

9

Organic Chemistry

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Christopher S.
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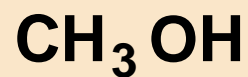
Alcohols and Thiols

Chapter 9

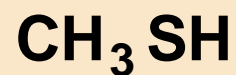
9-2

9 Structure

u In this chapter we study alcohols and thiols



Methanol
(an alcohol)



Methanethiol
(a thiol)

9 Structure - Alcohols

- u The functional group of an alcohol is an -OH group bonded to an sp^3 hybridized carbon
 - bond angles about the hydroxyl oxygen atom are approximately 109.5°
- u Oxygen is sp^3 hybridized
 - two sp^3 hybrid orbitals form sigma bonds to carbon and hydrogen
 - the remaining two sp^3 hybrid orbitals each contain an unshared pair of electrons

9 Structure - Thiols

- u The functional group of a thiol is an -SH (sulfhydryl) group bonded to an sp^3 hybridized carbon
- u The bond angle about sulfur in methanethiol is 100.3° , which indicates that there is considerably more p character to the bonding orbitals of divalent sulfur than there is to oxygen

9 Nomenclature-Alcohols

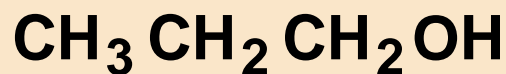
u IUPAC names

- the longest chain that contains the -OH group is taken as the parent.
- the parent chain is numbered to give the -OH group the lowest possible number
- the suffix **-e** is changed to **-ol**

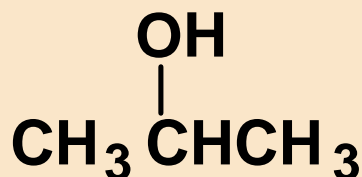
u Common names

- the alkyl group bonded to oxygen is named followed by the word **alcohol**

9 Nomenclature-Alcohols



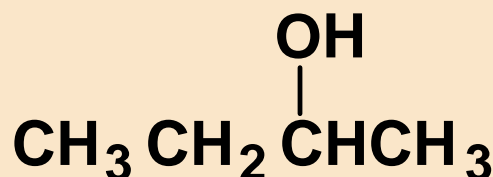
1-Propanol
(Propyl alcohol)



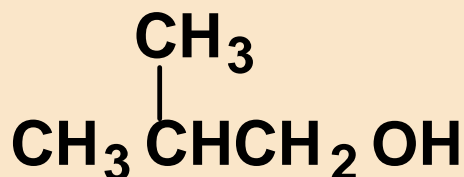
2-Propanol
(Isopropyl alcohol)



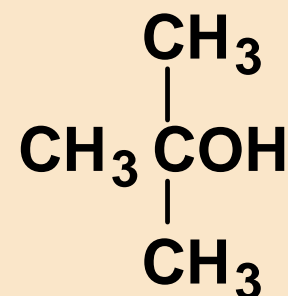
1-Butanol
(Butyl alcohol)



2-Butanol
(sec-Butyl alcohol)



