Determination of Reaction Mechanism

Non-Kinetic methods

1) Product analysis or identificaiton of products

2) Detection of intermediates

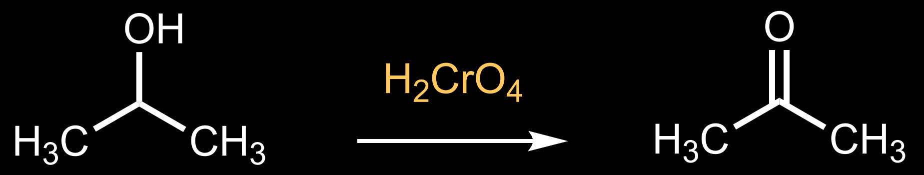
3) Trappng of intermediates

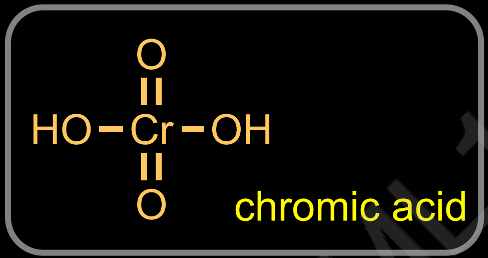
4) Isotopic labelling

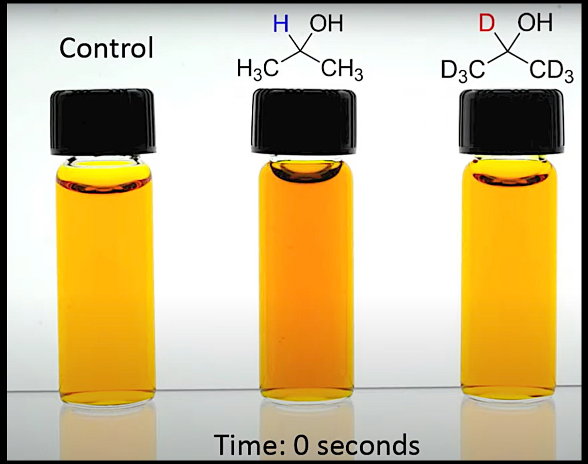
5) Isotopic effect

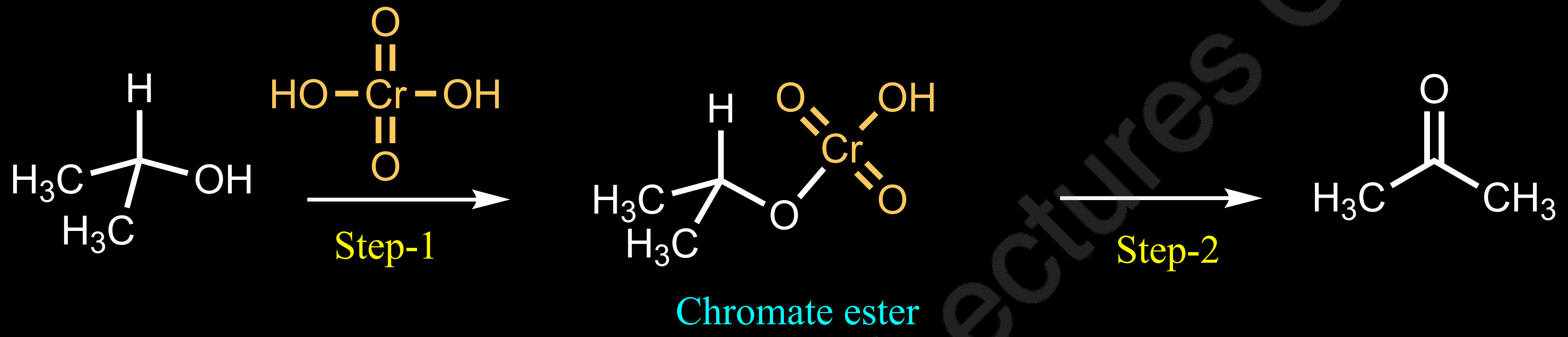
6) Stereochemical studies

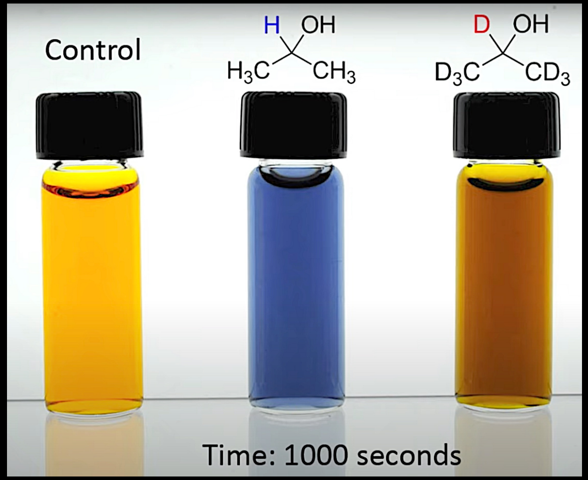
Kinetic Isotopic Effects

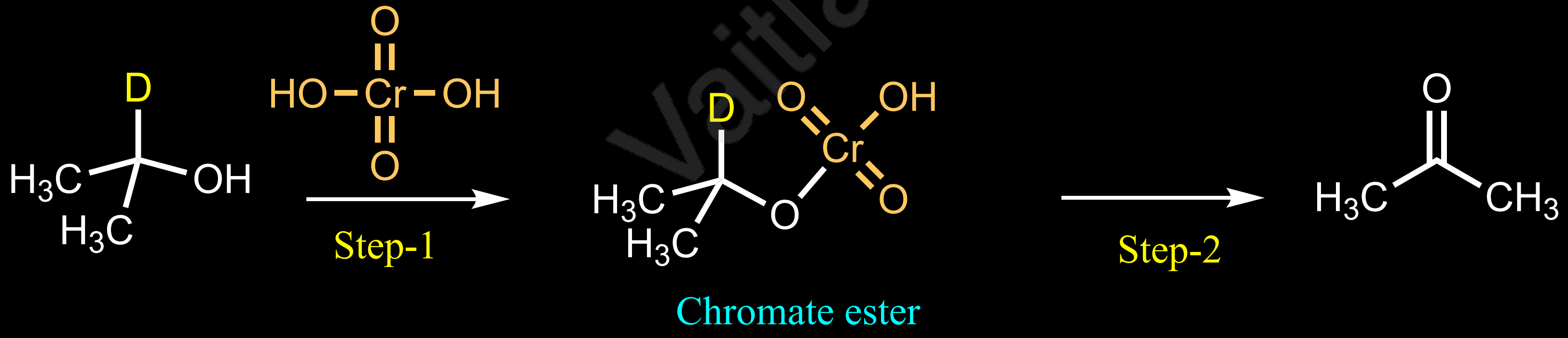






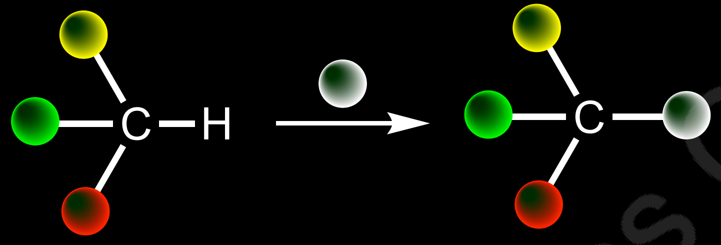






