

CHEM II ORGANIC

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C407

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C503

19 Lectures:

17 Survey Lectures

2 Afternoon Tutorials

1 Blackboard Tutorial

Class Record:

Class test

Labs

Tutorial questions

Section 2: Isomers

(Student Manual, Pages 13–17)

L.G 2.1 Isomers

Isomers are compounds with:

BUT: different

L.G 2.2 Two Classes of Isomers:

1) Structural isomers

eg: $\text{C}_4\text{H}_{10}\text{O}$

2) Stereoisomers

L.G 2.3 Three Types of Stereoisomers:

i) Conformational Isomers:

- Arise from **free rotation** about C-C single bonds
- **Interconvert rapidly**

ii) Geometric Isomers:

iii) Enantiomers:

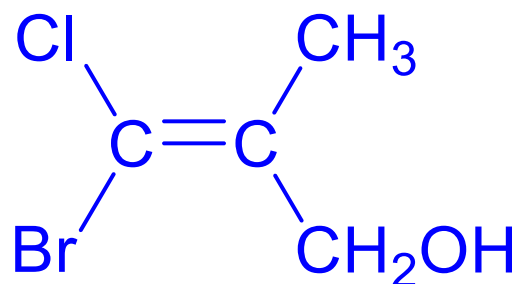
Geometric Isomers

Have a **RIGID** unit about which rotation is **NOT** possible.

e.g. π bond

e.g. Ring

L.G 2.4 What about systems like:



cis / *trans* meaningless! Need a new classification

- Substituents are assigned priorities by rules: **Cahn-Ingold-Prelog rules** (C.I.P rules)
- If groups of higher priority are on **same side** of C=C, isomer is called
- If groups of higher priority are on **opposite sides**, isomer is called

Cahn-Ingold-Prelog Sequence Rules

1) The higher the atomic number, the higher the priority

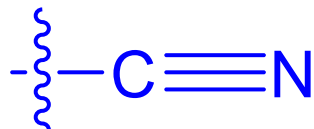
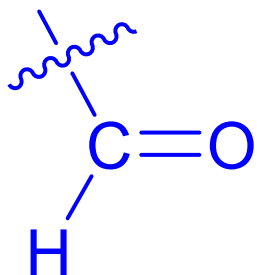
e.g.

2) If the bonded atoms have the SAME atomic number, look at the next atom along

e.g.

Cahn-Ingold-Prelog Sequence Rules cont.

- 3) For **multiple bonds** in substituents: **replace by equivalent number of single bonds** and then apply rules 1 and 2.

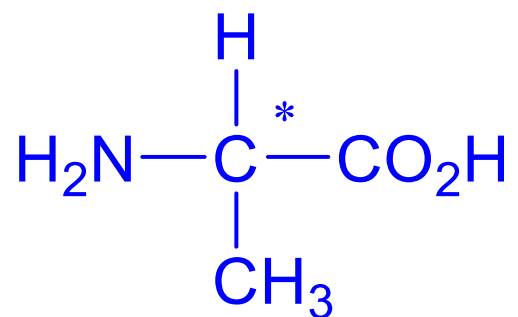


L.G 2.5 Enantiomers

- Molecules whose mirror images are not superimposable

Requirements: sp^3 carbon with four different substituents

e.g. Alanine:



Enantiomers are:

- almost indistinguishable
- very hard to separate

Can distinguish by interaction with polarised light

Plane of light is rotated either to the right
or to the left

Enantiomers cause EQUAL but OPPOSITE rotations

Enantiomers are also called:

Racemic Mixtures

- An **equal mixture** (1:1) of **(+) and (-) enantiomers** of a compound
- Net rotation of polarised light is **ZERO**

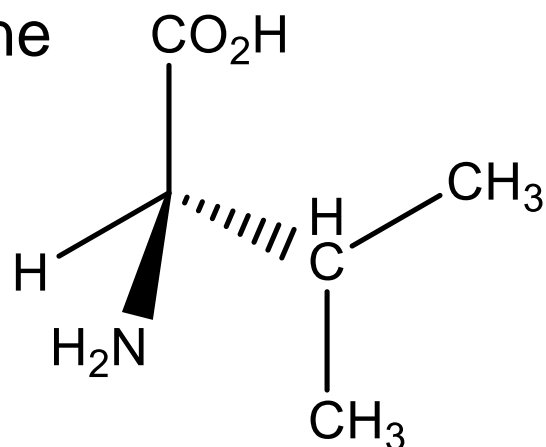
e.g. (\pm) – Alanine = 50% (+) - Alanine and 50% (–) - Alanine

L.G 2.6 Naming Enantiomers

- 1) Assign C.I.P priorities to the four substituents on the stereogenic carbon:
 - 2) With the substituent of lowest priority (4) pointing AWAY from you, look at the priority of the remaining 3 substituents:
 - If they are arranged CLOCKWISE, enantiomer is *R*
 - If they are arranged ANTICLOCKWISE, enantiomer is *S*
- i.e. the configuration at the stereogenic centre is *R* or *S*

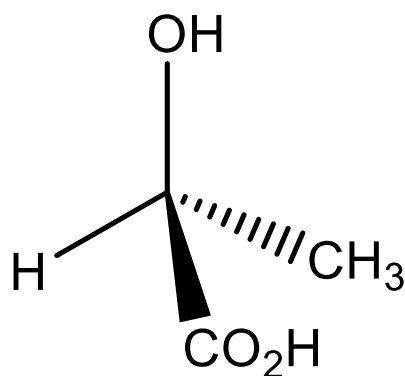
e.g. Valine

R/S?



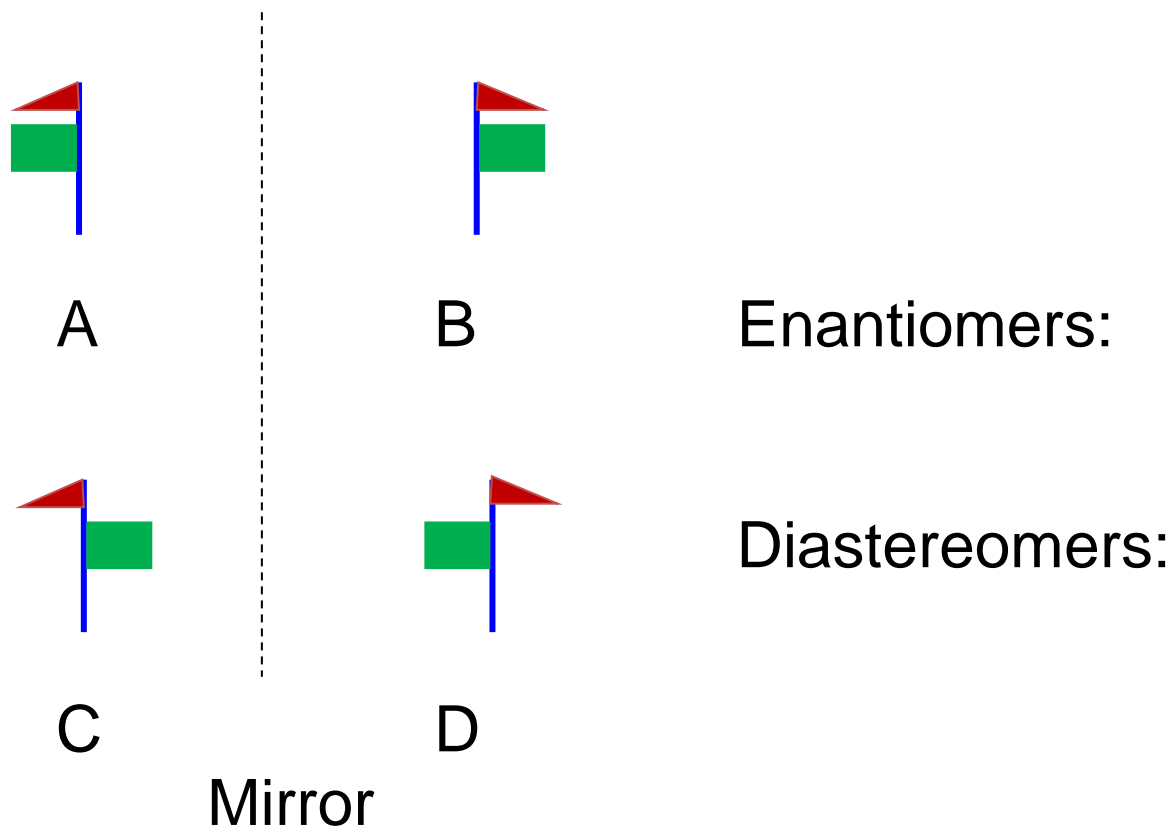
N.B. *R/S* bears **NO** relation to (+) / (-); this is determined experimentally

e.g (+) Lactic acid



Diastereomers

- More than one stereogenic centre gives rise to **DIASTEREOMERS**
- These are **stereoisomers** that are **NOT mirror images** of each other



Diastereomers

- For n stereogenic centres:
- Half of these are enantiomers of the other half
- All other relationships are DIASTEREOMERIC

Section 3: Aspects of Reactivity –I

(Student Manual, Pages 18–22)

Effects of bond polarity

a) Bond Breaking (L.G 3.3)

Non-polar

vs

Polar

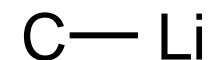
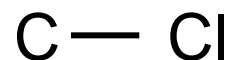
eg. Cl—Cl

H—Cl

b) Inductive Effects (L.G 3.6)

- i) **Electronic effects** transmitted through **σ -bond** framework of molecules

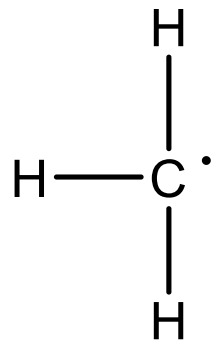
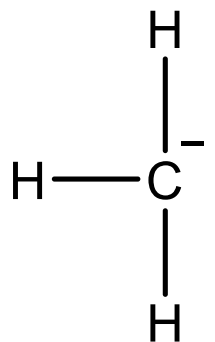
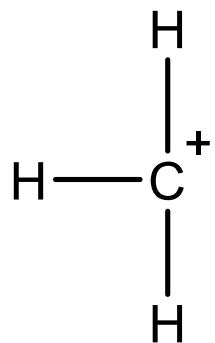
eg.



Effect falls off after about 3 bonds

- ii) **Alkyl groups** are electron donating

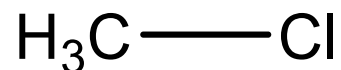
How will this influence cation and anion stability?