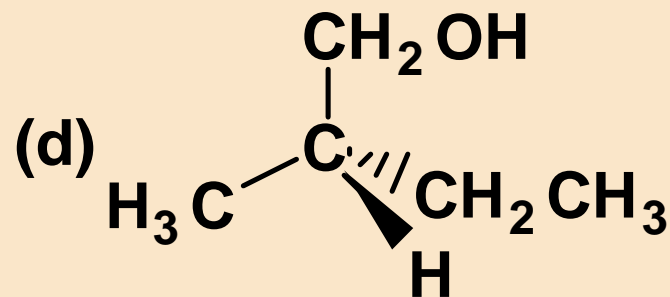
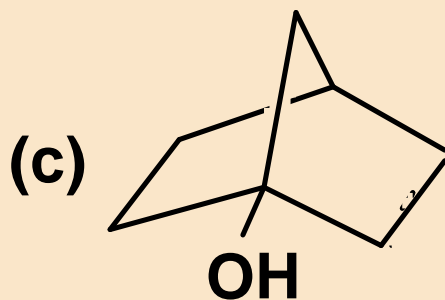
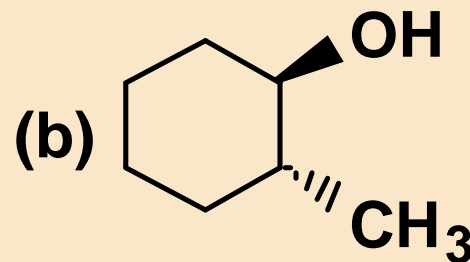
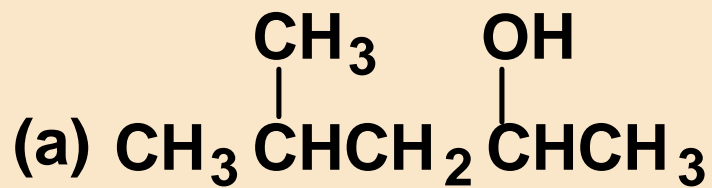
2-Methyl-1-propanol
(Isobutyl alcohol)



2-Methyl-2-propanol
(tert-Butyl alcohol)

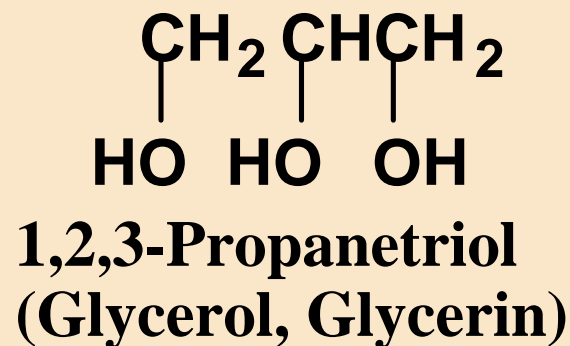
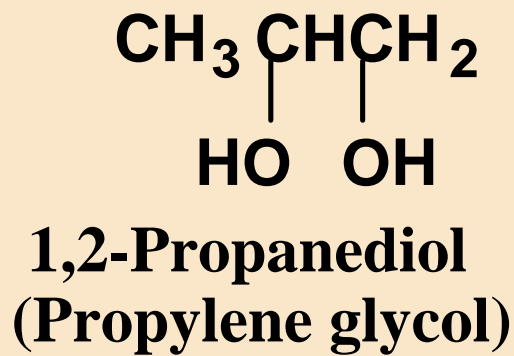
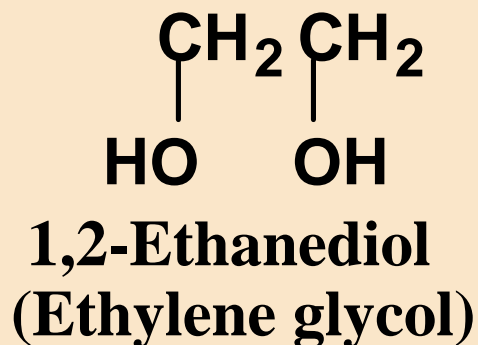
9 Nomenclature of Alcohols

u **Problem:** Write IUPAC names for these alcohols



9 Nomenclature of Alcohols

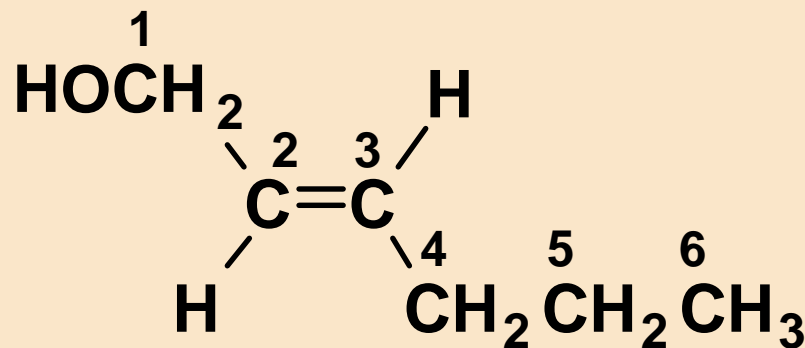
- u Compounds containing more than one -OH group are named diols, triols, etc.