Kinetic Isotopic Effects

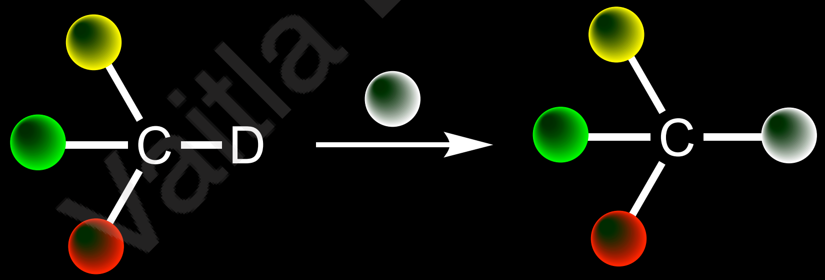
A method that gives insights into the Rate Determining Step



C-H functionalization

Find rate constant constant k_H

- *We would like to find weather C-H bond cleavage is r.d.s or not?*



C-D functionalization

Find rate constant constant k_D

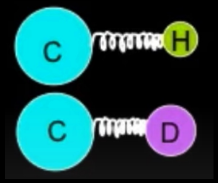
Then observe the k_H/k_D ratio

Kinetic Isotopic Effects

☆ The origins of the isotopic effect is the differences in the frequencies of various vibrational modes of a molecule, arising when one isotope is substituted for another.