Section 3: Aspects of Reactivity –II

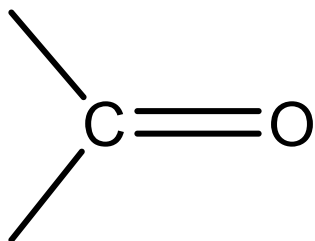
1. Inductive Effect

- through σ -bond



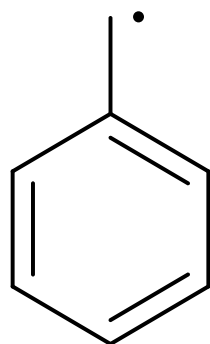
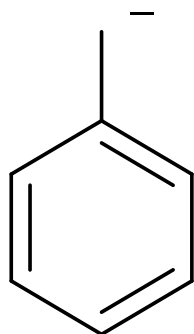
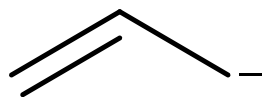
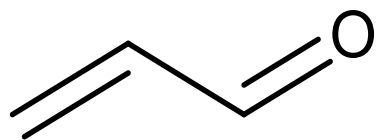
2. Mesomeric / Resonance Effect

- through π -bond

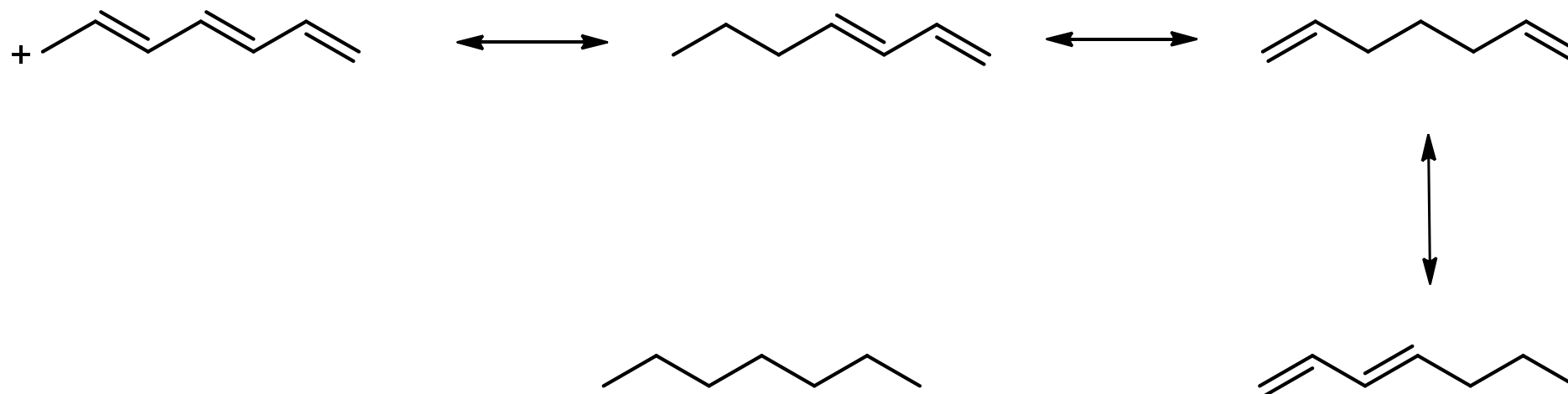


Delocalisation of charge gives rise to resonance structures

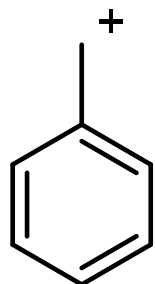
e.g. Conjugated systems:



NB: The greater the number of possible resonance forms, the greater the stability of the molecule



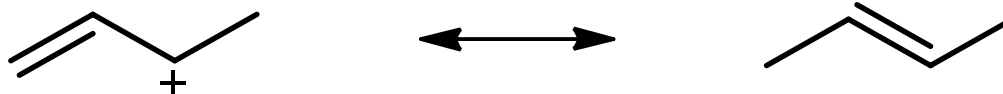
eg. Benzylic cation:



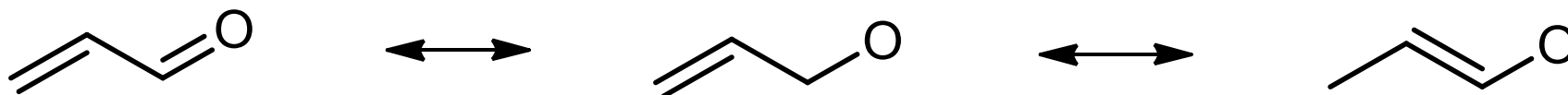
What influence does this have on reactivity?

Examples:

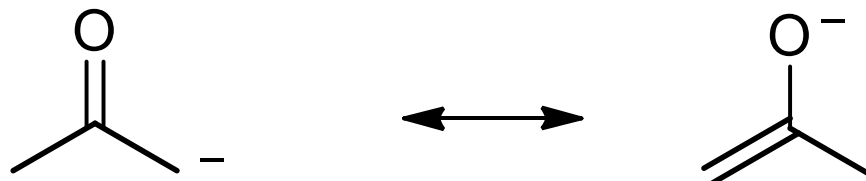
i)



ii)



iii)

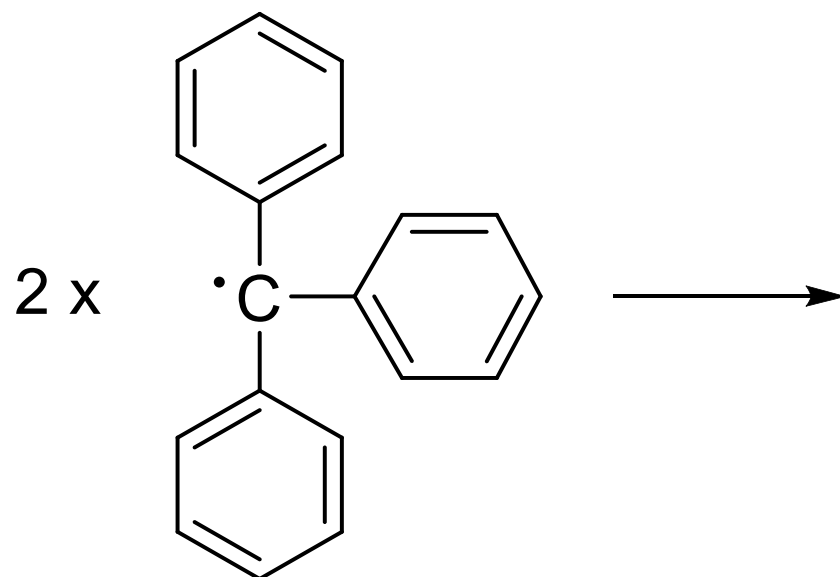


L.G 3.7 Steric Effects

- Due to:
- **Increasing bulk** often leads to:



But:



L.G 3.5 “Curly arrows”

NB lab exercise

- Represent:
- Arrow direction:

For paired electrons:

For unpaired electrons:

eg.



L.G 3.10 Descriptions of double bonds

- i) Isolated
- ii) Conjugated
- iii) Cross-conjugated
- iv) Cumulated

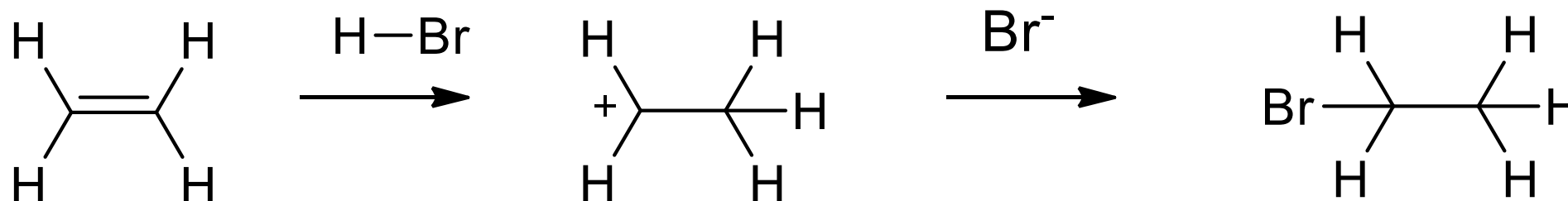
Section 5: Unsaturated hydrocarbons

(Student Manual, Page 30)

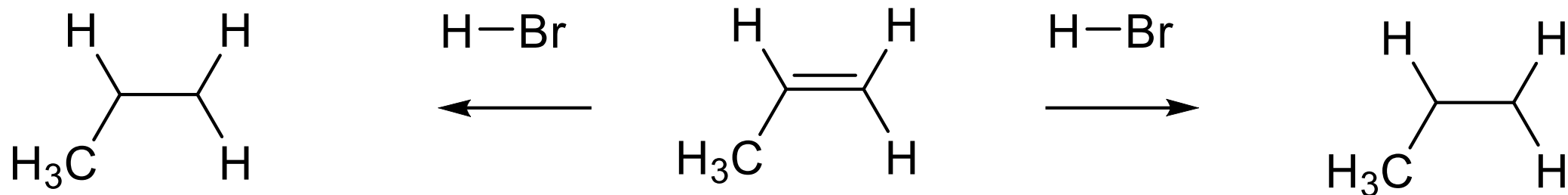
Addition reactions of alkenes

- Alkenes are **electron rich**;

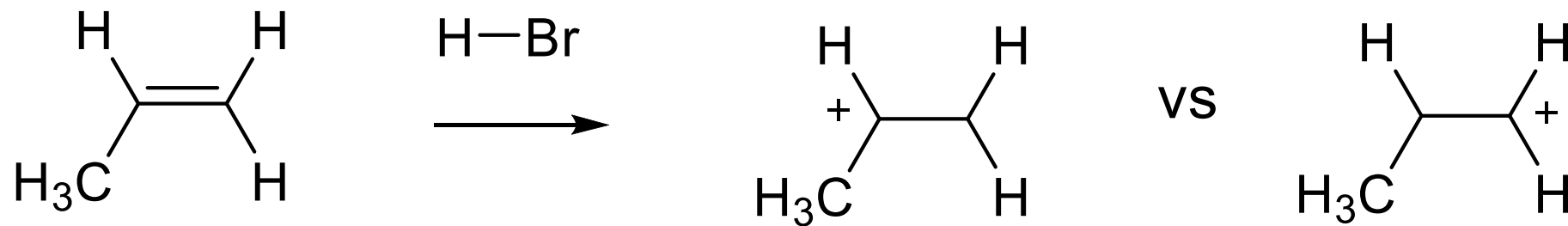
i) Addition of H-X



What about non-symmetrical alkenes?



Mechanism?



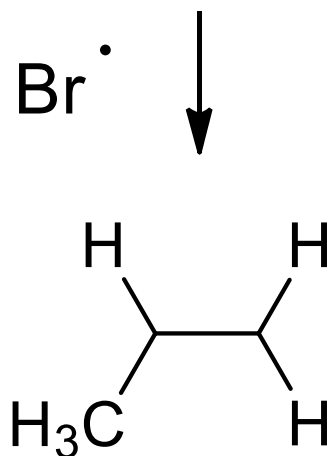
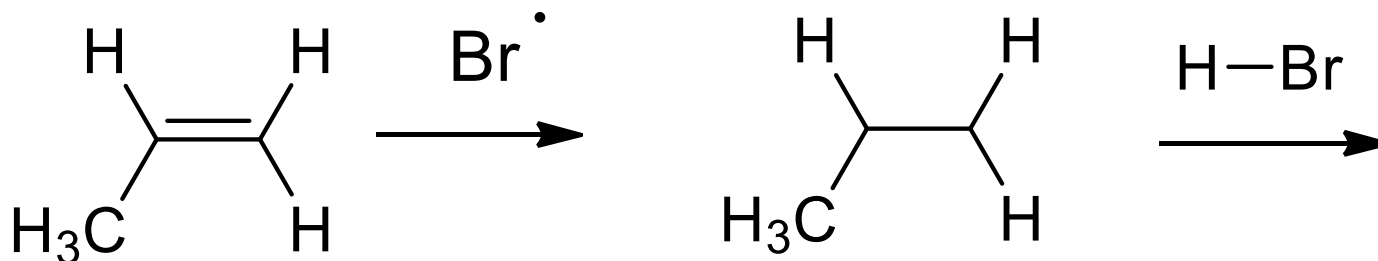
Anti-Markovnikov addition

