

CHEMISTRY

 59^{th} and 60^{th} Class, 29-11-2021

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Last class	SRV DISTITUTE OF SCIENCE & TECHNOLS (December of the University safe 3 of USC 600.)

- \Box Analysis S_N1 or S_N2 or E1 or E2
- ☐ Oxidation reaction reagents
- □ Reduction reaction, introduction

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In this class..



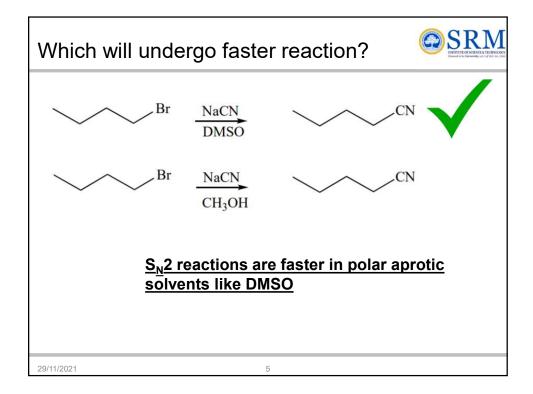
- ☐ Reduction reactions, reagents
- □ C-C bond formation reaction
- ☐ Synthesis of aspirin and paracetamol, scheme

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Examples



20/41/2024



Examples



For the above dibromo alkane determine which position will react faster (be more reactive) under $S_N 1$ and $S_N 2$ conditions. Explain your answer.

 $\frac{3^{\circ} \ fastest \ under \ S_{\underline{N}} 1 \ because \ carbocation}{1^{\circ} \ fastest \ under \ S_{\underline{N}} 2 \ because \ unhindered}$

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Example, solution
$$-3$$

$$\begin{array}{c} \text{Br} \\ \text{CH}_3\text{CHCH}_3 & + \text{CH}_3\text{CH}_2\text{O}^- & \text{CH}_3\text{CH}_2\text{OH} \\ \\ \text{Stronger bases favor E2 over S}_{\text{N}}\text{2} \\ \\ \text{CH}_3\text{CHCH}_3 & + \text{CH}_3\text{CH}_2\text{O}^- & \text{CH}_3\text{CH}_3\text{OH} \\ \\ \text{CH}_3\text{CHCH}_3 & + \text{CH}_3\text{CH}_2\text{O}^- & \text{CH}_3\text{CH}_3\text{OH} \\ \\ \text{20\%} & 80\% \\ \\ \end{array}$$

$$S_{N}1, S_{N}2, E1 \text{ or } E2 ??$$

$$CH_{3}CH_{2}CH_{2}CH_{2}CH_{2}CI + CH_{3}O^{-} \xrightarrow{CH_{3}OH}$$

$$CH_{3}CCH_{2}CH_{3} + CH_{3}CH_{2}O^{-} \xrightarrow{CH_{3}CH_{2}OH}$$

$$Br$$

$$CH_{3}CCH_{2}CH_{3} + CH_{3}CH_{2}O^{-} \xrightarrow{CH_{3}CH_{2}OH}$$

$$Br$$

$$CH_{3}CCH_{3} + CH_{3}CH_{2}O^{-} \xrightarrow{CH_{3}CH_{2}OH}$$

$$CH_{3}CCH_{2}CHCH_{3} + CH_{3}CCH_{2}O^{-} \xrightarrow{CH_{3}CH_{2}OH}$$

$$CH_{3}CCH_{2}CHCH_{3} + CH_{3}CO^{-} \xrightarrow{CH_{3}CH_{2}OH}$$

$$CH_{3}CCH_{2}CHCH_{3} + CH_{3}CO^{-} \xrightarrow{CH_{3}CH_{2}OH}$$

$$CH_{3}CCH_{2}CHCH_{3} + CH_{3}CCH_{2}OH$$

$$CH_{3}CCH_{2}CH$$

Solution - 1



$$CH_3CH_2CH_2CI + CH_3O^- \xrightarrow{CH_3OH}$$

The leaving group, Cl, is bonded to a primary carbon. Methoxide ion (CH_3O^-) is a strong nucleophile and a strong base but not sterically hindered, so the reaction will follow the S_N2 mechanism. Not much elimination should occur. There is no stereochemistry visible at the primary carbon.