☆ Different type of bond in a molecule have different frequency

☆ As Deuterium is heavier than Hydrogen,
The Vibrational Frequency of C-H bond will be more as compared to the C-D bond

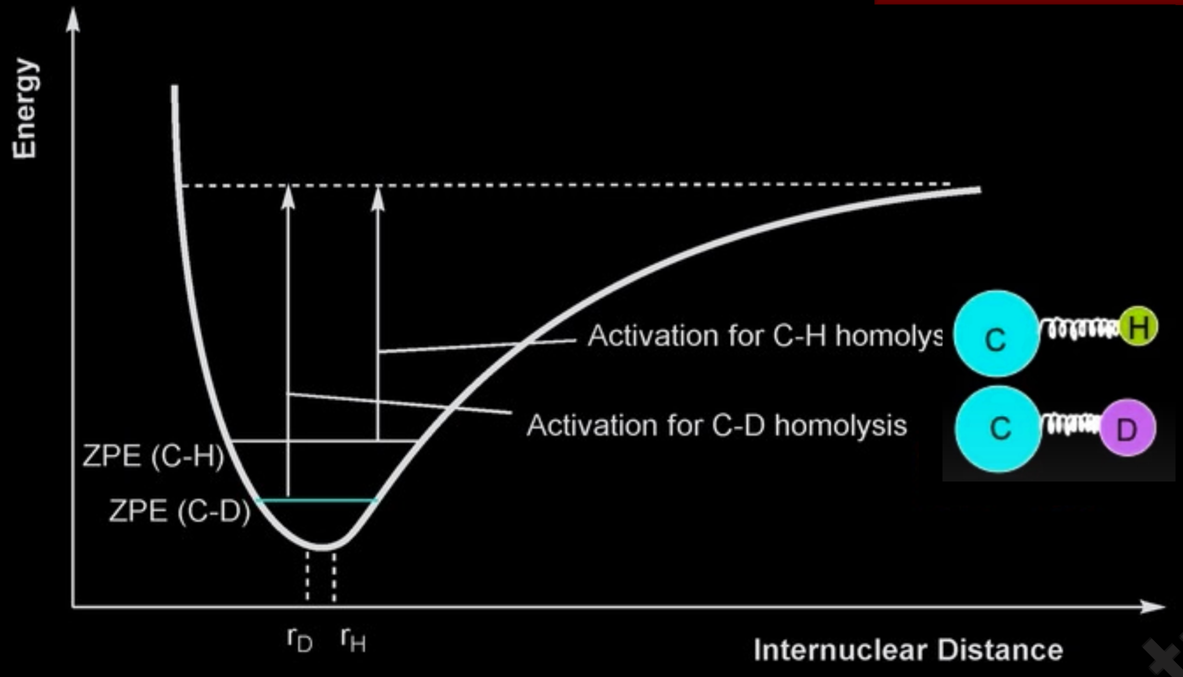


$$\text{Energy for bond breaking} \ \alpha \ \frac{1}{\text{Vibrational frequency}}$$

☆ Thus, Energy for C-H bond will be less compared to the C-D bond.

☆ ☆ Bond Strength: C-D > C-H (1.2 Kcal/mole)