Radical reaction

Initiation

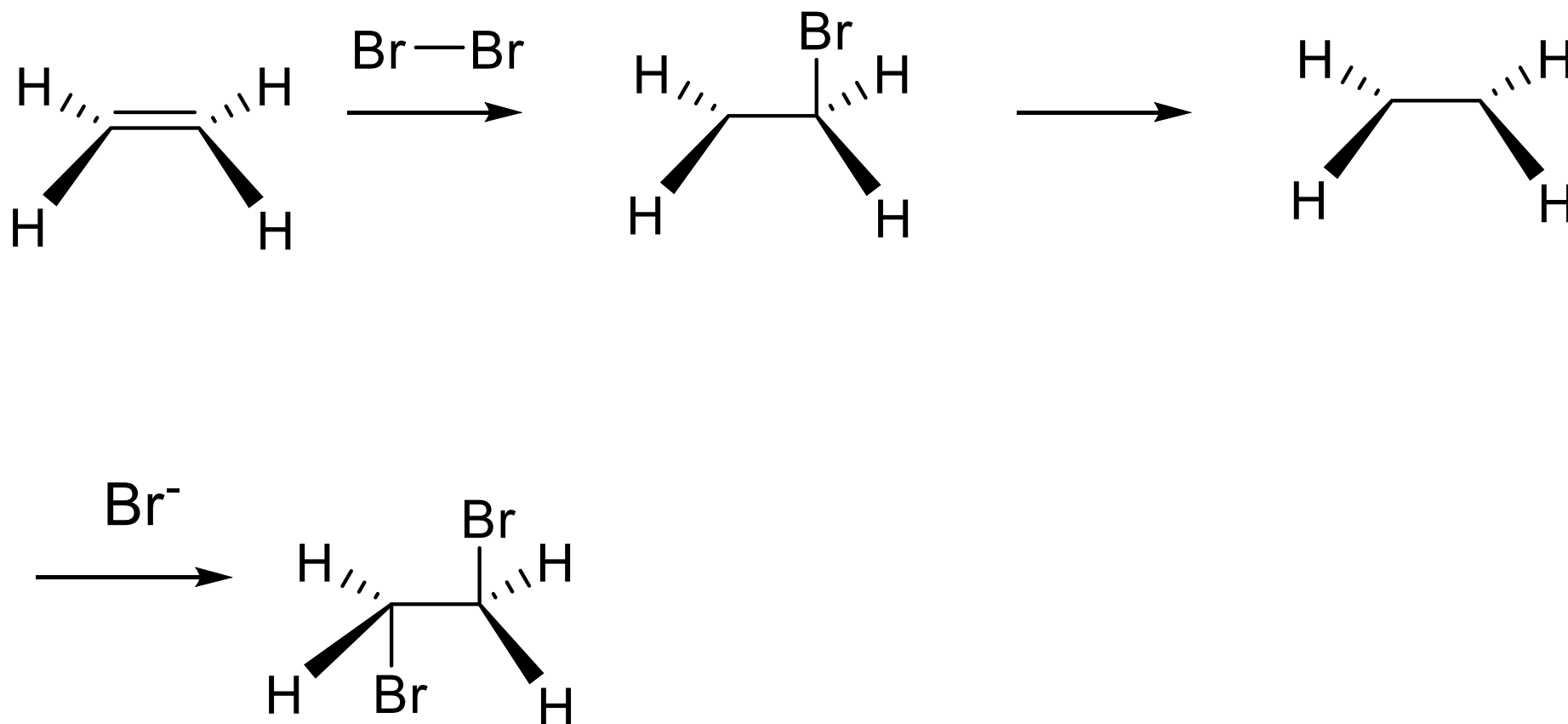


Propagation

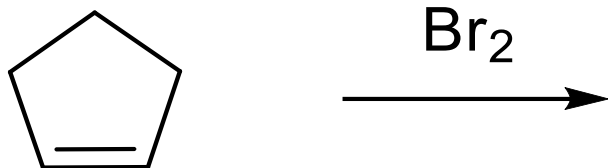


ii) Addition of Br₂

- Two bromine atoms add on **OPPOSITE** faces;

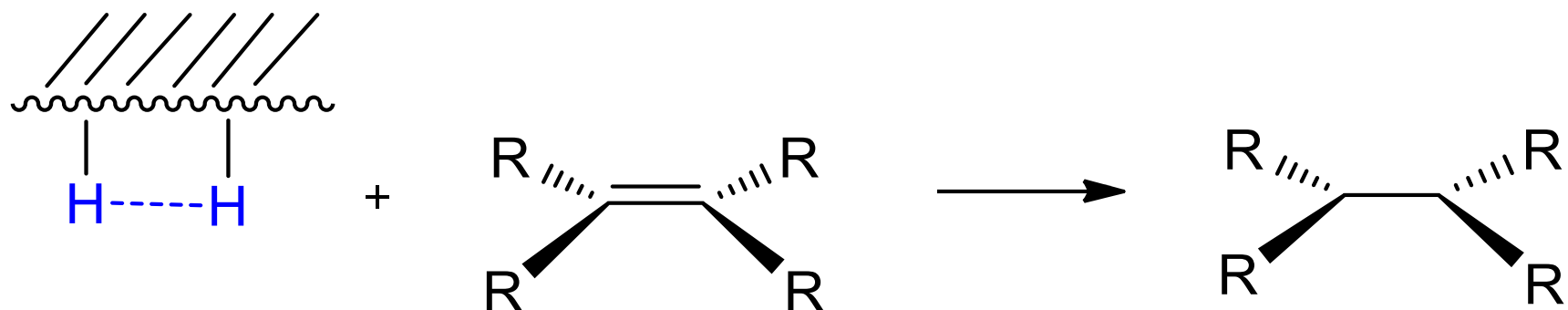


Eg:



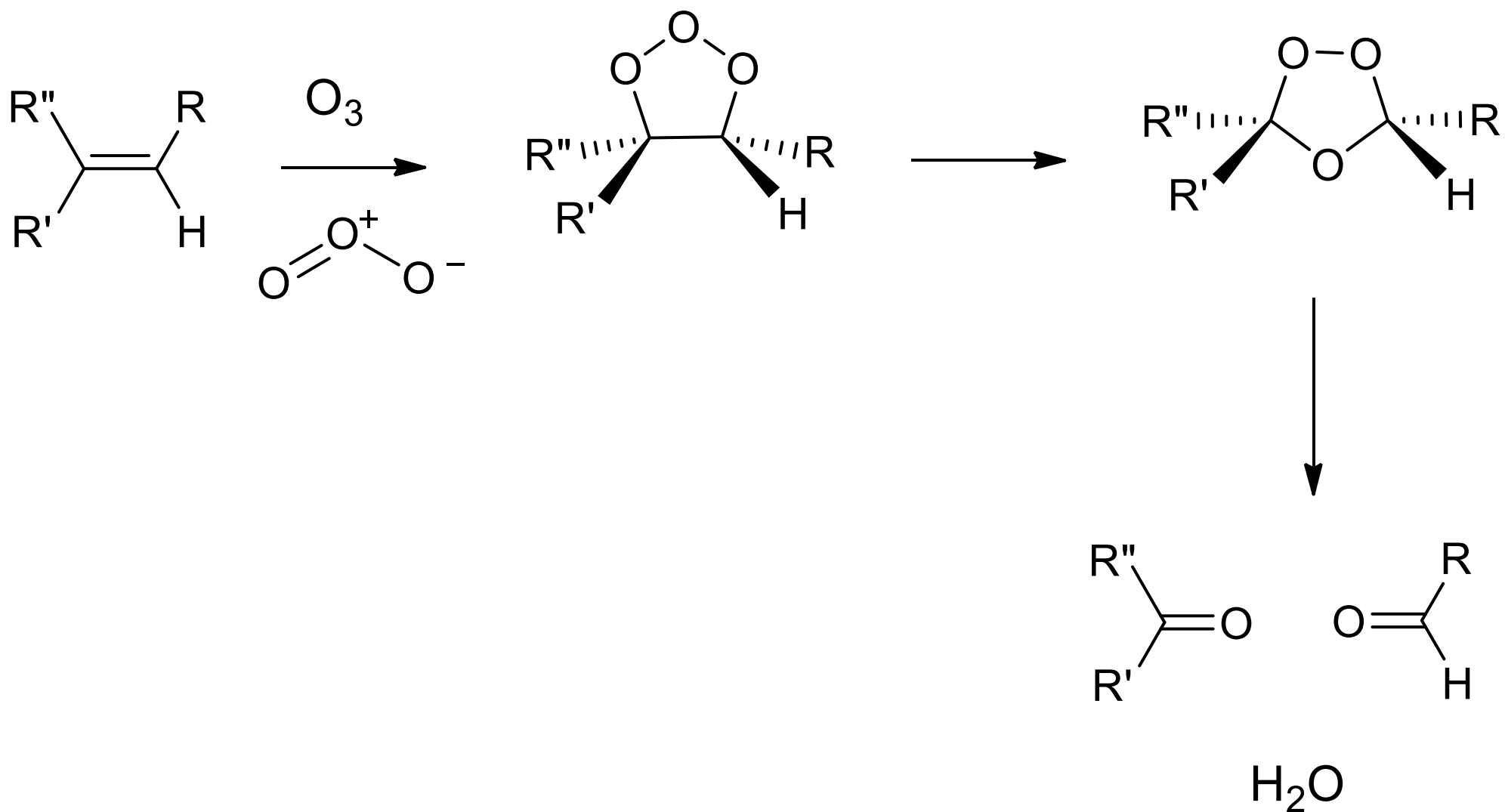
iii) Addition of H₂

- Catalyst needed: Pd or Pt (usually 1%- 5%)
- H-H bond strong:

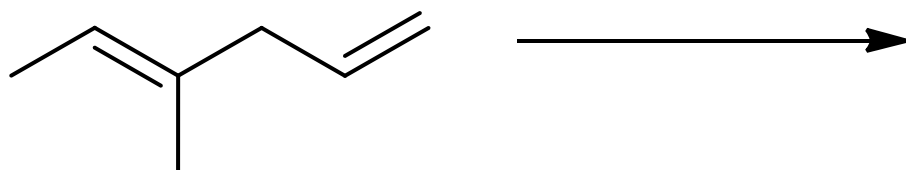
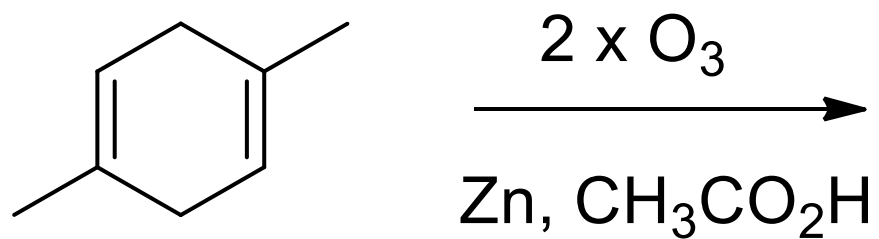


iv) O₃ Addition

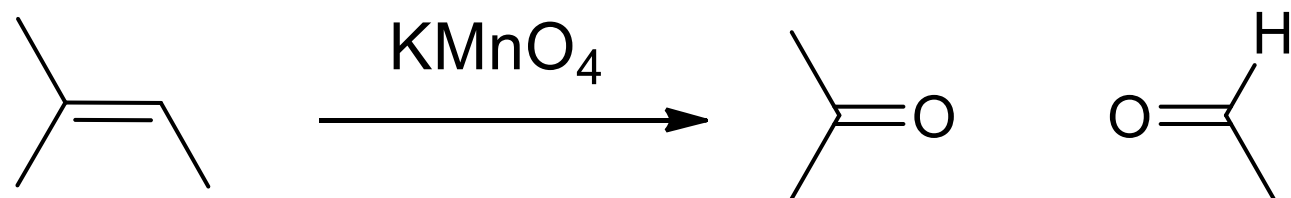
- Ozonolysis



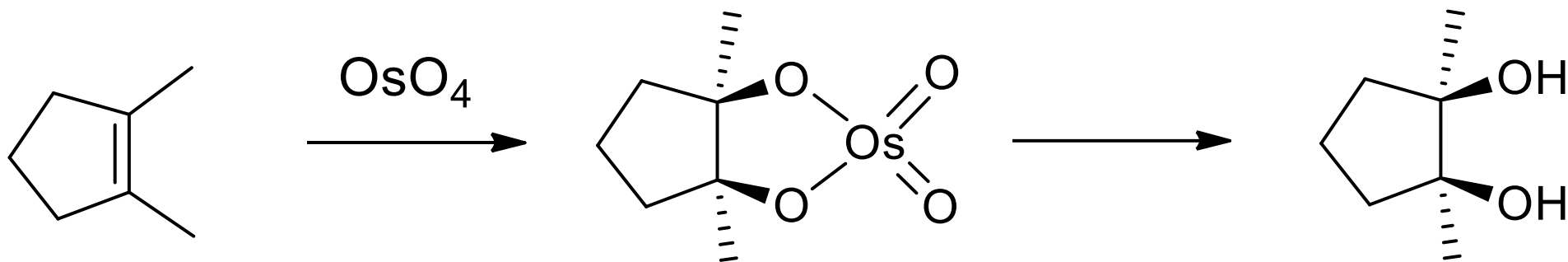
Examples:



Note:

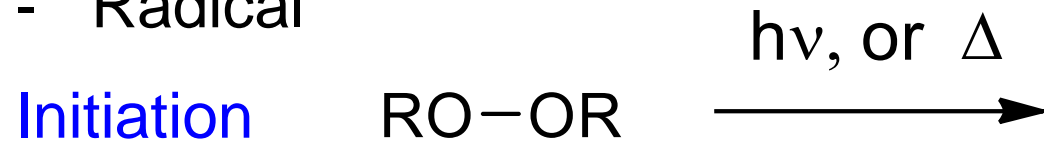


v) Reaction with Osmium tetroxide (OsO_4)