$$\begin{array}{cccc} \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CI} + \text{CH}_3\text{O}^- & \xrightarrow{\text{CH}_3\text{OH}} & \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OCH}_3 \end{array}$$

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Solution – 2



$$CH_3 \\ CH_3CCH_2CH_3 + OH \\ Br$$

The leaving group (Br) is bonded to a tertiary carbon. Hydroxide ion is a strong base, so the E2 mechanism should be followed. According to Zaitsev's rule, the more highly substituted alkene should be the major product.

$$\begin{array}{c} CH_3 \\ CH_3CCH_2CH_3 + OH \\ Br \end{array} \begin{array}{c} CH_3CH_2OH \\ H_3C \\ C=C \\ H_3C \\ CH_3 \\ CH_3 \end{array} \begin{array}{c} CH_3 \\ C=C \\ H_3C \\ CH_3 \\ CH_3CH_3 \\ CH_3$$

CH₃CHCH₃ + CH₃CH₂OH

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OCH₂CH₃

 $+ CH_3CH = CH_2$

CH₃CHCH₃

97%

Solution – 7

$$\begin{array}{c}
Br\\
CH_3CCH_3 + CH_3CH_2O^- \\
CH_3
\end{array}$$
Tertiary Substrates
no S_N2 (too hindered)
E2 favored with strong bases
HO -, RO - (NaOH, NaOEt)

$$\begin{array}{c}
CH_2\\
CH_3CCH_3
\end{array}$$

$$\begin{array}{c}
CH_2\\
CH_3CCH_3$$

$$\begin{array}{c}
CH_2\\
CH_3CCH_3
\end{array}$$

Solution - 8



The leaving group is on a tertiary carbon and there is no strong base present, so the reaction follows the $S_{\rm N}1$ and E1 mechanisms. Substitution is usually the major product, but a significant amount of elimination product is also formed. According to Zaitsev's rule, the more highly substituted product should predominate among the alkenes.

$$Cl + CH_3CH_2OH$$
 EtOH OCH₂CH₃ + CH_3CH_2OH $EtOH$ $ETOH$

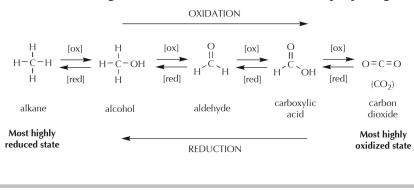
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Definitions

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- ☐ In reference to organic molecules, oxidation is a process by which a carbon atom gain bonds to more electronegative elements, most commonly oxygen
- ☐ Reduction is a process by which a carbon atom gain bonds to less electronegative elements, most commonly hydrogen



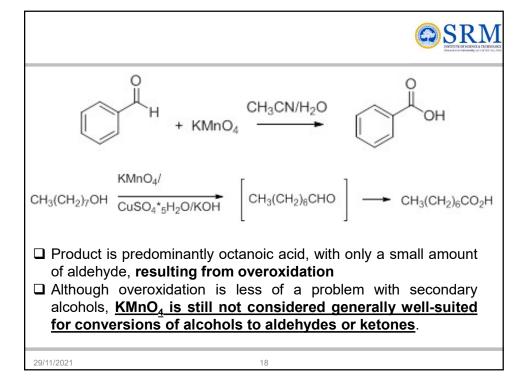
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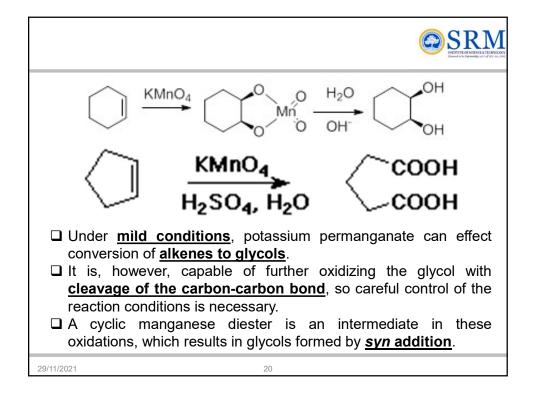
KMnO₄, potassium permanganate