Kinetic Isotopic Effects



$$\frac{k_H}{k_D}$$ = Deuterium kinetic isotopic effect

$$\frac{k_H}{k_D} = 2 - 8$$ Primary kinetic isotopic effect

⇩

C-H bond is breaking at r.d.s

$$\frac{k_H}{k_D} = 0.7 - 1.5$$ Secondary kinetic isotopic effect

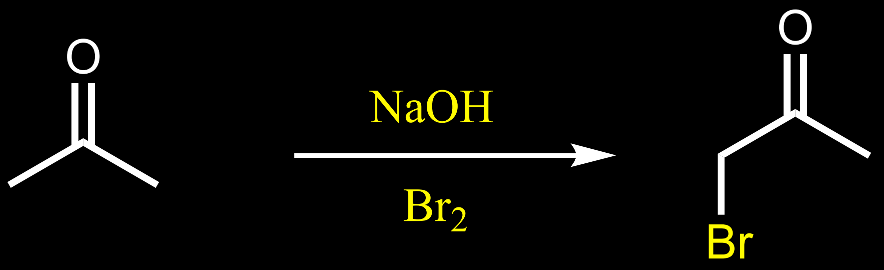
⇩

C-H bond is not breaking at r.d.s

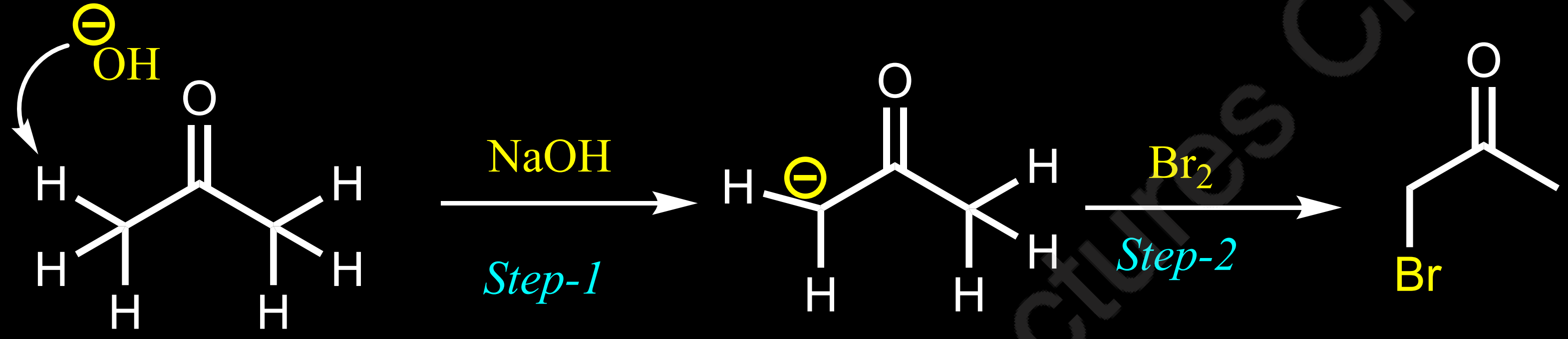
✻ The larger mass of deuterium causes C-D bonds to be Shorter and Stronger than C-H bonds

✻ The difference in bond strength is due to a mass dependent Quantity known as zero-point vibrational energy