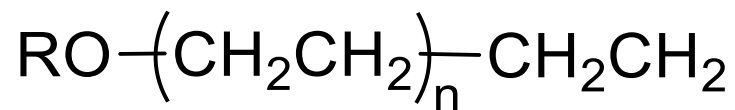
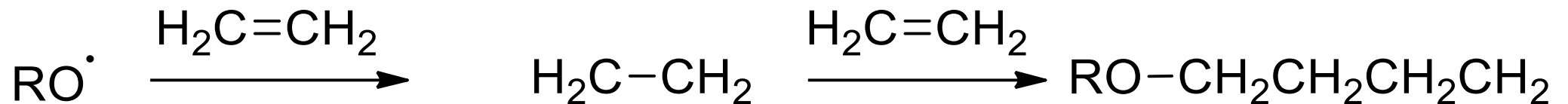


vi) Addition Polymerisation

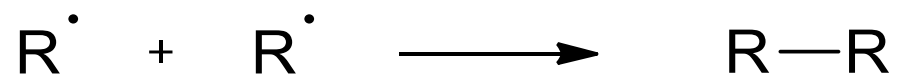
- Radical



Propagation

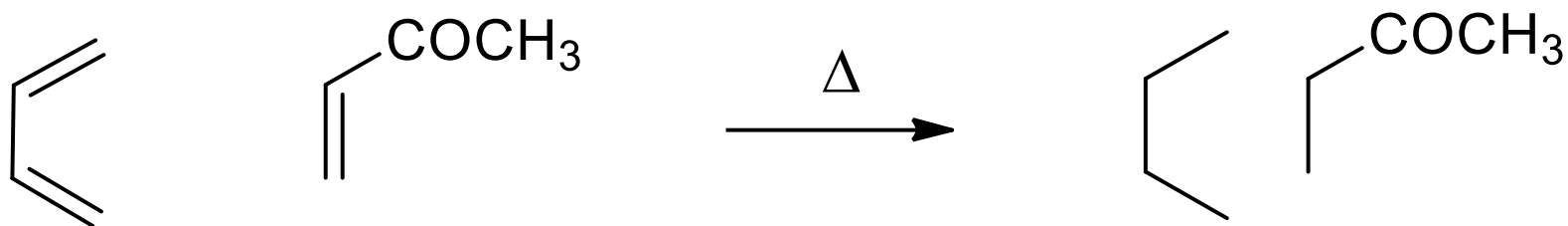


Termination



vii) Pericyclic Reactions

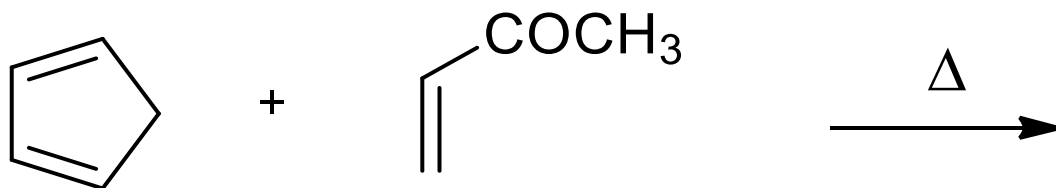
- Diels-Alder cycloaddition reaction



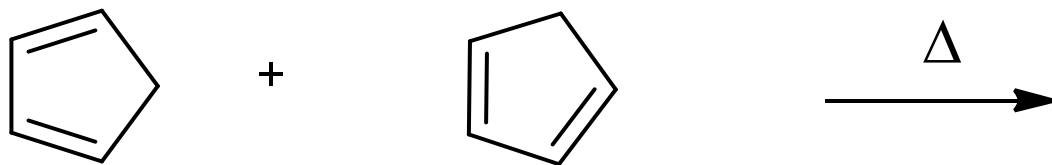
6-membered ring with alkene

Examples:

i)



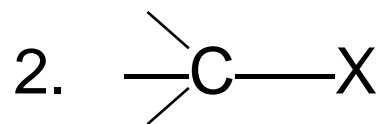
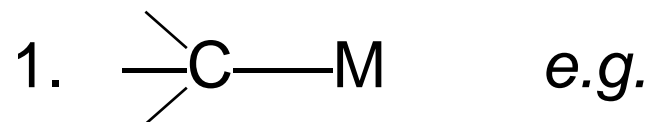
ii)



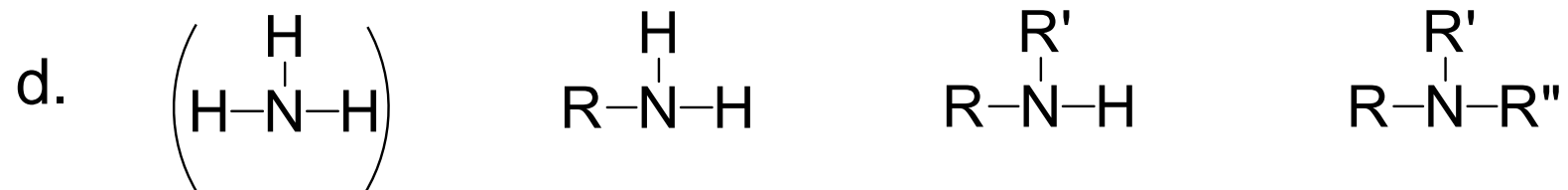
Section 6: Saturated Heteroatom Compounds

(Student Manual, Pages 34–44)

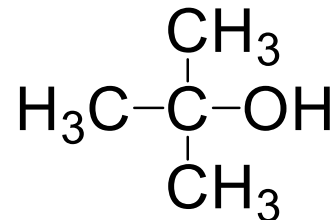
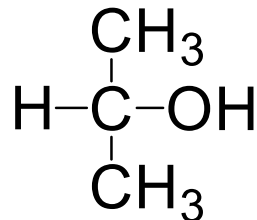
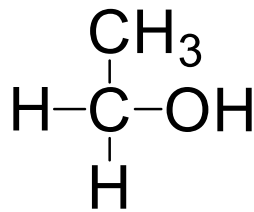
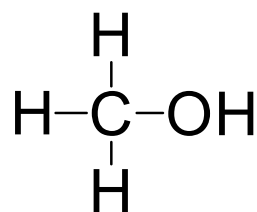
Bonds are *polarised*. Two classes:



Most important functional groups:



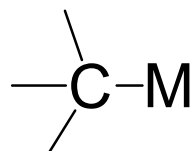
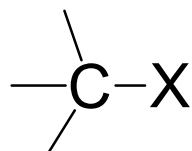
Also note:



Reminders from First Year:

Reactivity of the C—X bond is due to:

1. Bond Polarisation



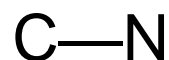
Reacts with:

2. Lone Pairs On X (or empty orbitals on M)

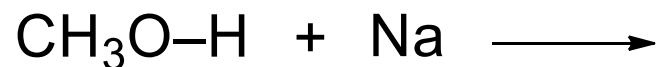
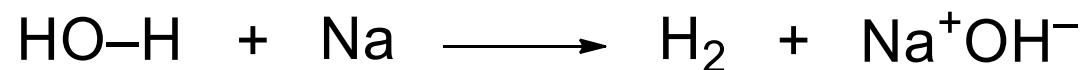
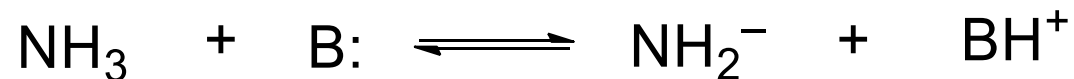
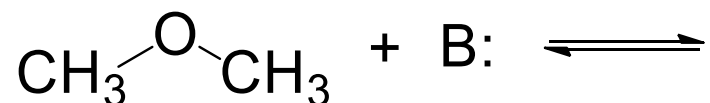
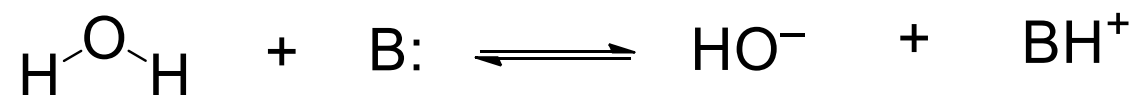
Leads to acid–base behaviour

3. Bond Strengths

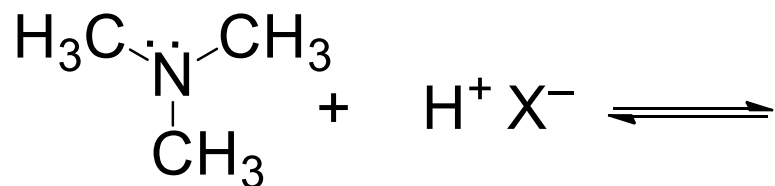
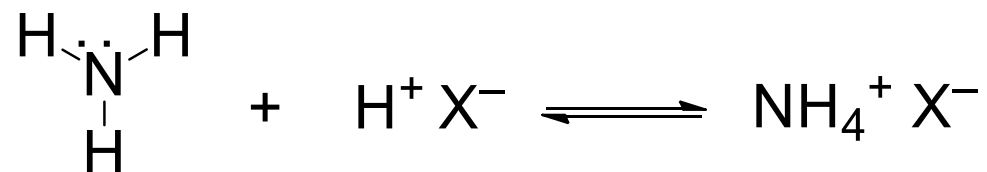
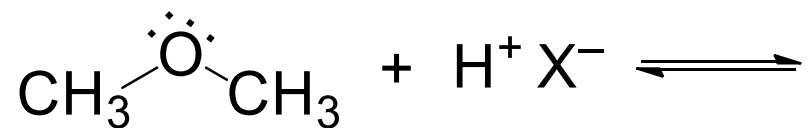
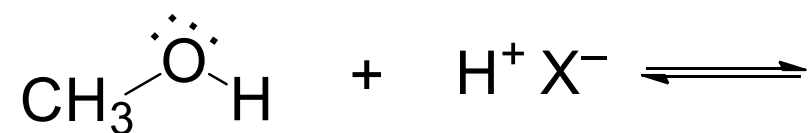
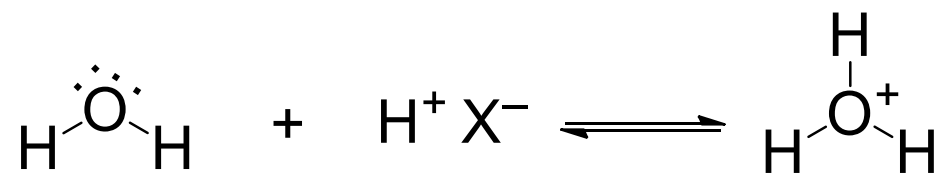
C—X is weaker than C—H



Acid–Base Properties: 1. Behaviour as Acids:

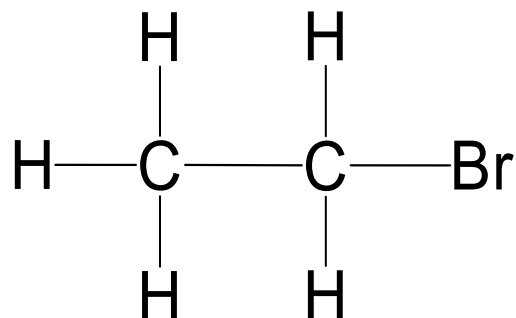


2. Behaviour as Bases:

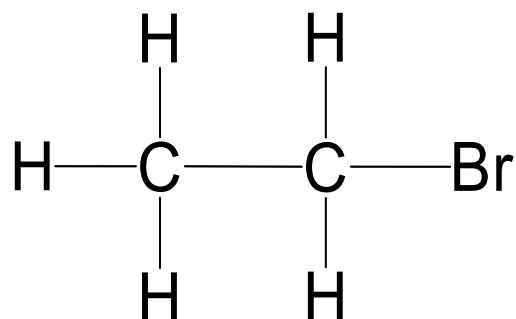


Typical Reactions of Compounds with C—X Bonds

Substitution:



Elimination:



N.B.: substitution and elimination *always* compete with each other!