- Manganese can function as oxidant when it is in +7 oxidation state. KMnO₄ is one such oxidant. It is a very strong oxidizing agent.
- ☐ KMnO₄ is used to oxidize primary alcohol and aldehyde to corresponding carboxylic acid
- □ Alkyl side chains on aromatic rings are oxidized to carboxylic acid group. This method is more generally applied to methyl group, however, longer side chains can also be cleaved



Oxidation of alcohols, $K_2Cr_2O_7$ $CH_3CH_2CH_2CH_2CH_2OH \text{ a primary alcohol} \qquad H_2CrO_4 \text{ ich}_3CH_2CH_2CH_2CH \text{ oxidation} \qquad CH_3CH_2CH_2CH_2CH \text{ a carboxylic acid}$ $CH_3-C-OH \text{ in aldehyde} \qquad CH_3-C-OH \text{ in a primary alcohol} \qquad Propanone$ $CH_3-C-OH \text{ in a primary alcohol} \qquad Propanone$





☐ Treatment of an alkylbenzene with potassium permanganate results in oxidation to give the benzoic acid

- ☐ The reaction only works if there is at least one hydrogen attached to the carbon. However, if there is at least one hydrogen, the oxidation proceeds all the way to the carboxylic acid.
- ☐ When no hydrogens are present on the benzylic carbon, no reaction occurs

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Reduction



Broadly speaking, reductions can be grouped into 2 mechanistic classes:

A. Catalytic hydrogenation

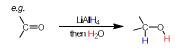
e.g.
$$\searrow = \zeta' \xrightarrow{H_2} \longrightarrow \zeta - \zeta'$$
Pd catalyst $\longrightarrow H H$

- g.

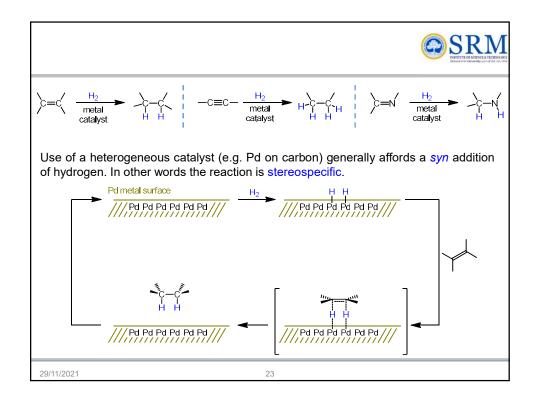
 pd catalyst

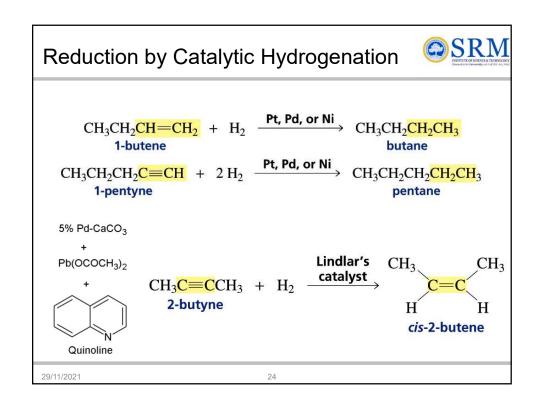
 nonpolar substrates
 usually gives syn addition