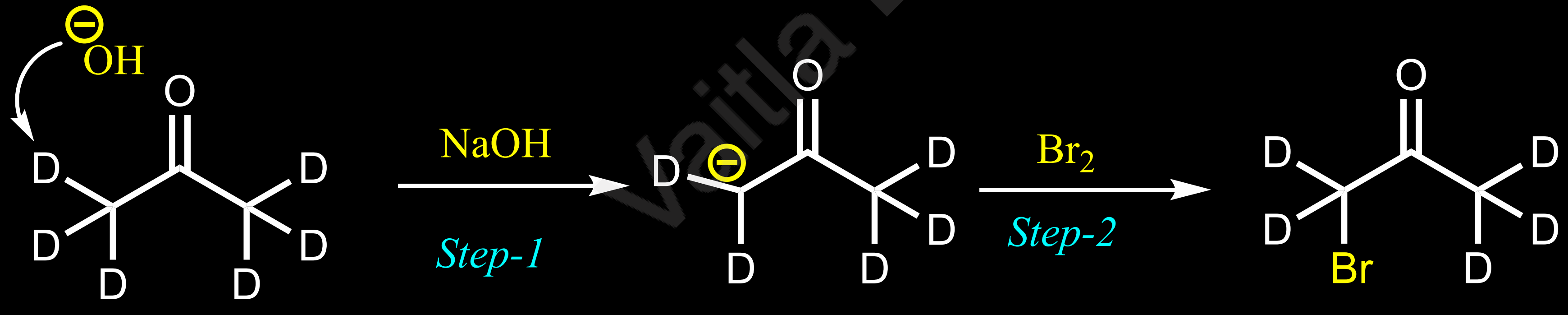
Kinetic Isotopic Effects



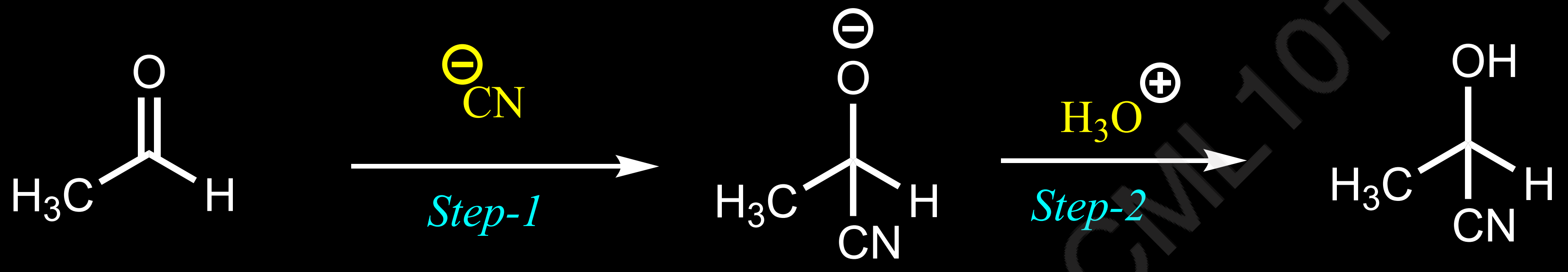
$$\frac{k_H}{k_D} = 6.1$$



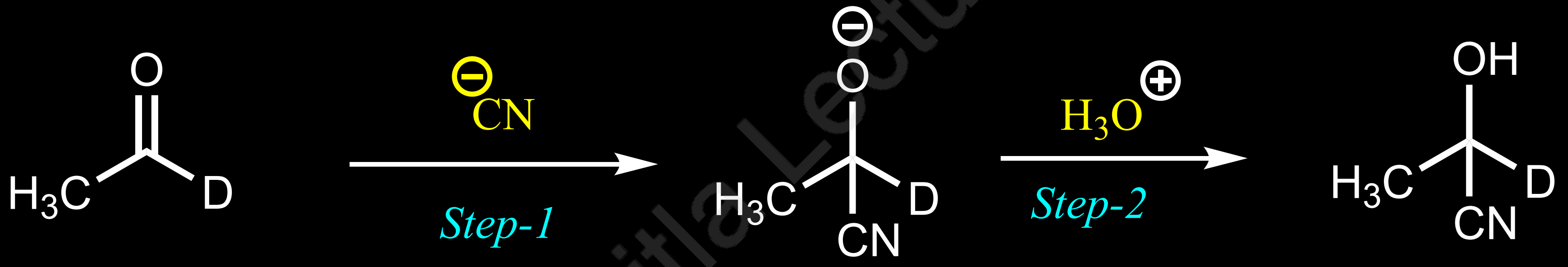
Rate $k_H > k_D$



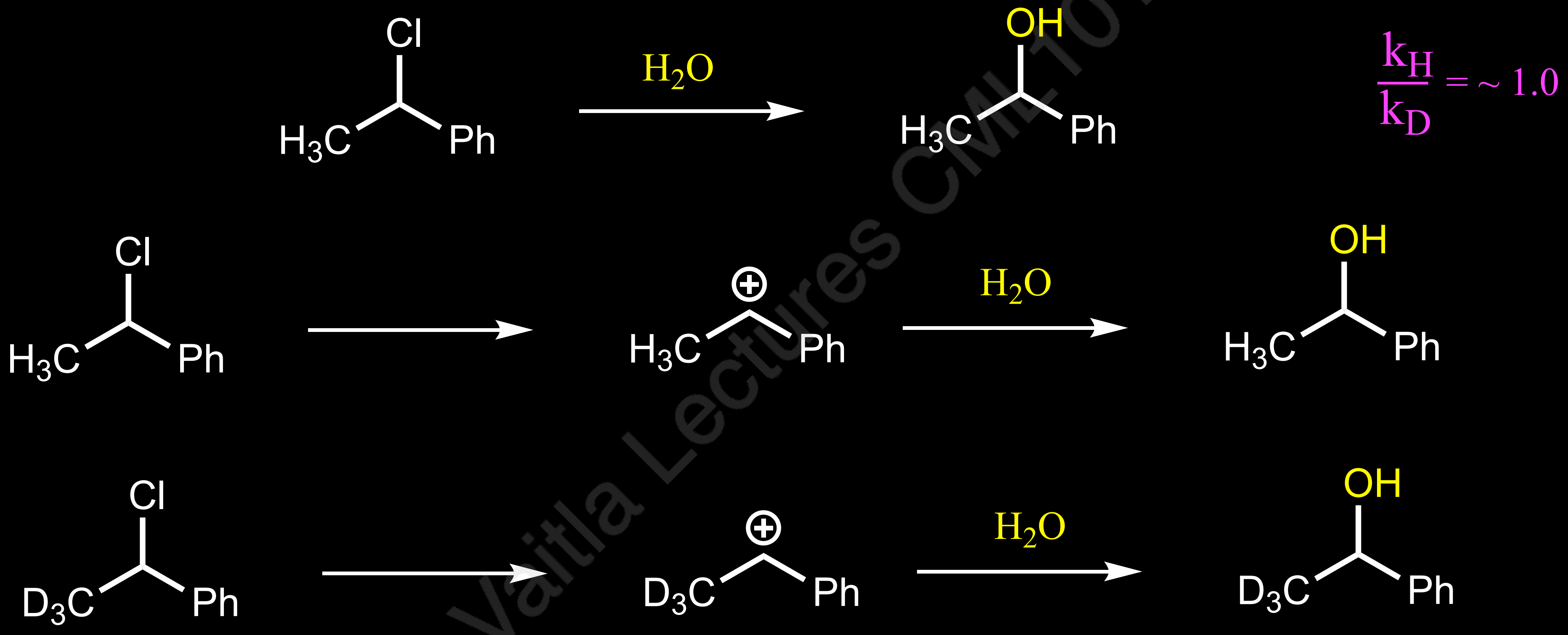
Kinetic Isotopic Effects



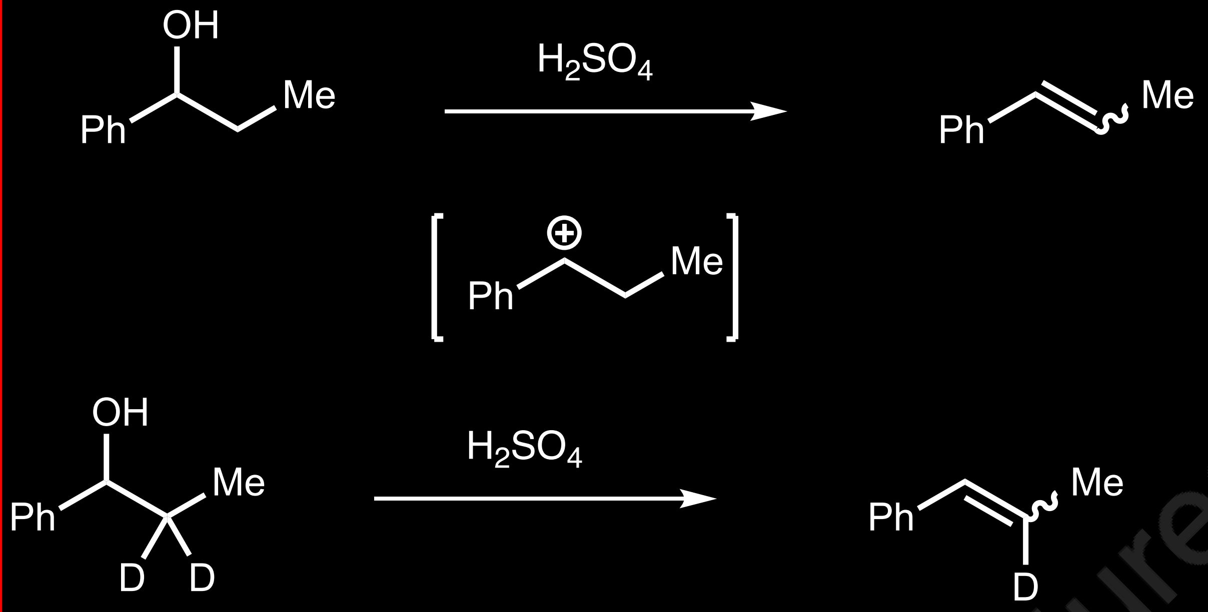
$$\frac{k_H}{k_D} = 0.8$$



Kinetic Isotopic Effects