Competition between S_N And E

1) Effect of Nu:

The more *basic* the Nu, the more chance of *elimination*
(*i.e.*, attack at H⁺ rather than at C^{δ+})

OH⁻ *versus* H₂O

H₂O *versus* NH₃

2) Size Effects:

S_N: attack is at C

E: attack is at H

∴ Any *steric hindrance* favours E

- Bulky Nu
- Crowded C^{δ+} site

3) Higher Temperature favours E: from $\Delta G = \Delta H - T\Delta S$

Further Aspects of Nucleophilic Substitution



In principle, this process is reversible.

To favour the forward S_N reaction:

- A good Nu should be a poor LG; and
- A good LG should be a poor Nu.

What makes a nucleophile “good”?

- A **good nucleophile** tends to be a **good base**.

e.g. OH^- H_2O CH_3O^- CH_3OH

e.g. $(\text{CH}_3)_2\text{NH}$ CH_3NH_2 NH_3

Less clear cases, *e.g.* CH_3O^- vs CH_3CO_2^-

Look at their conjugate acids: **stronger acid** implies **weaker conjugate base**.

What makes a nucleophile “good”?

- Going down a group in the periodic table gives **better nucleophiles** (**lower electronegativity**; atoms can “donate” electrons more readily).



Nu	H ₂ O	NH ₃	Cl ⁻	OH ⁻	CH ₃ O ⁻	I ⁻	SH ⁻
Relative reactivity	1	700	1000	16000	25000	100000	125000

Taken from McMurry, 6th edition, page 353

What makes a leaving group “good”?

- As above: **poor Nu** usually means **good L**; but
- The **weaker** the **C—L bond**, the **better** the **leaving group**.



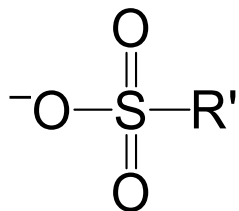
Note the oddity: I^- is one of the best nucleophiles, but also one of the best leaving groups!

- For anions, the **weakest bases** (*i.e.*, derived from the strongest acids) are the **best leaving groups**.



What makes a leaving group “good”?

- Stabilised anions are better leaving groups than unstabilised anions.



For the reaction: $\text{CH}_3\text{--L} + \text{Nu}^- \rightarrow \text{CH}_3\text{--Nu} + \text{L}^-$

L^-	OH^-	Cl^-	Br^-	I^-	$\text{R}'\text{SO}_2\text{O}^-$
Relative reactivity	$\ll 1$	200	10000	30000	60000

Taken from McMurry, 6th edition, page 354

- Poor L can be changed into better L by modifying them:



Activate the leaving group with H^+ :



Nucleophilic Substitution (S_N) Reactions: Mechanisms

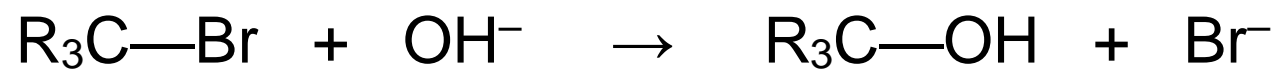
Reaction mechanisms are **detailed descriptions** of:

- The **events** that occur **during chemical reactions** including
 - The **order** in which **bonds are broken** and **formed**;
 - The **relative rates** of different **steps** in the reaction;
 - **Stereochemical features**.

Two main mechanisms for S_N reactions:

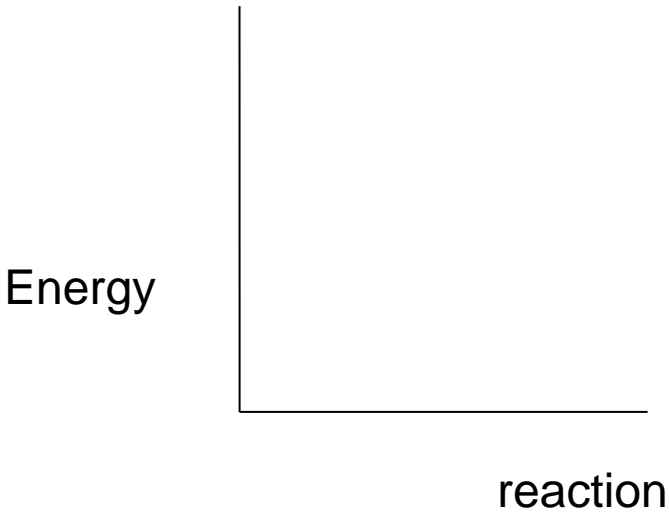
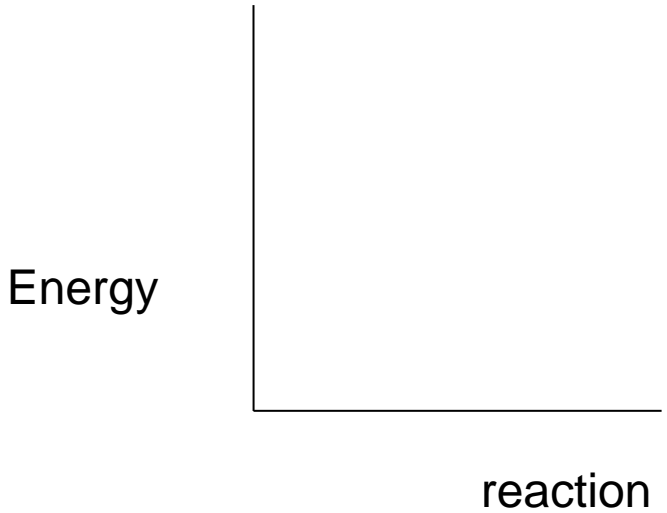
S_N1

S_N2



$\text{S}_{\text{N}}1$	$\text{S}_{\text{N}}2$
L leaves <i>before</i> Nu attacks	Nu attacks, L leaves <i>simultaneously</i>

S_N1	S_N2
Kinetics and Rate Law	
Unimolecular	Bimolecular

S_N1	S_N2
Energy profile	
 <p>Energy</p> <p>reaction</p> <p>The diagram shows a vertical axis labeled 'Energy' and a horizontal axis labeled 'reaction'. The energy profile for an S_N1 reaction starts at a baseline, rises to a single peak representing the transition state, and then falls to a lower energy level than it started at, indicating an exothermic process.</p>	 <p>Energy</p> <p>reaction</p> <p>The diagram shows a vertical axis labeled 'Energy' and a horizontal axis labeled 'reaction'. The energy profile for an S_N2 reaction starts at a baseline, rises to a single peak representing the transition state, and then falls back to the same energy level it started at, indicating a thermoneutral process.</p>

S _N 1	S _N 2
Stereochemistry	

S_N1	S_N2
Effect of Structure	
Importance of C^+ :	Direction of Nu: Approach is NB

S _N 1	S _N 2
Effect of Nu Strength	
Effect of Leaving Group	
Effect of Solvent	

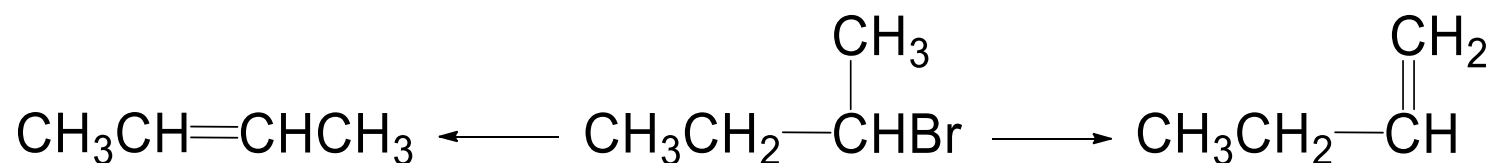
Further Aspects of Base- Induced Elimination

In S_N reactions, Nu attacks carbon

In eliminations, Nu attacks hydrogen

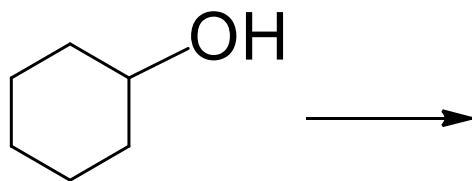
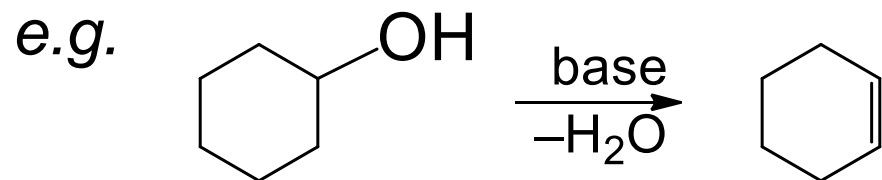


Depending on reactant's structure, different products are possible:



Preferences?

Can **modify poor leaving groups** to facilitate reaction (same as with S_N).

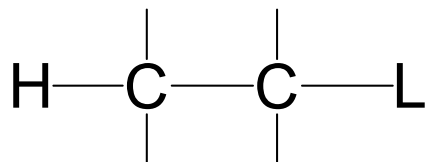


Mechanisms of E reactions

Two main mechanisms: E1 E2

The E1 Mechanism:

Leaving group leaves *before* the base attacks (similar to S_N1)



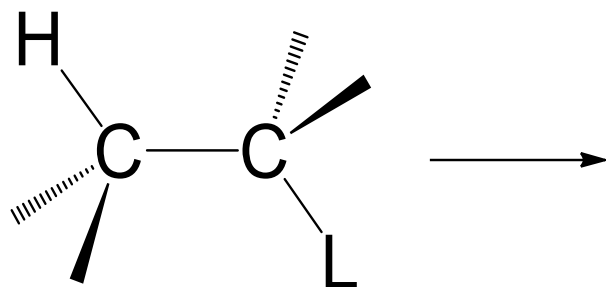
Similar arguments to S_N1 for:

- Kinetics
- Solvent effects
- Structural effects: more chance of E1 mechanism with

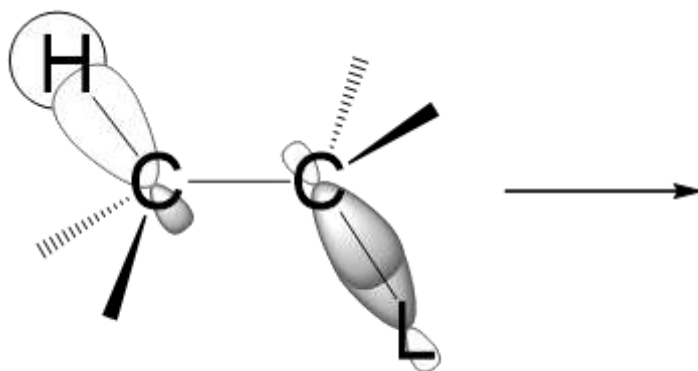
The E2 Mechanism:

Base attacks H, L leaves *simultaneously*, i.e. *concerted* (similar to S_N2)

But note **stereochemical condition**: H and L must be aligned

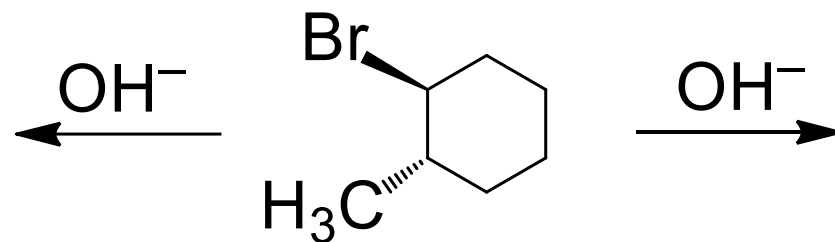


Orbitals must overlap to make the π bond:

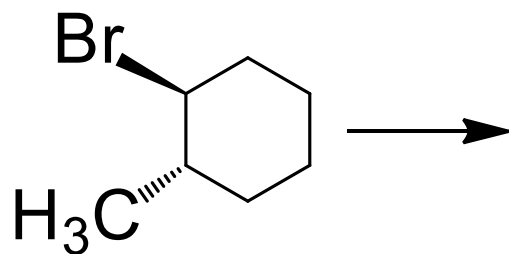


Kinetics:

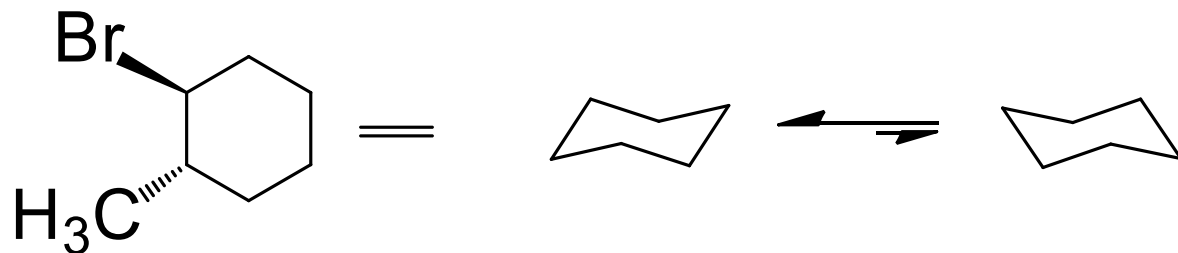
An Example of E1 *versus* E2



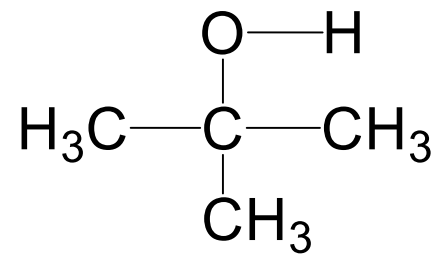
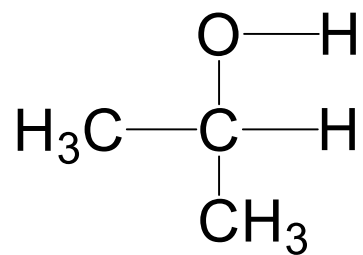
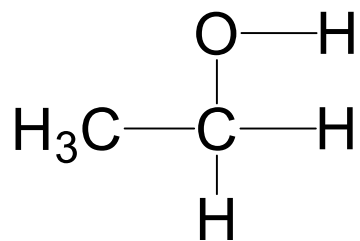
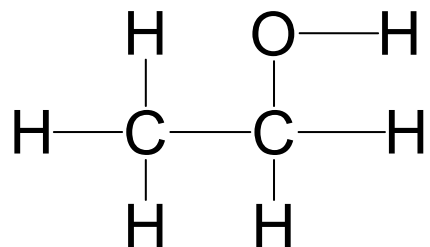
If E1 operates:



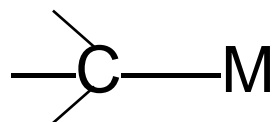
If E2 operates:



Alternative Eliminations



Organometallics



Preparation: by exchange with halides

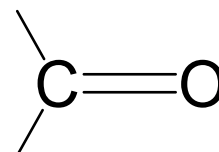
Reactivity:

Section 7: Unsaturated Heteroatom Compounds

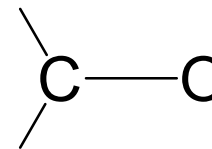
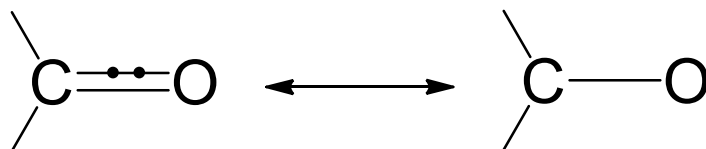
(Student Manual, Pages 45–50)



1. Inductive effect through σ -bond

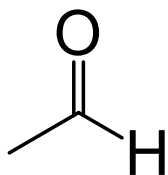


2. Resonance (mesomeric) effect

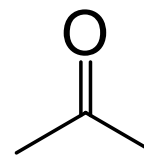


Examples:

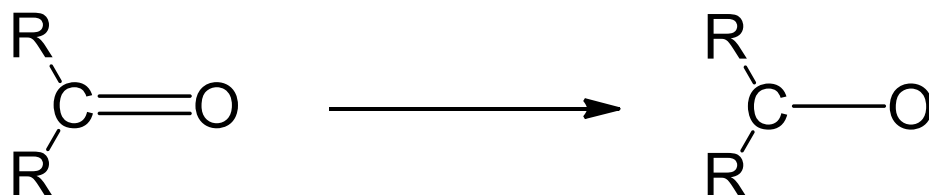
Aldehydes



Ketones



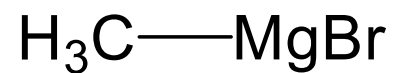
Typical reactions of compounds with C=O bonds: [Nucleophilic addition](#)



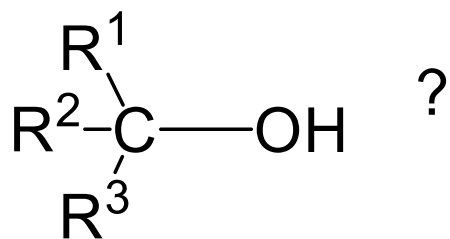
◆ Timing?

Good Nu: attack first!

Example

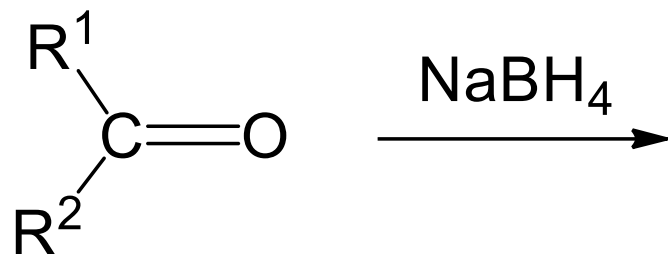


Strategies to make



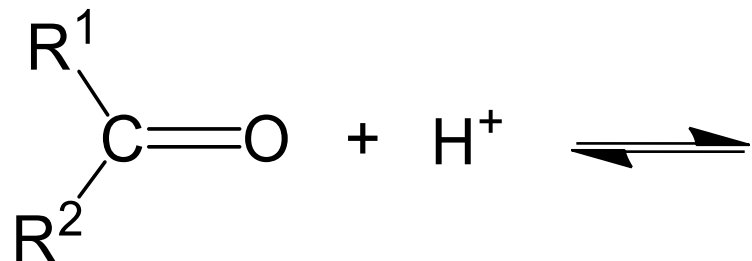
Good Nu: "H⁻"

Sources: Na⁺BH₄⁻, Li⁺AlH₄⁻
(Complex hydrides)



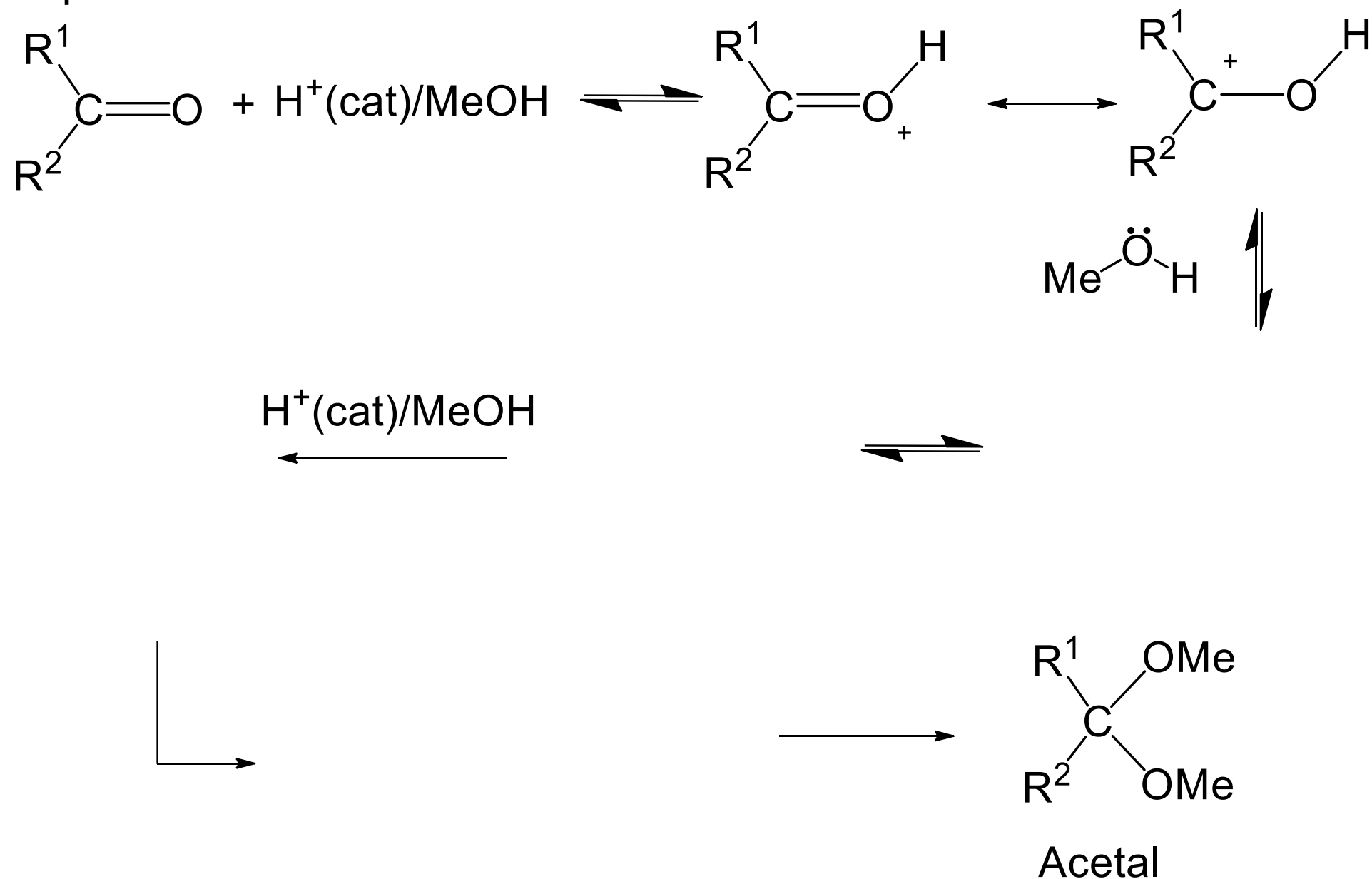
Poorer Nu: H₂O, ROH, RSH

N.B.: Catalyse the reaction with H⁺

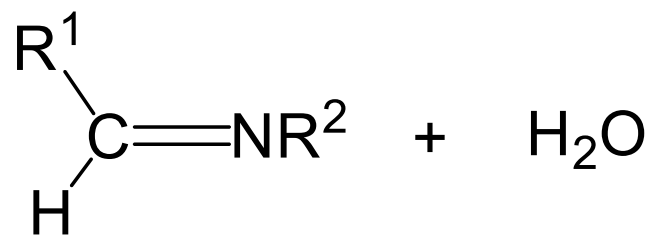
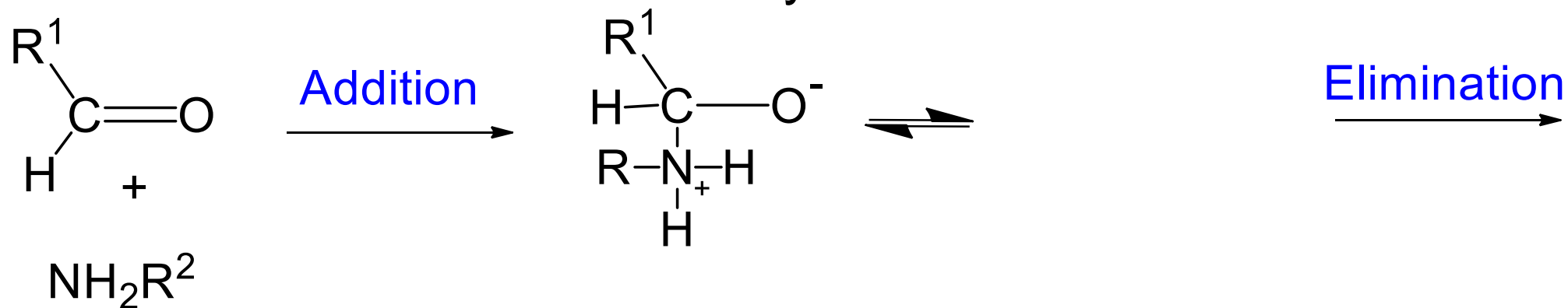