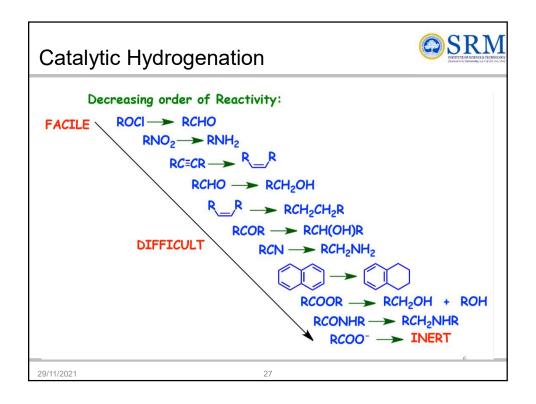
 storogeneous catalyst is used
- B. Nucleophilic reduction

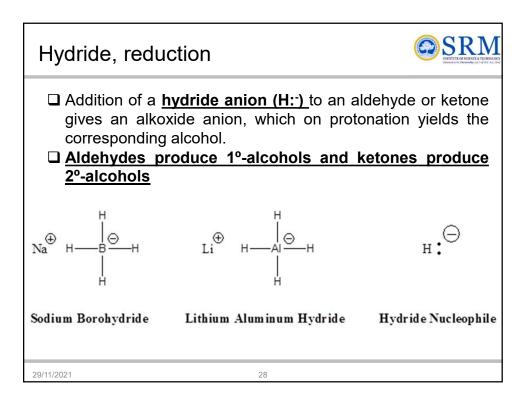


- requires а substrate, eg.
 - polarized
- usually <u>not stereospecific</u>









Reduction by Addition of a Hydride Ion and a Proton



- ☐ The most common sources of the hydride Nucleophile are lithium aluminium hydride (LiAlH₄) and sodium borohydride (NaBH₄).
- ☐ The hydride anion is not present during this reaction; rather, these reagents serve as a source of hydride due to the presence of a polar metal-hydrogen bond.
- □ Because aluminium is less electronegative than boron, the Al-H bond in LiAlH₄ is more polar, thereby, making LiAlH₄ a stronger reducing agent.
- □ Addition of a hydride anion (H:) to an aldehyde or ketone gives an alkoxide anion, which on protonation yields the corresponding alcohol. Aldehydes produce 1°-alcohols and ketones produce 2°-alcohols.

$$N_a^{\oplus}$$
 H \longrightarrow B \longrightarrow H \longrightarrow Li $^{\oplus}$ H \longrightarrow H \longrightarrow H \longrightarrow

Sodium Borohydride Lithium Aluminum Hydride Hydride Nucleophile

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Mechanism - Reduction



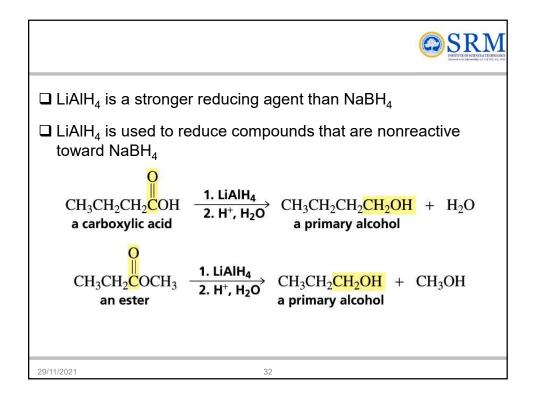
This mechanism is for a LiAlH₄ reduction. The mechanism for a NaBH₄ reduction is the same except methanol is the proton source used in the second step.