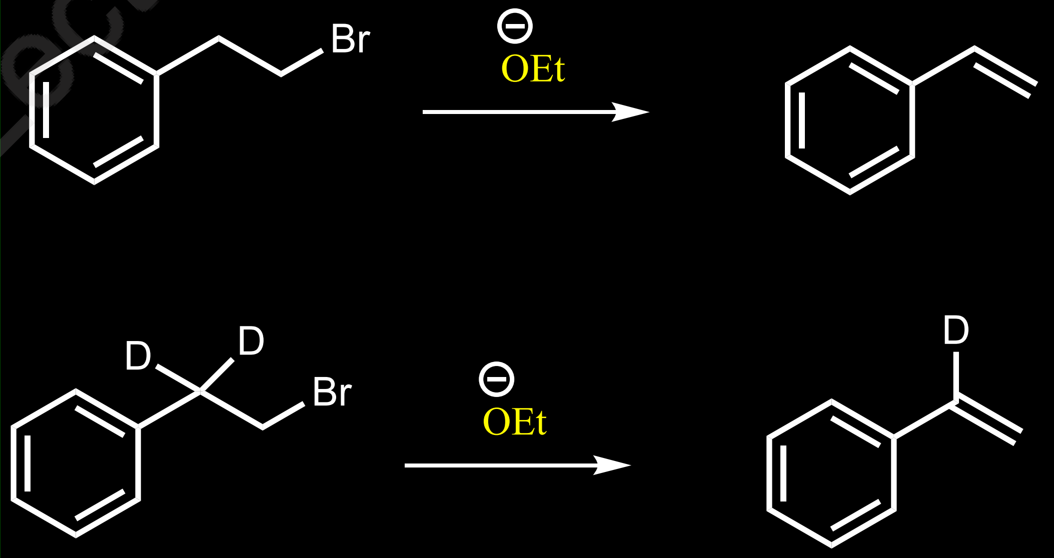


Kinetic Isotopic Effects



$$\frac{k_H}{k_D} = \sim 1.0$$

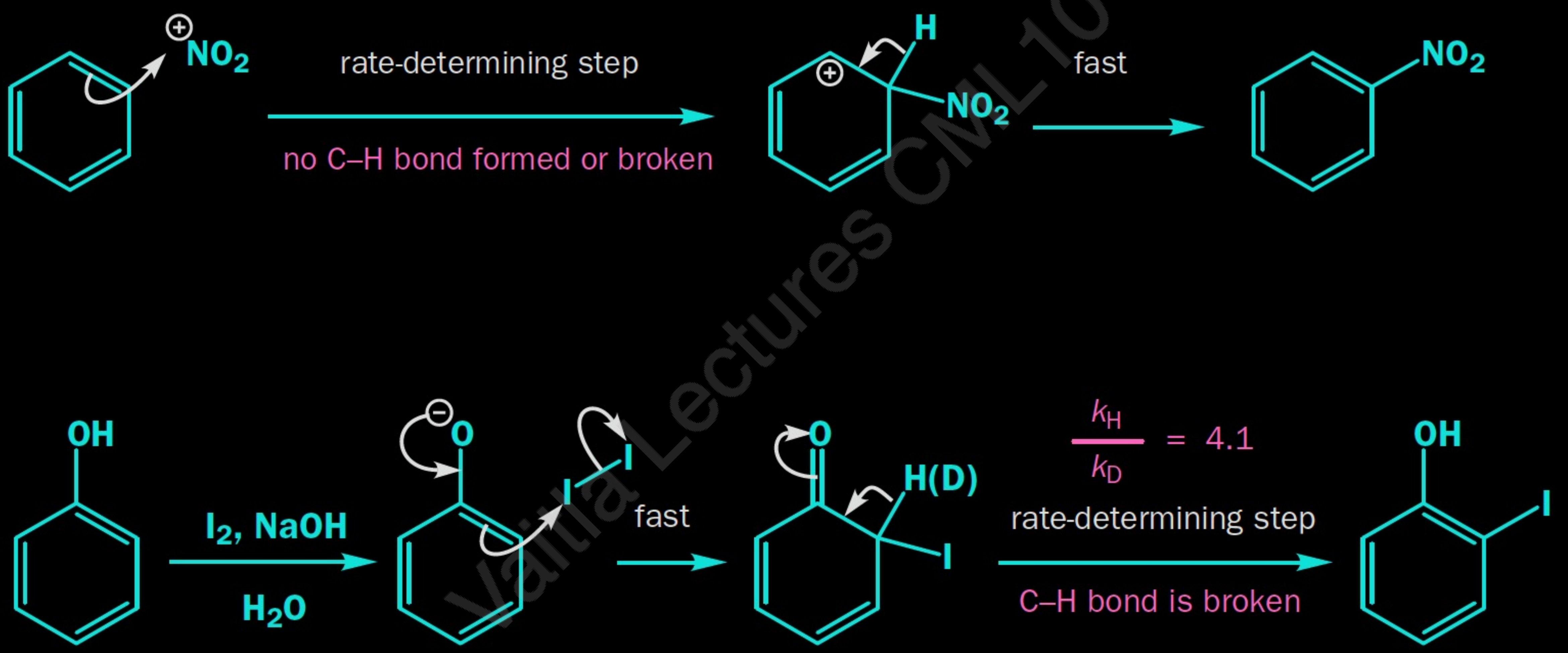
☆ ☆ E1 reaction



$$\frac{k_H}{k_D} = 7.1$$

☆ ☆ E2 reaction

Kinetic Isotopic Effects



Non-Kinetic methods

1) Product analysis or identificaiton of products

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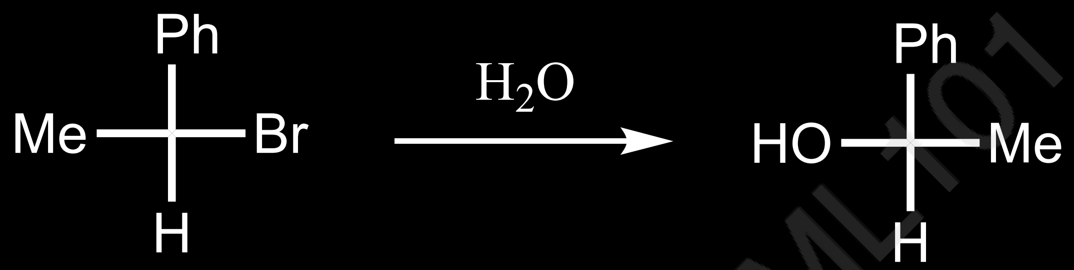