Improved chance of attack by Nu

Example: Formation of Acetals



Extension: Addition Followed By Elimination

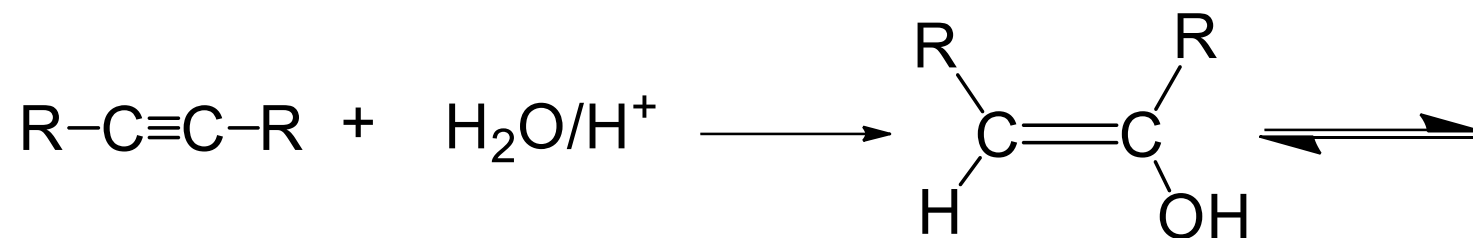


$\text{R}^2 = \text{H or C}$

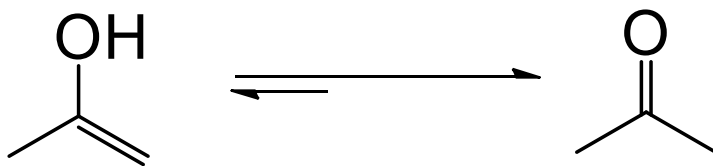
$\text{R}^2 = \text{OH}$

$\text{R}^2 = -\text{NH}_2$

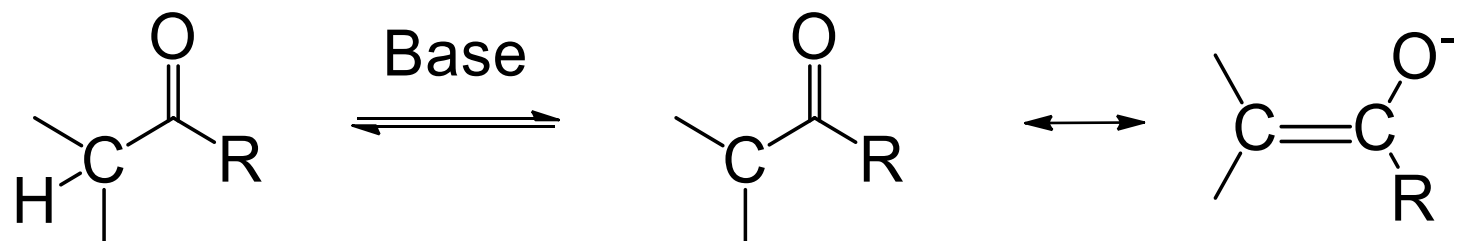
Tautomerism



In general: ENOL \rightleftharpoons KETO

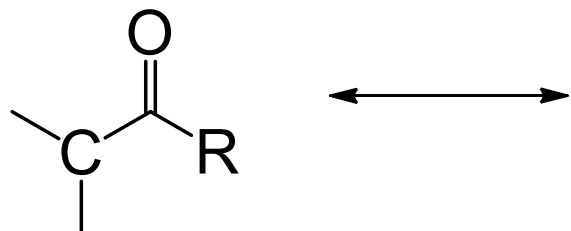


α -Substitution Reactions

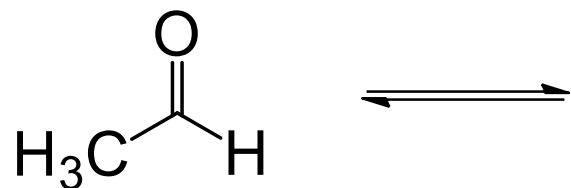


Enolate Anion:

Reactions of Enolates



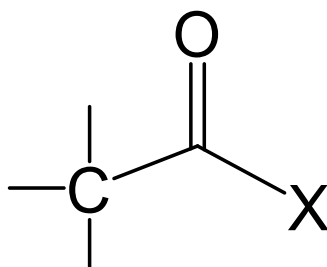
Example: Aldol Reactions



Base-catalyzed dimerization

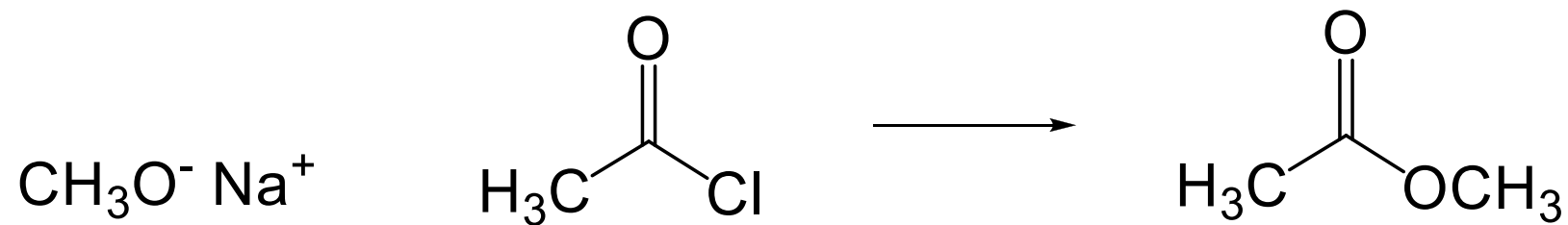
Section 8: Composite Functional Groups

(Student Manual, pages 51–56)