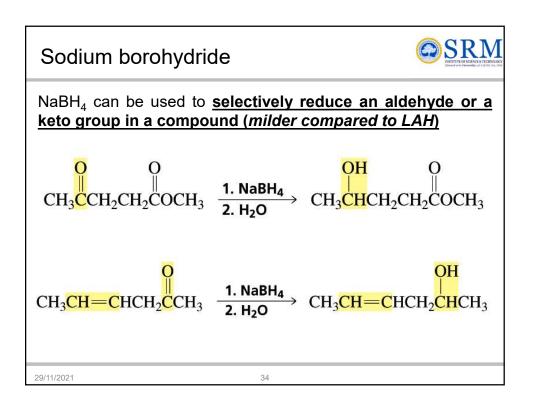
1) Nucleopilic attack by the hydride anion

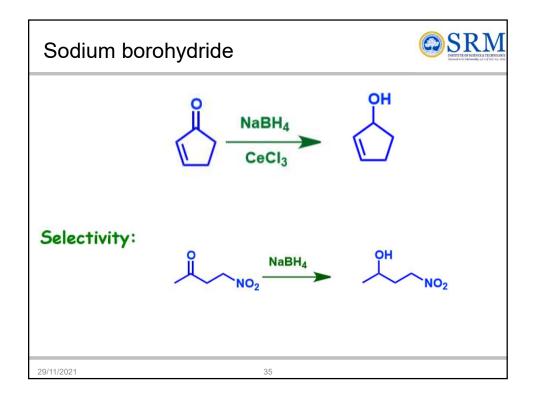
2) The alkoxide is protonated

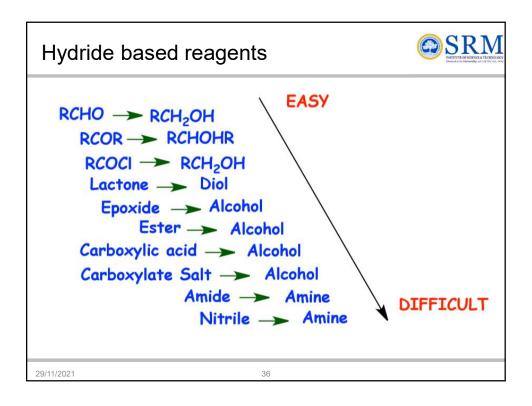
In simple terms....

Change the CO Double Bond To a Single B ond Add an H to the Carbon and an H to the Oxygen



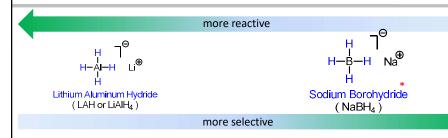






Hydride based reagents, summary





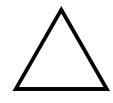
- LiAlH₄ will reduce almost anything: aldehydes, ketones, alcohols and esters (to provide the corresponding alcohols), nitriles (to 1° amines), and even under forcing conditions carboxylic acids! These reagents can even reduce alkyl tosylates!!
- NaBH₄ will only reduce more reactive species: aldehydes, ketones, imines, etc.
- NaBH₄ is compatible with water (and therefore other alcohols) whereas LiAlH₄ will catch fire if exposed to water!

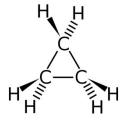
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Examples, (not) common



$$\begin{array}{ccccc} \text{CH}_3\text{CH}_2\text{CH}=\text{CH}_2 & + & \text{H}_2 & \xrightarrow{\text{Pt, Pd, or Ni}} & \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3 \\ & & \text{butane} & & \text{butane} \end{array}$$



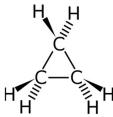


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Cyclopropane



- ☐ Cyclopropane has a <u>triangular planar structure</u> due to which, the bond angles between carboncarbon bonds are **expected to be 60°**
- ☐ This is far less than the thermodynamically stable angle of 109.5° as per the sp³ hybridisation of the carbon atoms. Due to this there is a considerable amount of ring strain in the cyclopropane molecule



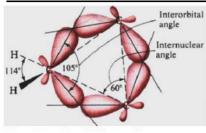
- ☐ In addition to this angular strain, cyclopropane also suffers additional torsional-strain
- ☐ The torsional strain is due to the coplanar arrangement of the carbon atoms wherein leading to the eclipsed arrangement of the C- H bonds