6) Stereochemical studies

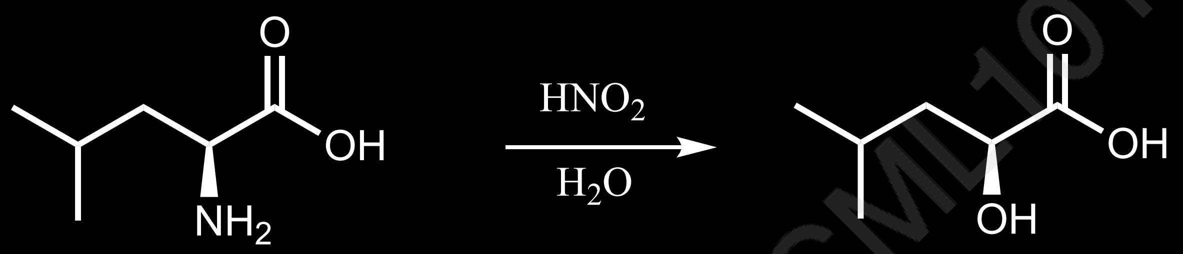
☆ Stereochemical evidence



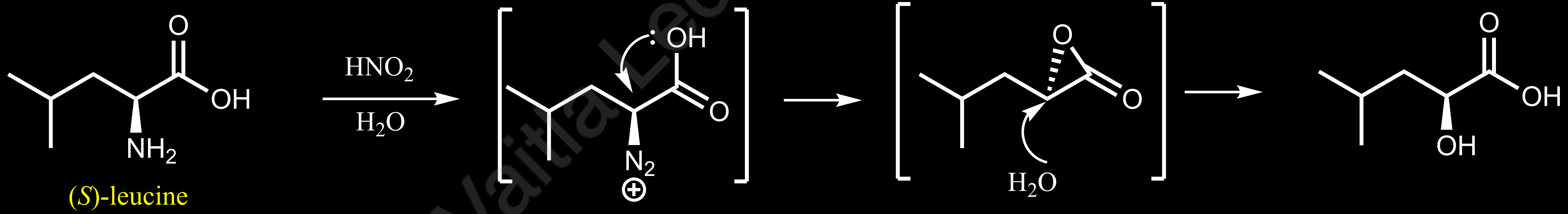
Optically pure

Racemic mixture

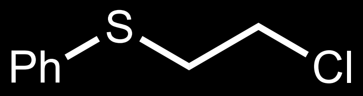
☆ Stereochemical evidence



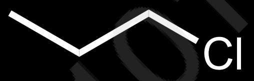
☆ NGP

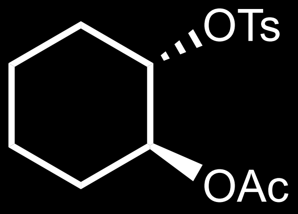


Neighboring Group Participation (Anchimeric assistance)

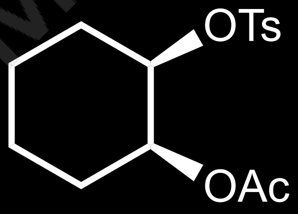


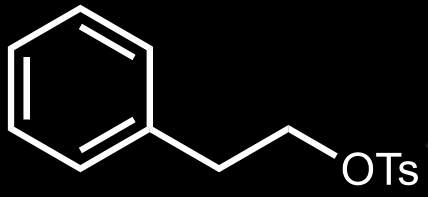
Reacts with water
600 times faster than



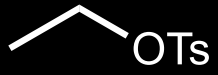


Reacts with CF_3CO_2H
3000 times faster than





Reacts with CH_3CO_2H
670 times faster than



Reacts with CH_3CO_2H
10^6 times faster than