9 Nomenclature of Alcohols

u Unsaturated alcohols-

- the double bond is shown by the infix **-en-**
- the hydroxyl group is shown by the suffix **-ol**
- number the chain to give OH the lower number



(E)-2-Hexene-1-ol
(trans-2-Hexen-1-ol)

9 Nomenclature-Thiols

u IUPAC names:

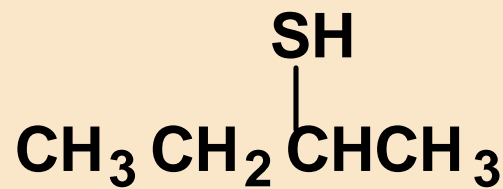
- the parent is the longest chain that contains the -SH group
- change the suffix **-e** to **-thiol**

u Common names:

- name the alkyl group bonded to sulfur followed by the word **mercaptan**



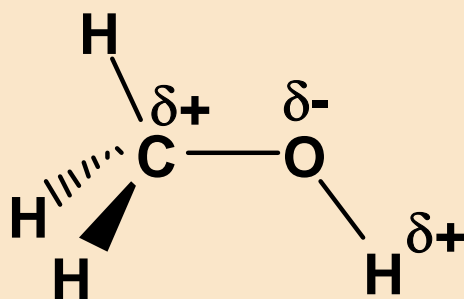
1-Butanethiol
(Butyl mercaptan)



2-Butanethiol
(sec-Butyl mercaptan)

9 Physical Properties

u Alcohols are polar compounds



u They interact with themselves and with other polar compounds by dipole-dipole interactions

u **Dipole-dipole interaction:** the attraction between the positive end of one dipole and the negative end of another

9 Physical Properties

- u **Hydrogen bonding:** when the positive end of one dipole is an H bonded to F, O, or N (atoms of high electronegativity) and the other end is F, O, or N
- u The strength of hydrogen bonding in water is approximately 5 kcal/mol
- u Hydrogen bonds are considerably weaker than covalent bonds
- u Nonetheless, they can have a significant effect on physical properties

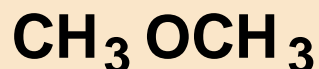
9 Physical Properties

- u Ethanol and dimethyl ether are constitutional isomers.
- u Their boiling points are dramatically different
 - ethanol forms intermolecular hydrogen bonds which increases attractive forces between its molecules, which results in a higher boiling point



Ethanol

bp 78°C



Dimethyl ether

bp -24°C

9 Physical Properties

- u In relation to alkanes of comparable size and molecular weight, alcohols
 - have higher boiling points
 - are more soluble in water

- u The presence of additional -OH groups in a molecule further increases solubility in water and boiling point

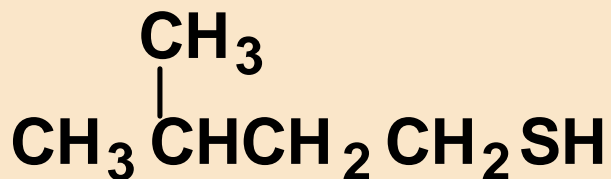
9 Physical Properties

Formula	Name	MW	bp (°C)	Solubility in Water
CH_3OH	methanol	32	65	infinite
CH_3CH_3	ethane	30	-89	insoluble
$\text{CH}_3\text{CH}_2\text{OH}$	ethanol	46	78	infinite
$\text{CH}_3\text{CH}_2\text{CH}_3$	propane	44	-42	insoluble
$\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$	1-propanol	60	97	infinite
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3$	butane	58	0	insoluble
$\text{HO}(\text{CH}_2)_4\text{OH}$	1,4-butanediol	90	230	infinite
$\text{CH}_3(\text{CH}_2)_4\text{OH}$	1-pentanol	88	138	2.3 g/100 g
$\text{CH}_3(\text{CH}_2)_4\text{CH}_3$	hexane	86	69	insoluble

9 Physical Properties Thiols

u Low-molecular-weight thiols - STENCH

- the scent of skunks is due primarily to these two thiols



3-Methyl-1-butanethiol



2-Butene-1-thiol

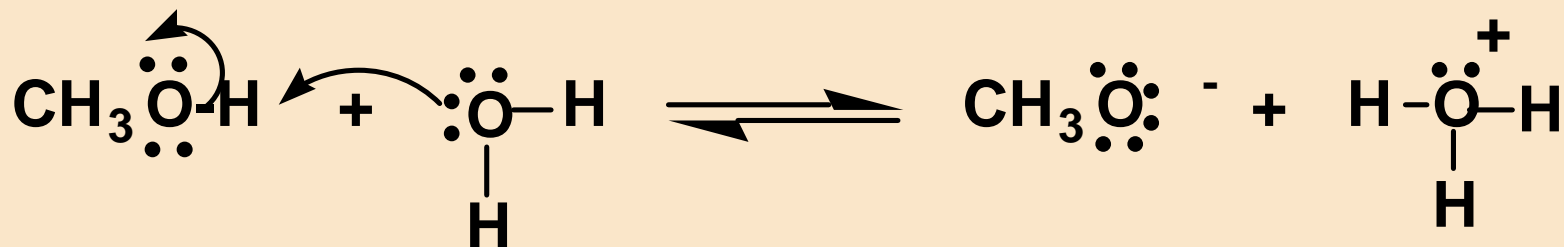
9 Physical Properties-Thiols

- u The difference in electronegativity between S (2.5) and H (2.1) is 0.4. Because of the low polarity of the S-H bond, thiols
- show little association by hydrogen bonding
 - have lower boiling points and are less soluble in water than alcohols of comparable MW

Thiol	bp (°C)	Alcohol	bp (°C)
methanethiol	6	methanol	65
ethanethiol	35	ethanol	78
1-butanethiol	98	1-butanol	117

9 Acidity of Alcohols

u In dilute aqueous solution, alcohols are weakly acidic



$$K_a = \frac{[\text{CH}_3\text{O}^-][\text{H}_3\text{O}^+]}{[\text{CH}_3\text{OH}]} = 15.5$$

9 Acidity of Alcohols

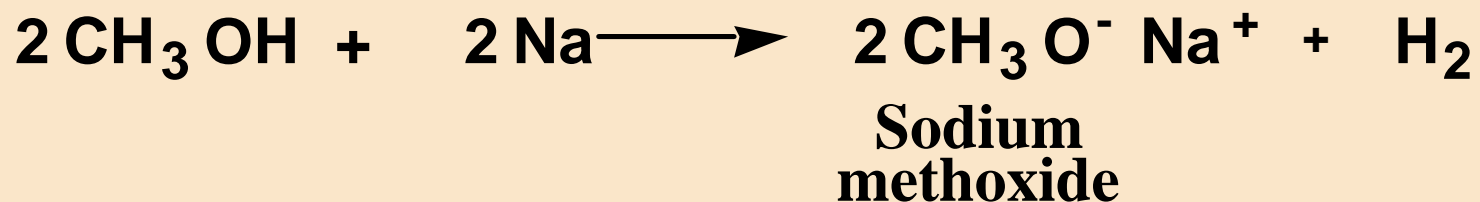
Compound	Formula	pK _a	
hydrogen chloride	HCl	-7	Stronger acid
acetic acid	CH ₃ CO ₂ H	4.8	
methanol	CH ₃ OH	15.5	
water	H ₂ O	15.7	
ethanol	CH ₃ CH ₂ OH	15.9	
2-propanol	(CH ₃) ₂ CHOH	17	
2-methyl-2-propanol	(CH ₃) ₃ COH	18	Weaker acid

9 Acidity of Alcohols

- u **Acidity depends primarily on the degree of stabilization and solvation of the alkoxide ion**
 - **the negatively charged oxygens of methanol and ethanol are about as accessible as hydroxide ion for solvation. These alcohol are about as acidic as water.**
 - **as the bulk of the alkyl group increases, the ability of water to solvate the alkoxide decreases and the acidity of the alcohol decreases**

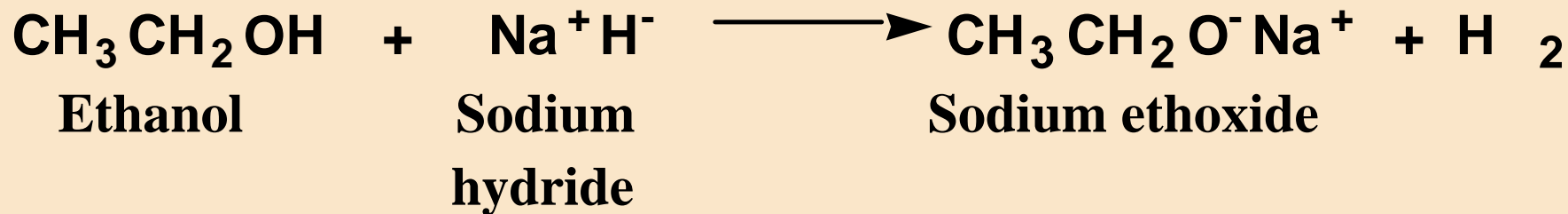
9 Reaction with Metals

- u Alcohols react with Li, Na, K, and other active metals to liberate hydrogen gas and form metal alkoxides



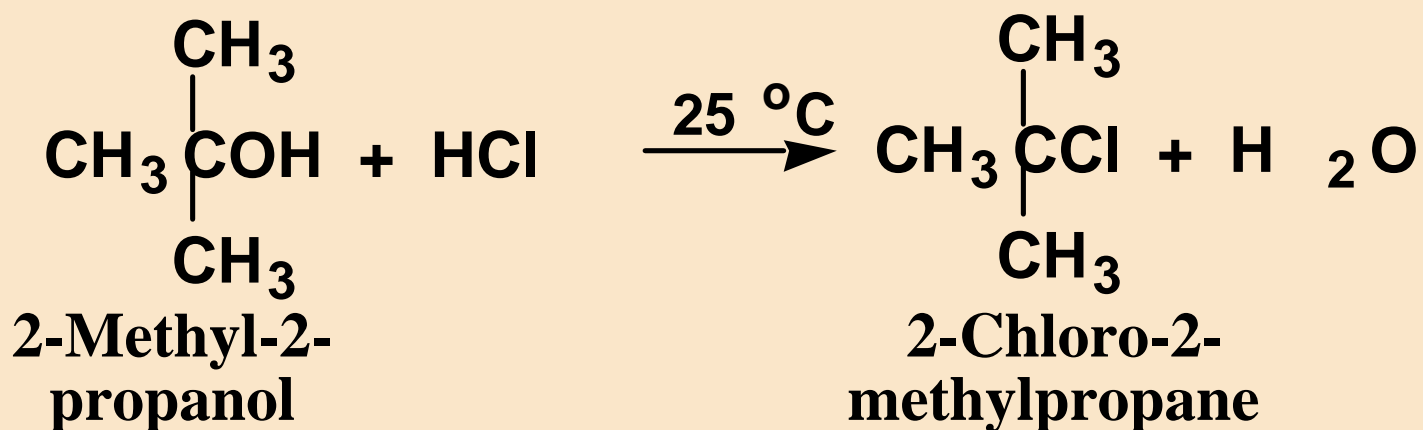
9 Reaction with NaH

- u Alcohols are also converted to metal salts by reaction with bases stronger than the alkoxide ion. One such base is sodium hydride



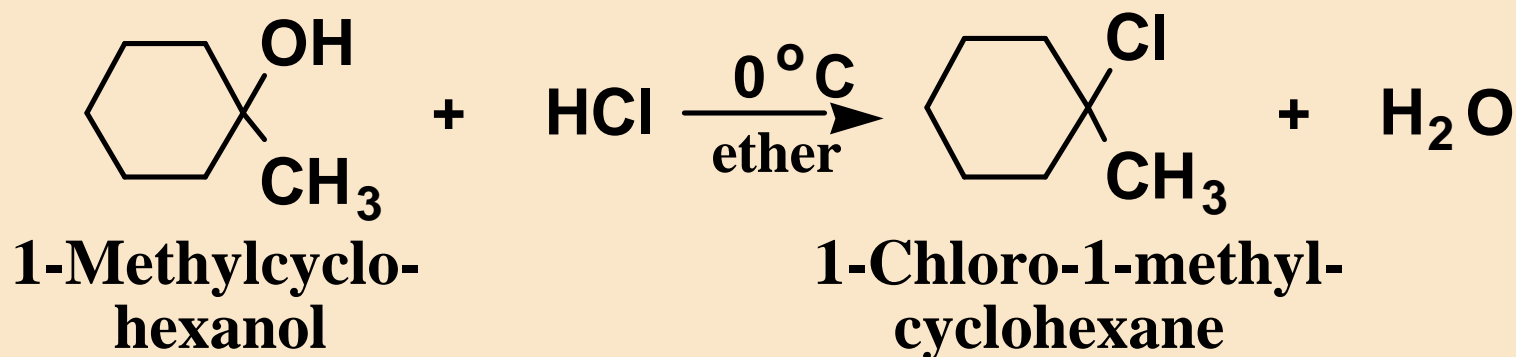
9 Reaction with HX

- u 3° Alcohols react very rapidly with HCl, HBr, and HI. Low-molecular-weight 1° and 2° alcohols are unreactive under these conditions



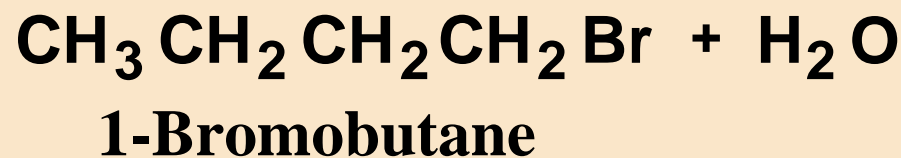
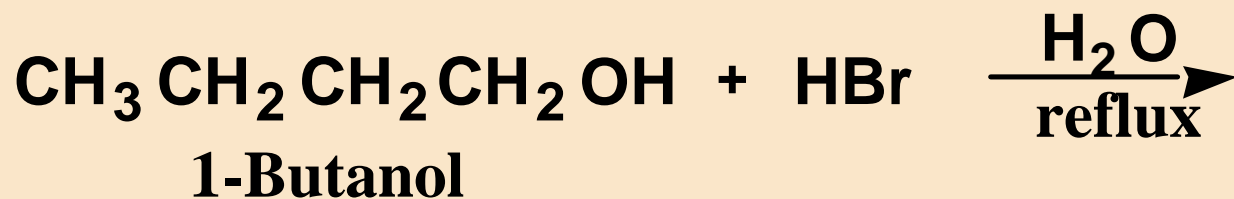
9 Reaction with HX

- u Water-insoluble 3° alcohols react by bubbling gaseous HX through a solution of the alcohol dissolved in diethyl ether or THF