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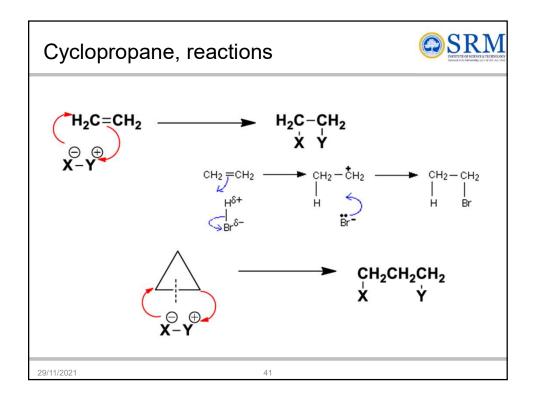
Cyclopropane

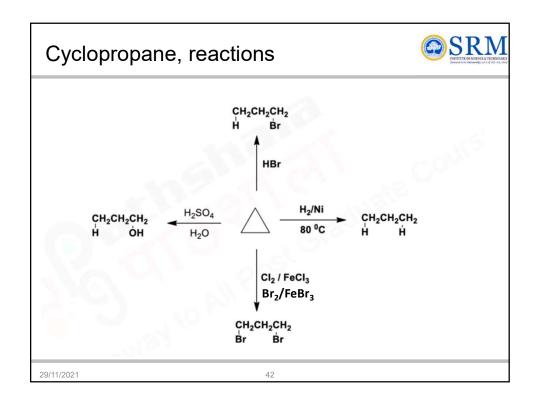


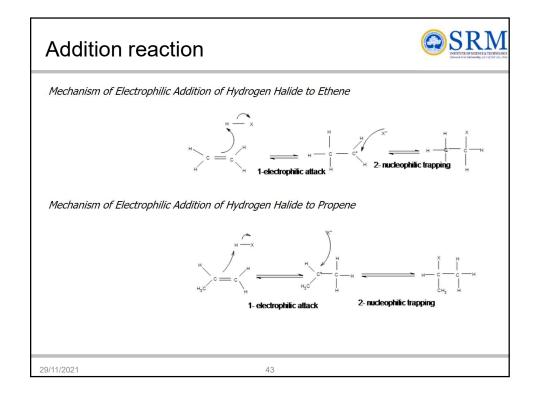
- □ It has been suggested that significant re-hybridization occurs in cyclopropane and bonding between the carbon centres occurs in terms of 'bent' bonds (Coulson-Moffitt model) wherein the carbon-carbon bonds are bent outwards so that the inter-orbital angle is 104° which consequently reduces the level of bond strain
- \square So it is <u>intermediate between σ and π bonding</u>. These bonds are also sometimes called "banana bonds"

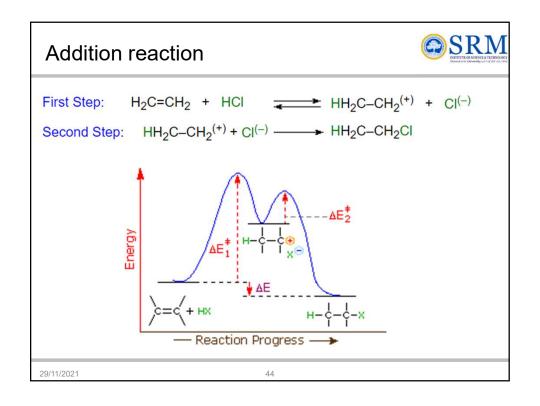












Addition reaction



All alkenes undergo addition reactions with the hydrogen halides. A <u>hydrogen atom joins to one of the carbon atoms</u> <u>originally in the double bond, and a halogen atom to the other.</u>

For example, with ethene and hydrogen chloride, you get chloroethane:

With but-2-ene you get 2-chlorobutane:

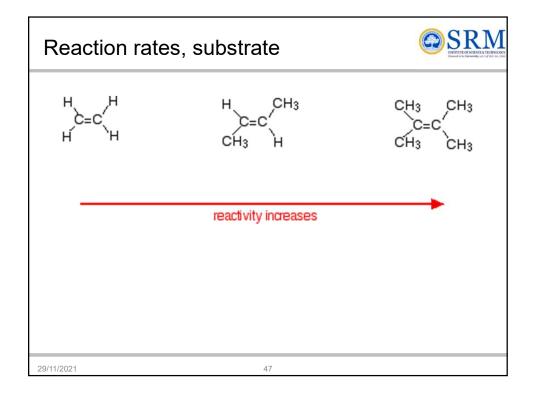
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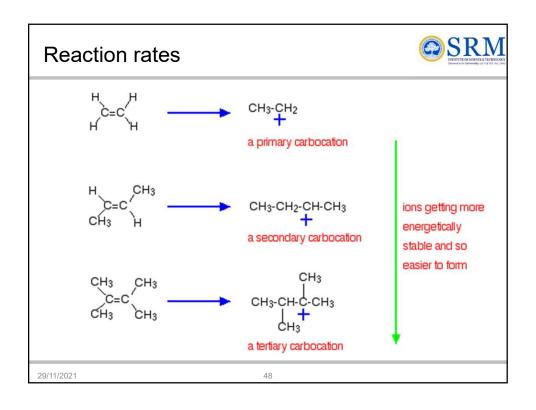
Reaction rates

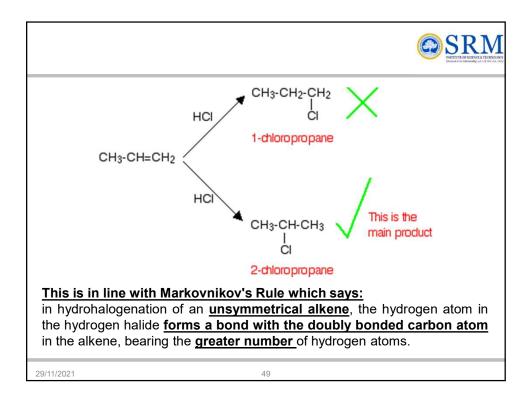


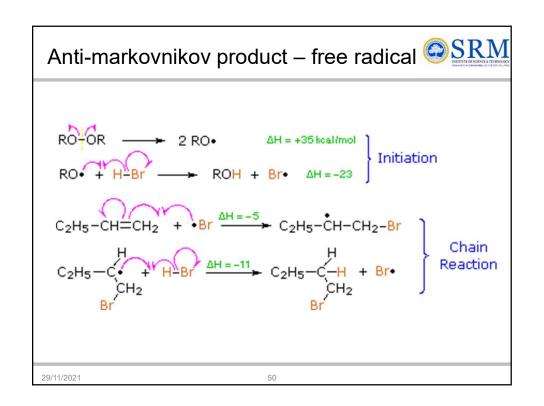
- ☐ Variation of rates when you **change the halogen?**
- Reaction rates increase in the order <u>HF HCI HBr HI</u>. Hydrogen fluoride <u>reacts much more slowly</u> than the other three, and is normally ignored in talking about these reactions.
- ☐ When the hydrogen halides react with alkenes, the hydrogen-halogen bond has to be broken.
- ☐ The bond strength falls as you go from HF to HI, and the hydrogen-fluorine bond is particularly strong. Because it is difficult to break the bond between the hydrogen and the fluorine, the addition of HF is bound to be slow.