X = OH, OR, NH₂, Cl

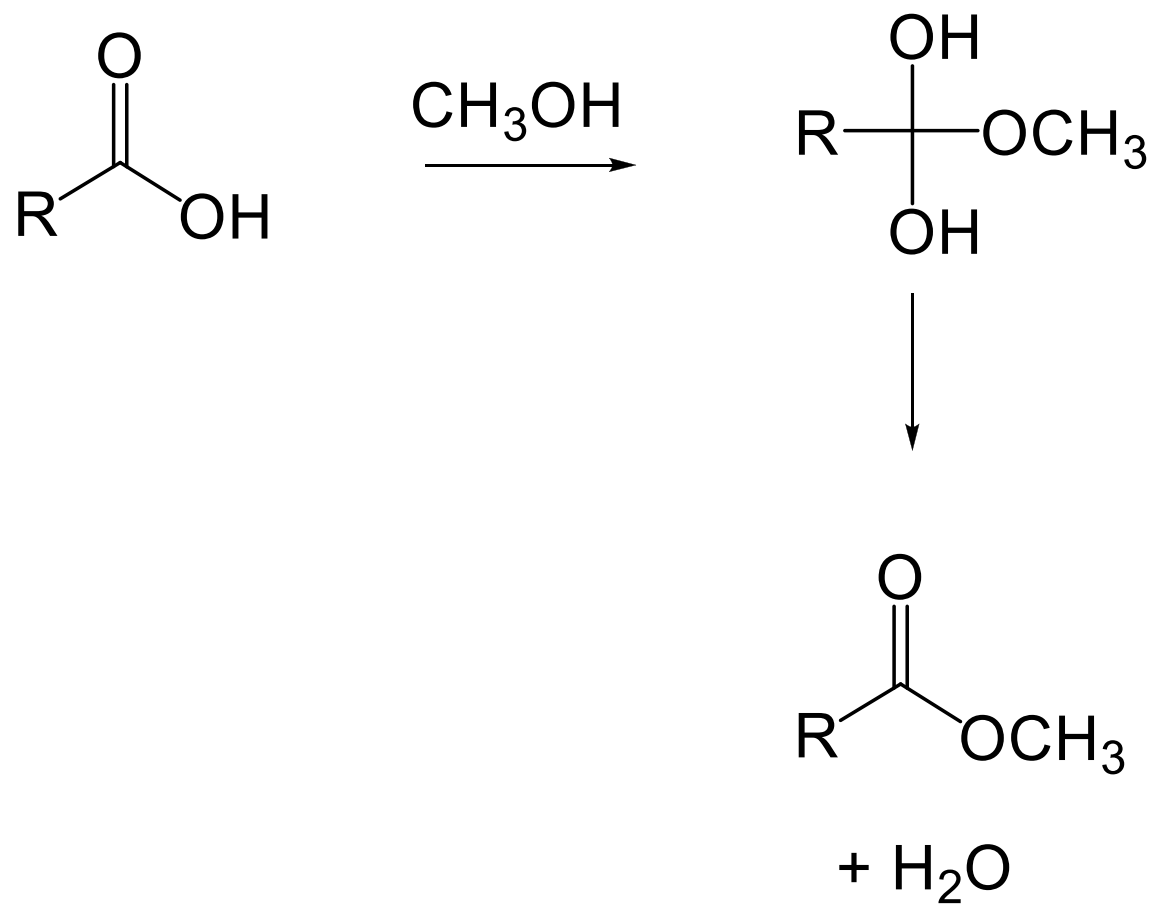
“Substitution” Occurs



Example: Grignard Addition



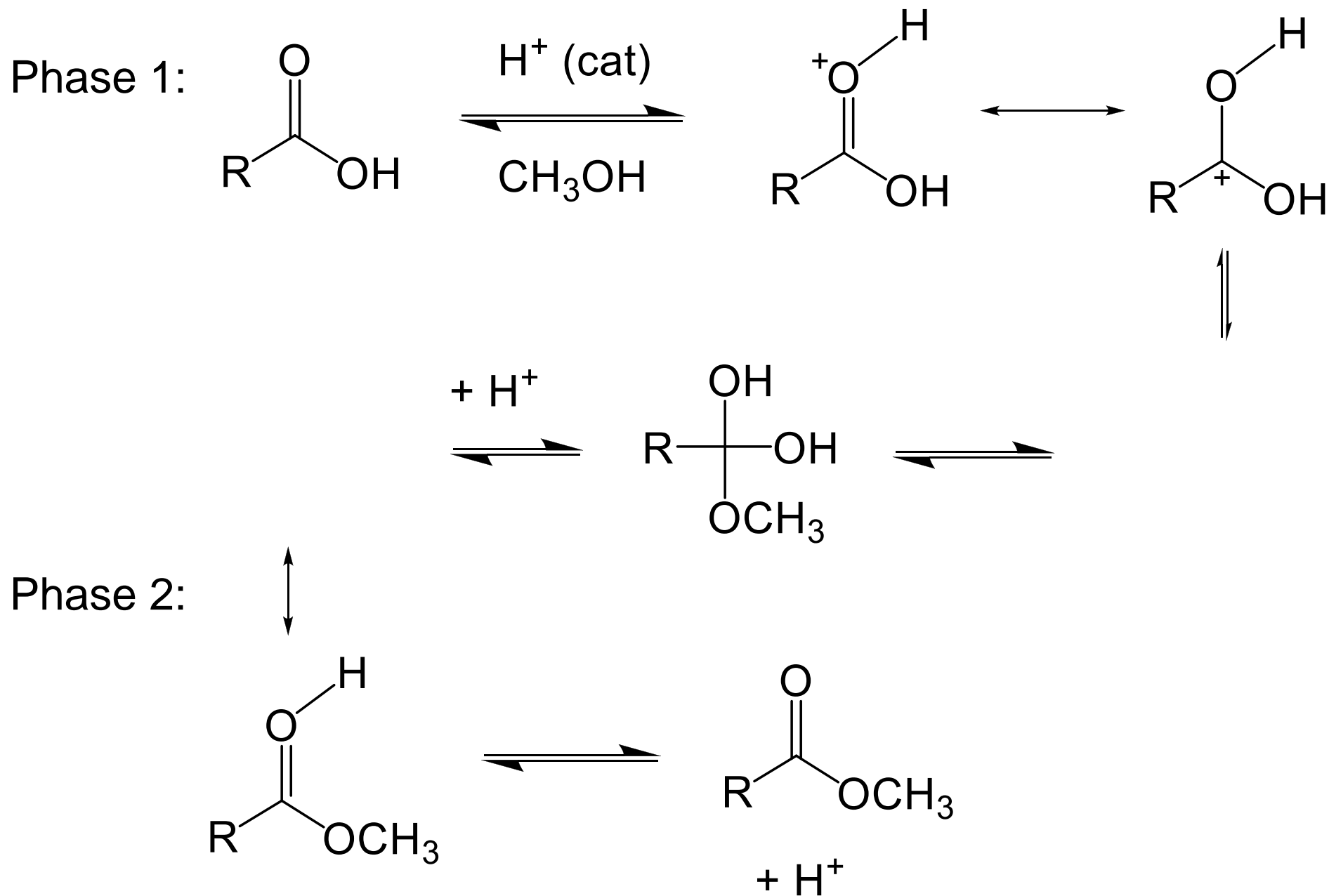
Example: Ester Formation



Overall: Substitution

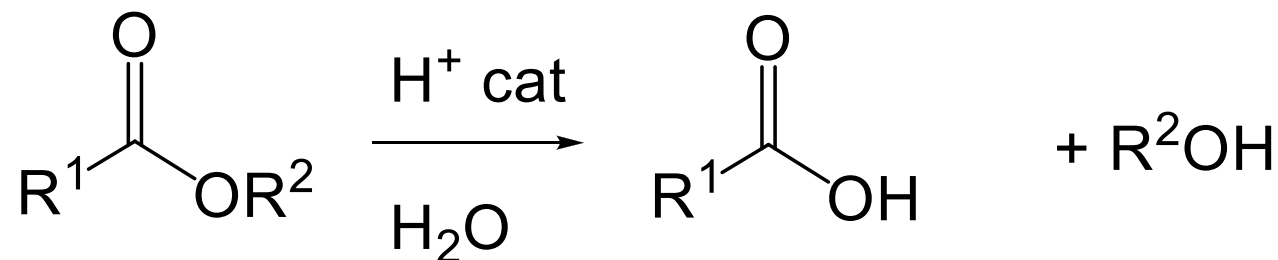
How?

Ester Formation: Mechanism

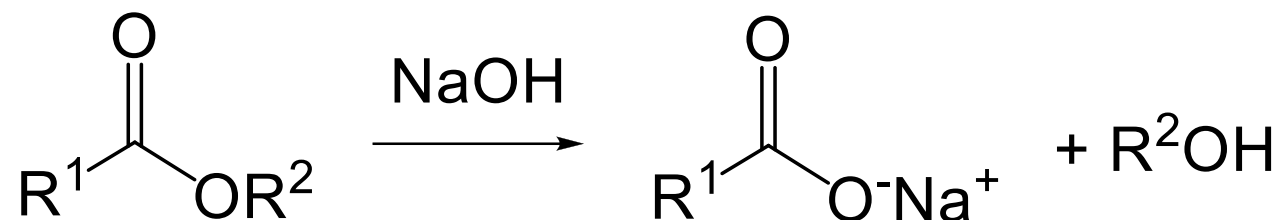


You must know:

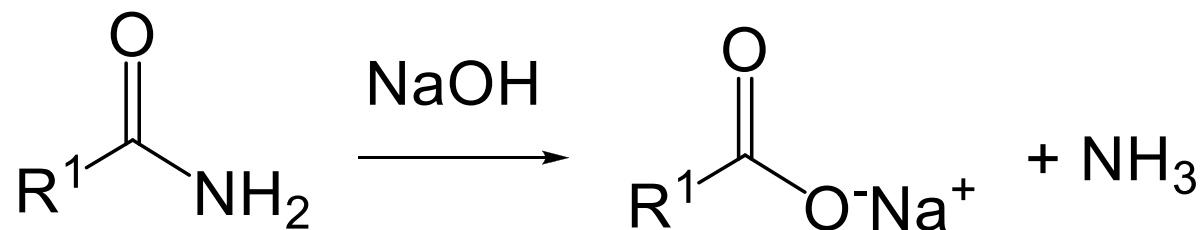
1) Ester Hydrolysis (**acid**)



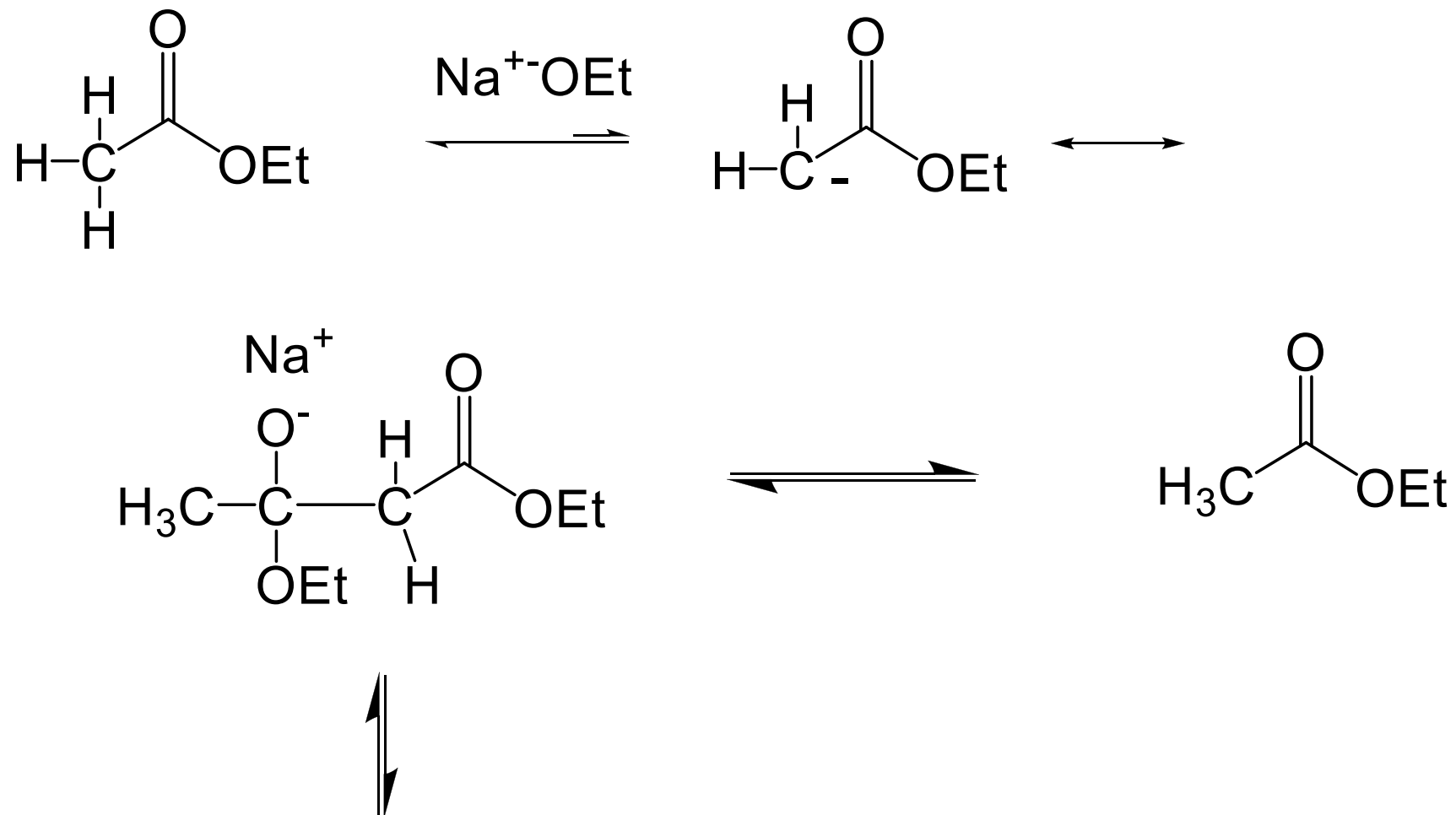
2) Ester Hydrolysis (**base**)



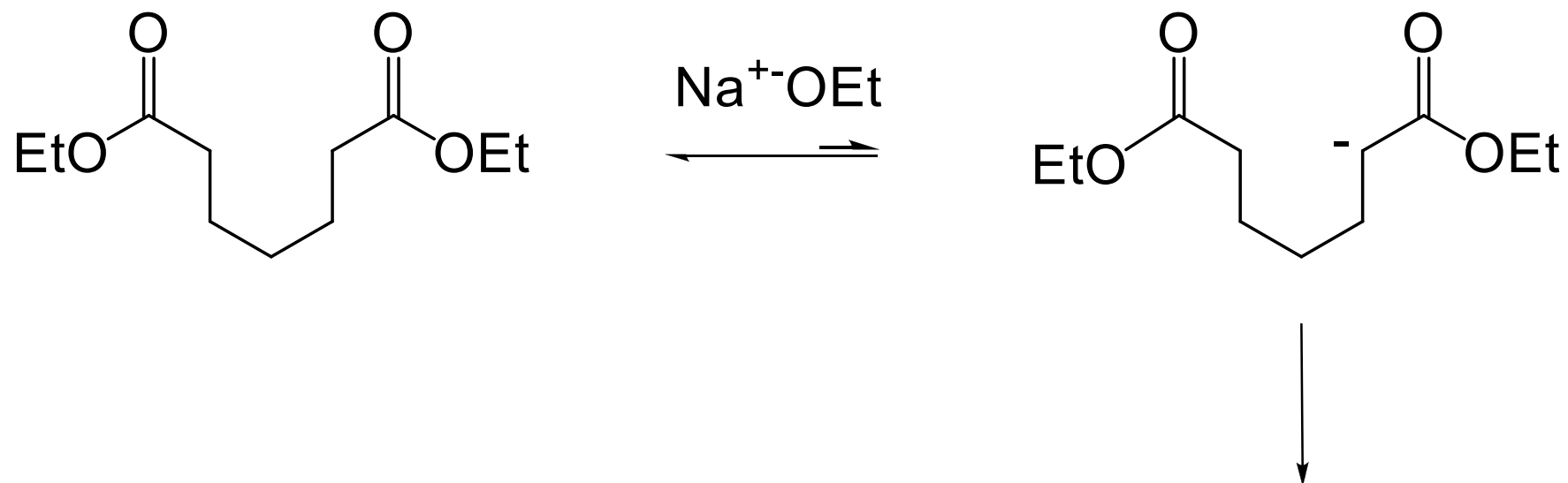
3) Amide Hydrolysis



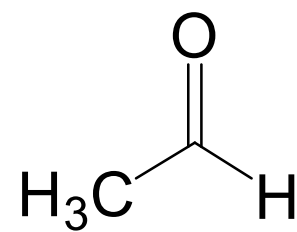
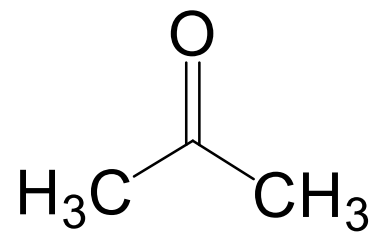
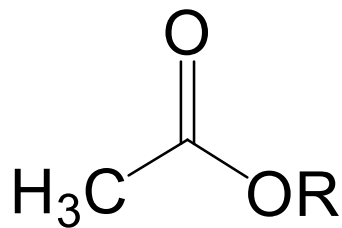
Enolate Chemistry:



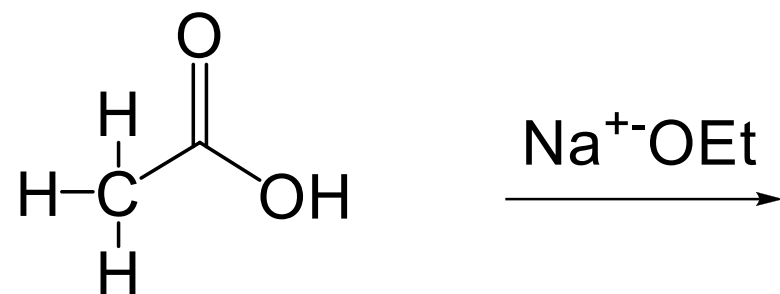
Example:



Carbonyl Electrophilicity



NB: – Don't overlook acid-base properties



Better to use esters:

