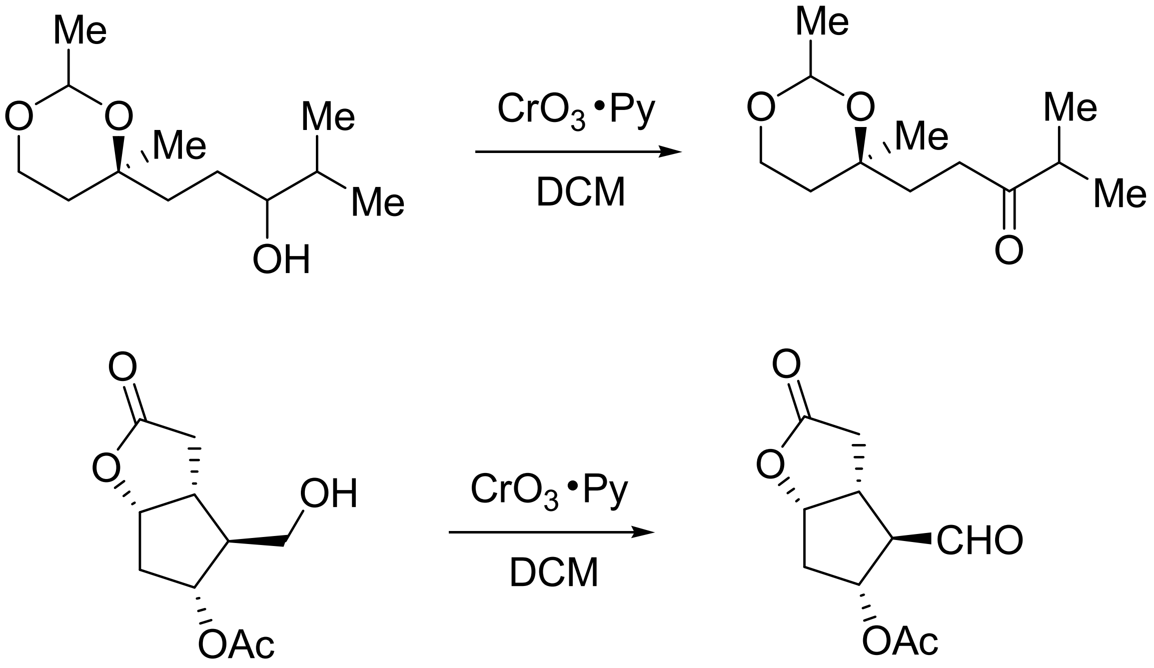


- Preparation: Addition of CrO_3 to dry Py (2 equiv.) in DCM.

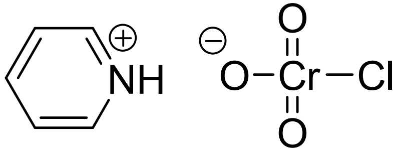
- Disadvantage: 5-fold excess reagent is required for the reaction.

- Advantage: It is the preferred reagent over PCC and PDC (discussed later) when an acid sensitive group is present in the substrate.

- Examples:


Me
O
O
Me
Me
Me
OH
CrO$_3$•Py
DCM
Me
O
O
Me
Me
Me
O
O
O
OH
OAc
CrO$_3$•Py
DCM
O
O
CHO
OAc

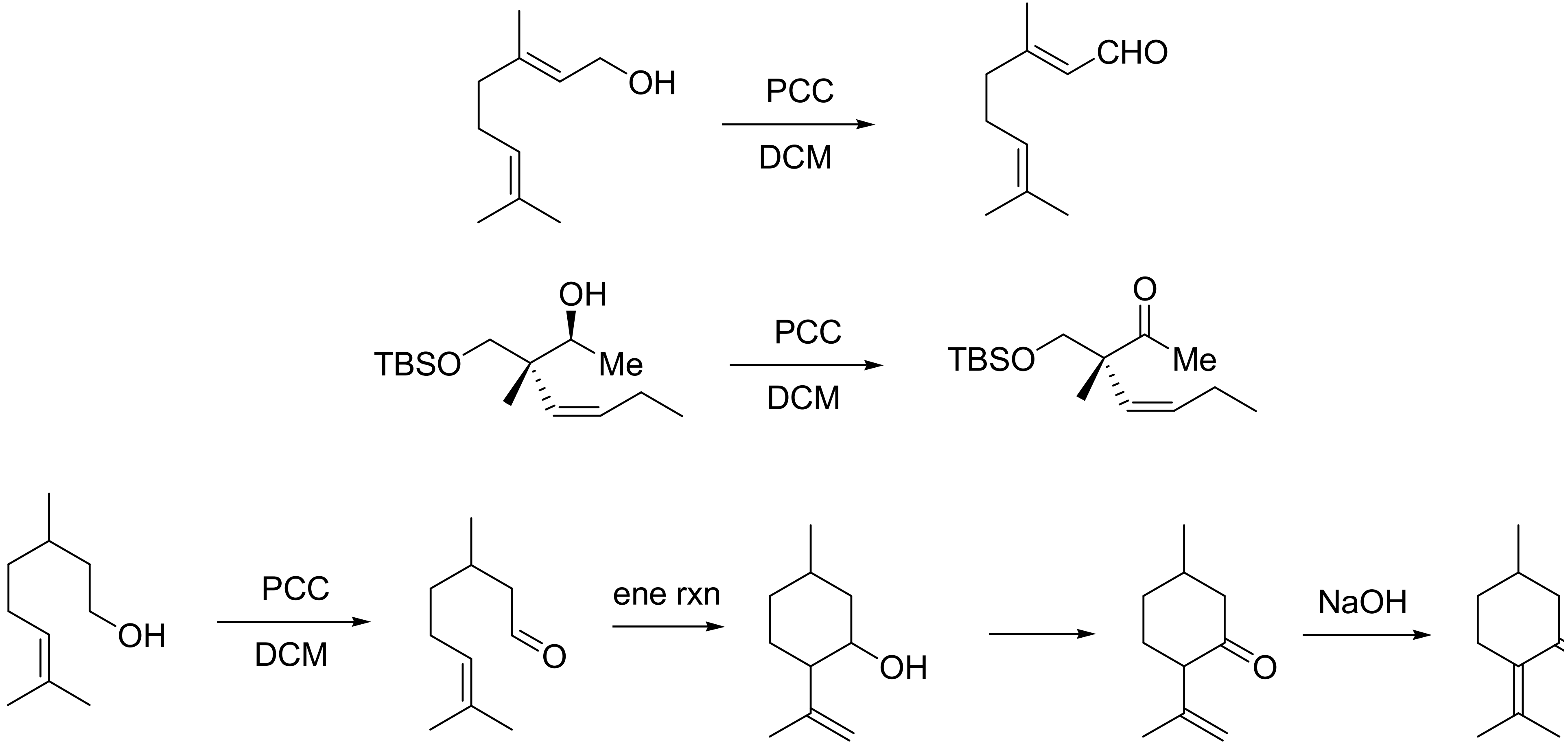
Pyridinium chlorochromate (PCC):



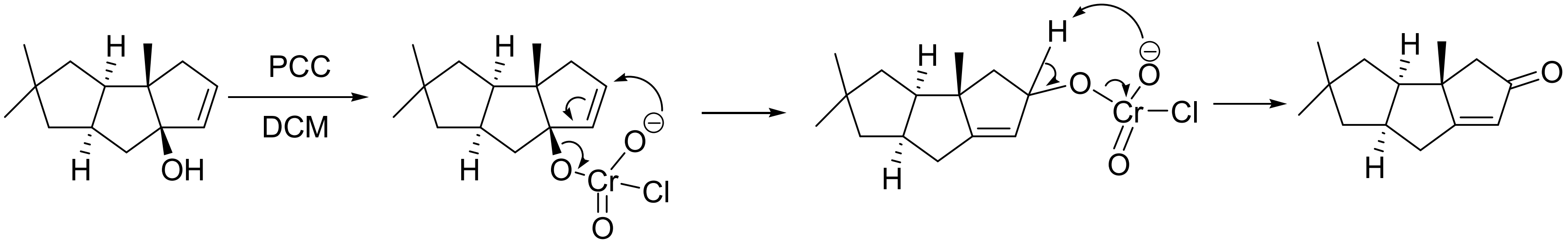
- ➢Preparation: Addition of Py to a cold solution of CrO_3 in con. HCl.

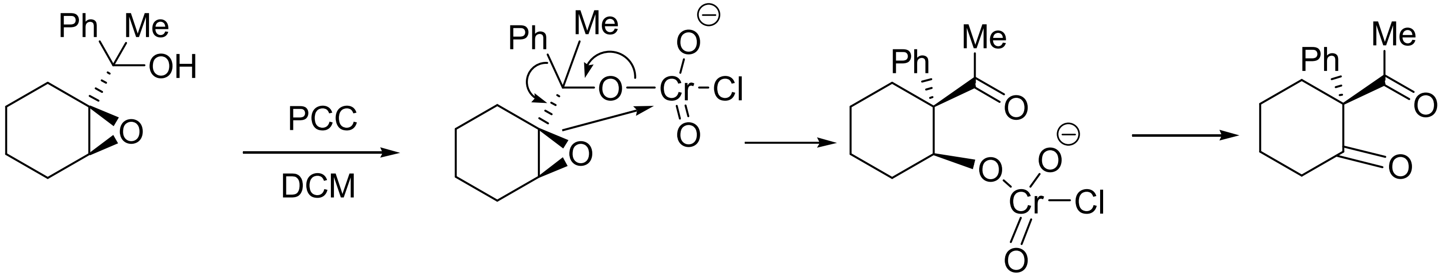
- ➢Mildly acidic and not suitable for acid-sensitive compounds. But, NaOAc may be used to neutralize the acidity.

Examples:

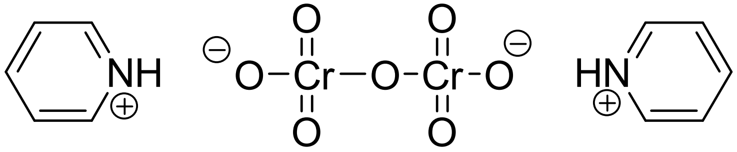


Note: Rearrangement often takes place in cases of tertiary alcohols.


PCC
DCM
H
OH
O
Cr
Cl
O


Ph
Me
OH
O
PCC
DCM
Cr
Cl

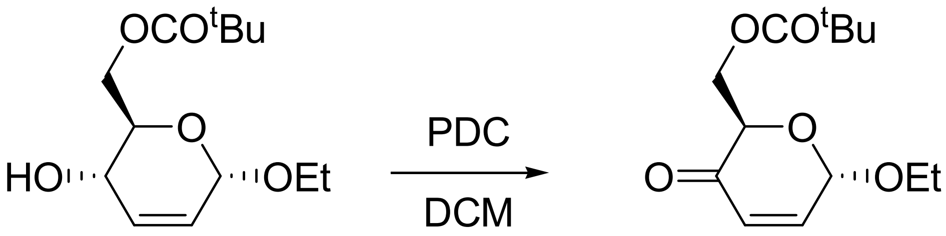
- **Pyridinium dichromate (PDC):** (also called Cornforth reagent)



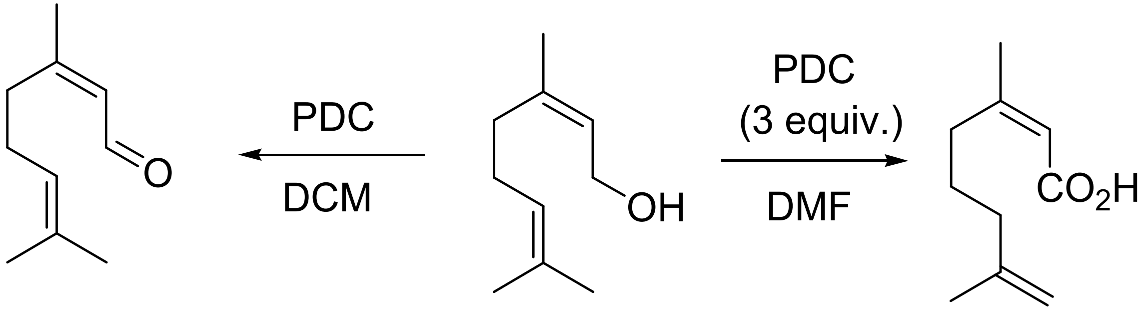
Preparation: Addition of con. aq. solution of CrO_3 to Py.

Less acidic than PCC and hence suitable for acid-sensitive compounds.

Examples:

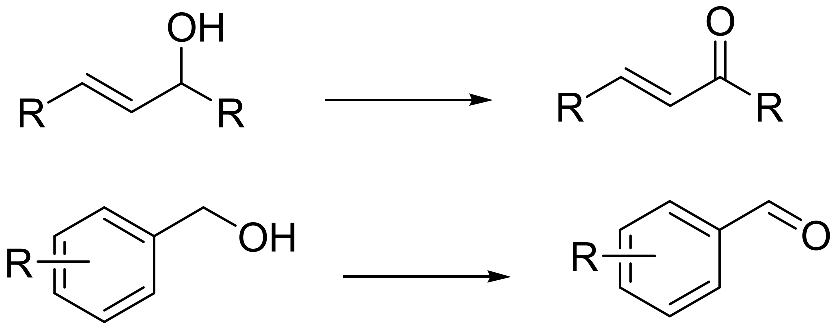


Note: PDC oxidizes primary alcohols to aldehydes in DCM and, to acids in DMF (about 3 equiv of PDC is required in the later case).

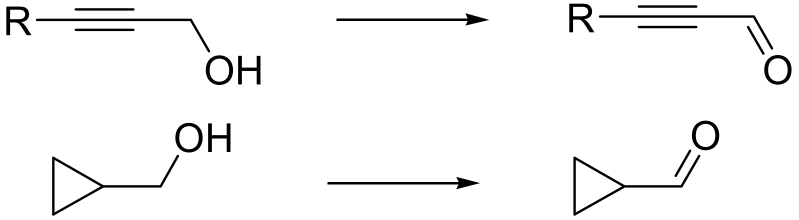


Manganese dioxide (MnO_2):

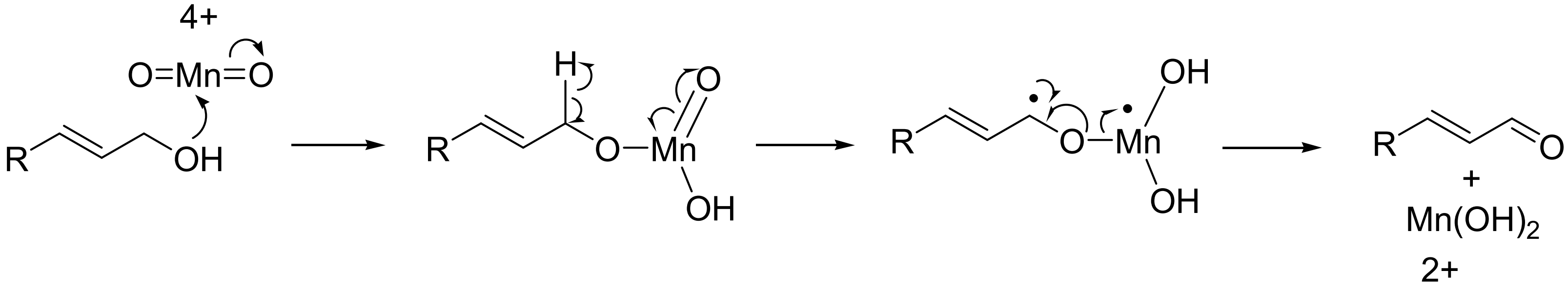
MnO_2 is highly specific mild oxidant for allylic and benzylic alcohols (to obtain the corresponding aldehydes or ketones). It seldom oxidizes saturated alcohols.



It also oxidizes hydroxyl group adjacent to triple bond and cyclopropyl ring.

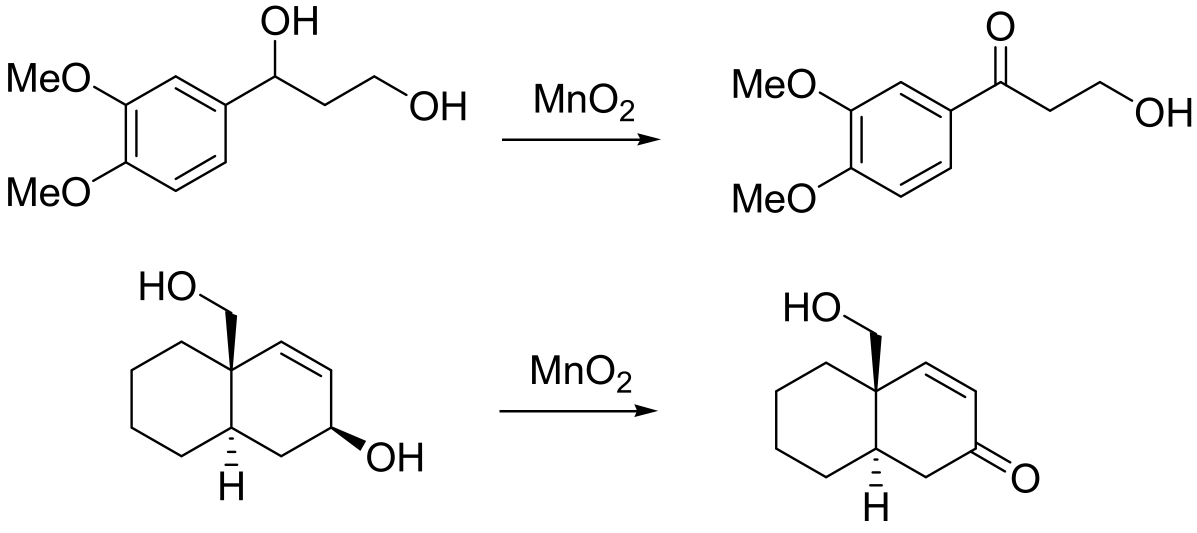


Mechanism:

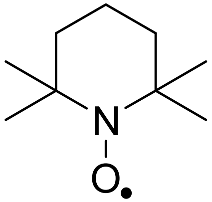


The intermediate allyl radical is stabilized by resonance. This also explains why the reaction is specific to allylic and benzylic alcohols.

Examples:



TEMPO



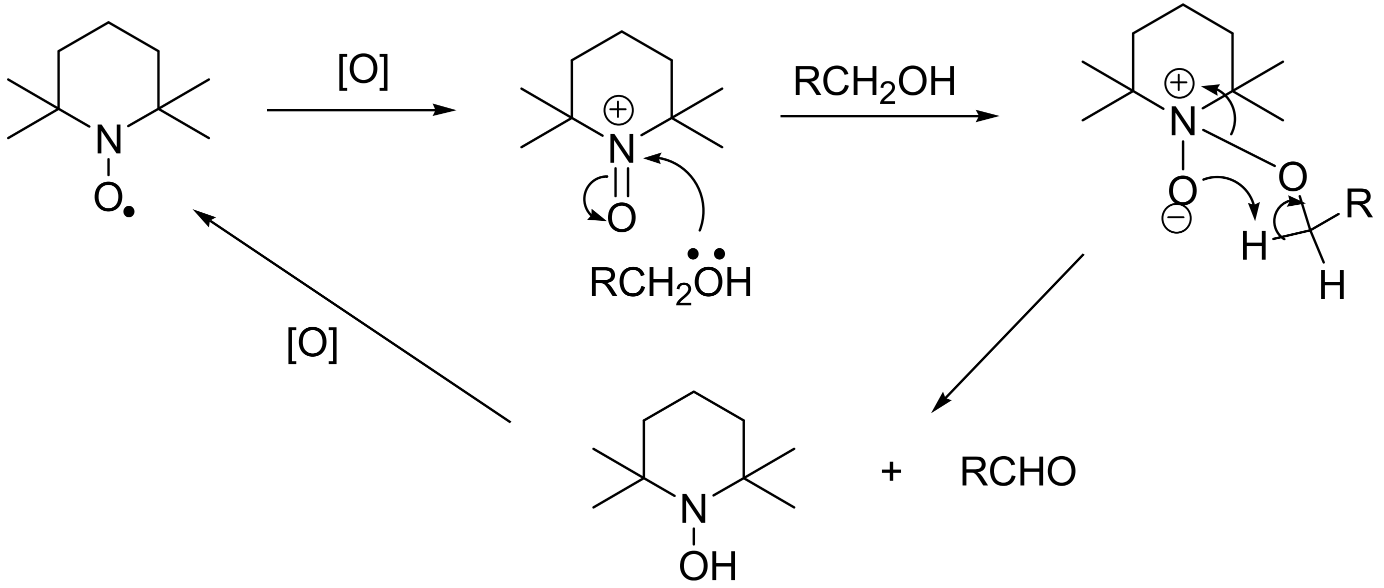
- Tempo: 2,2,6,6-tetramethylpiperidin-1-oxyl

- Stable nitroxyl radical

- Prepared by the oxidation of 2,2,6,6-tetramethylpiperidine

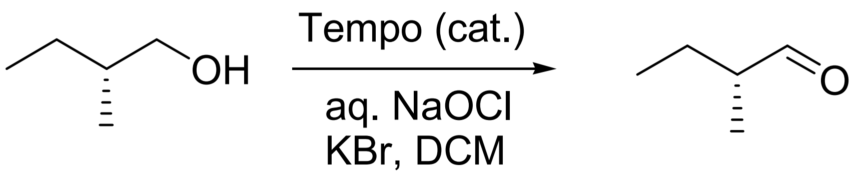
- Use: (1) Probe in ESR, (2) radical trap, (3) mediator for radical polymerization and (4) oxidizing reagent in organic synthesis

Mechanism:



Examples:

1) Oxidation of 1° alcohols to aldehydes



Similarly, oxidation of 2° alcohols to ketones is done.

2) Oxidation of 1° alcohols to acids (stereochemistry not affected)