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C-C bond formation, reaction

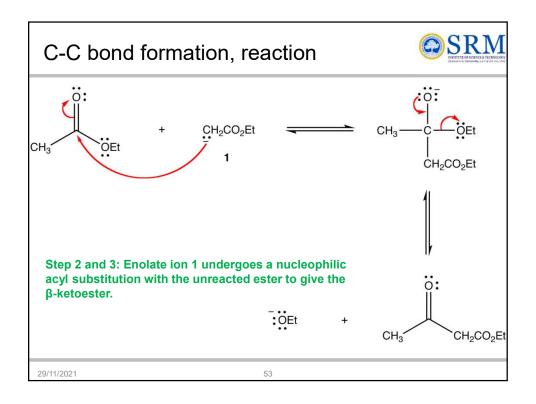


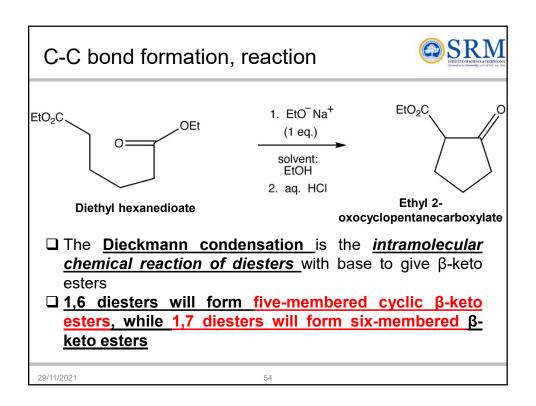
- The Claisen condensation is a <u>carbon-carbon bond forming reaction that occurs between two esters or one ester and another carbonyl compound in the presence of a strong base, resulting in a β-keto ester or a β-diketone.</u>
- □ At least one of the reagents <u>must be enolizable (have an α-proton</u> and <u>be able to undergo deprotonation</u> to form the enolate anion).
- ☐ The base used must not interfere with the reaction by undergoing nucleophilic substitution or addition with a carbonyl carbon.

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C-C bond formation, reaction

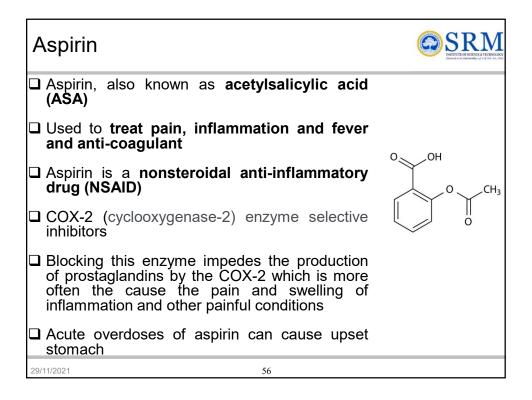


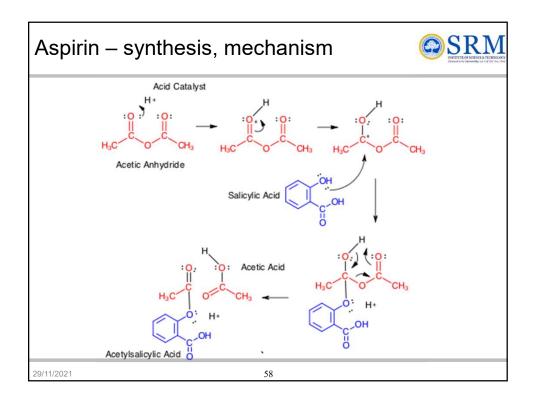




C-C bond formation, reaction

$$CH_2 - C - OC_2H_5$$





Paracetamol



- □ Paracetamol, also known acetaminophen N-acetyl-paraor aminophenol or APAP
- ☐ Used to treat pain and fever
- ☐ Paracetamol is classified as a mild analgesic, part of the class of drugs known as "aniline analgesics"
- ☐ Acute overdoses of paracetamol can cause potentially fatal liver damage
- ☐ Paracetamol is lethal to snakes, and has been suggested as a chemical control program

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Paracetamol – synthesis, boots method SRM



Paracetamol – synthesis, boots method SRM



ethanoic anhydride

paracetamol ethanoic acid

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Thank you all for your attention

Information presented here were collected from various sources textbooks, articles, manuscripts, internet and newsletters. All the researchers and authors of the above mentioned sources are greatly acknowledged.

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