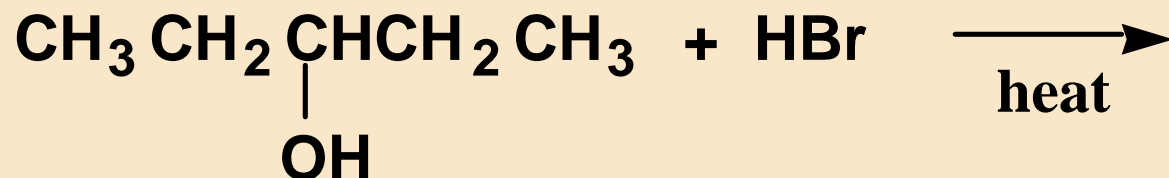
9 Reaction with HX

- u 1° and 2° alcohols require concentrated HBr and HI to form alkyl bromides and iodides

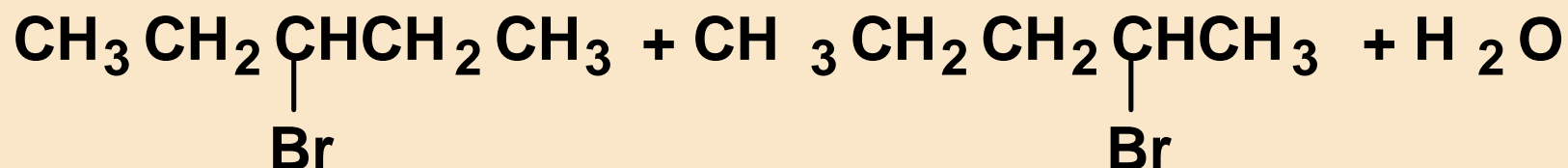


9 Reaction with HX

u With HBr and HI, 2° alcohols generally give some rearrangement



3-Pentanol

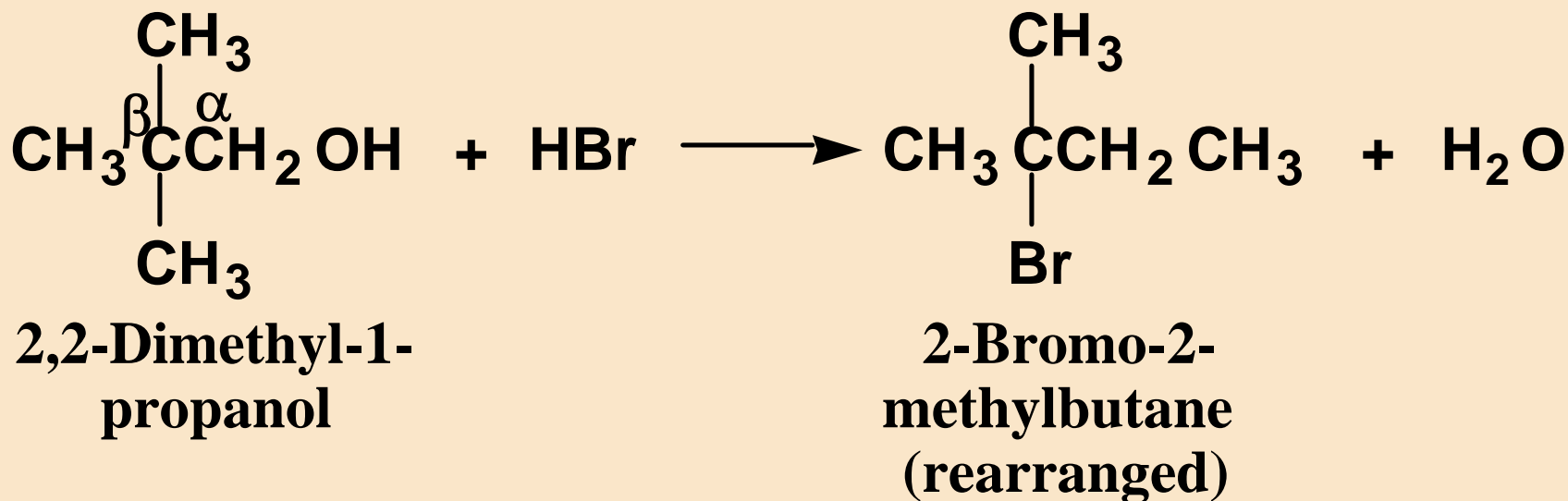


3-Bromopentane
(major product)

2-Bromopentane

9 Reaction with HX

- u 1° alcohols with extensive β -branching give large amounts of rearranged product



9 Reaction with HX

u Based on

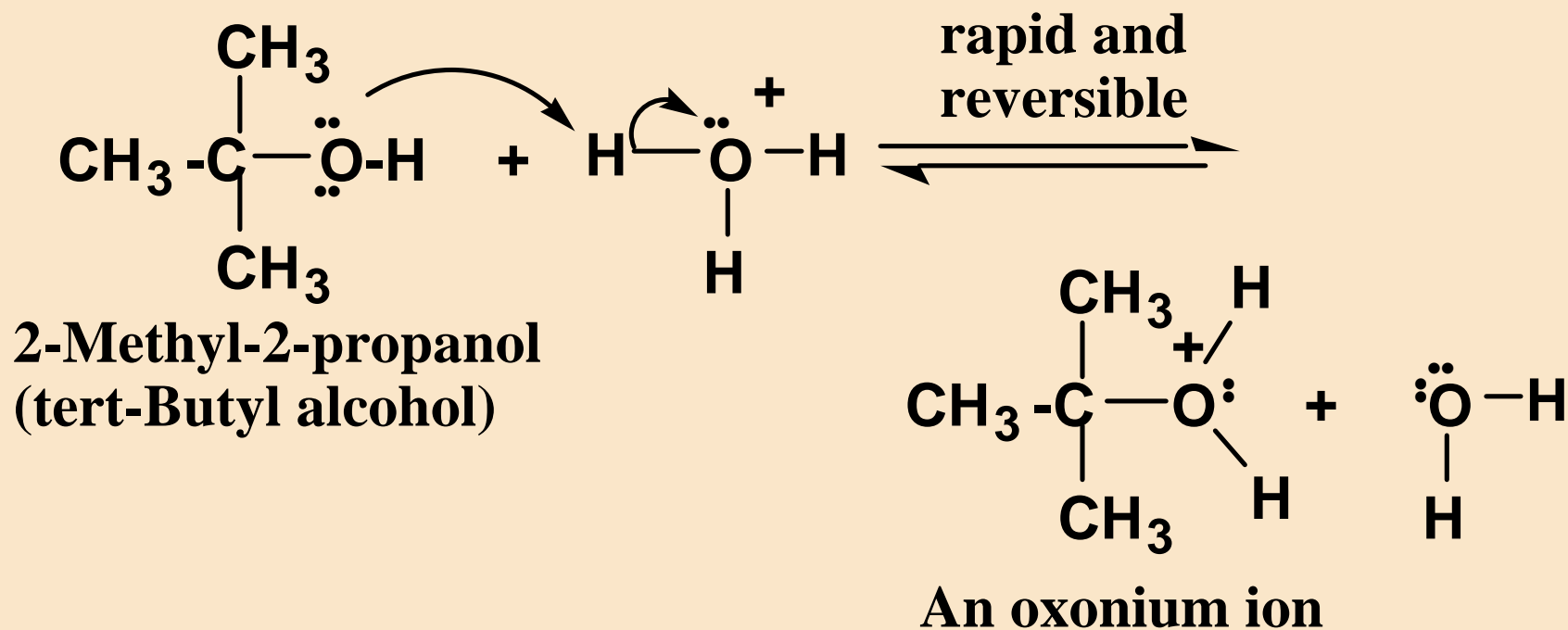
- the relative ease of reaction of alcohols with HX ($3^\circ > 2^\circ > 1^\circ$) and
- the occurrence of rearrangements,

u chemists propose that reaction of 2° and 3° alcohols with HX

- occurs by an S_N1 mechanism, and
- involves a carbocation intermediate

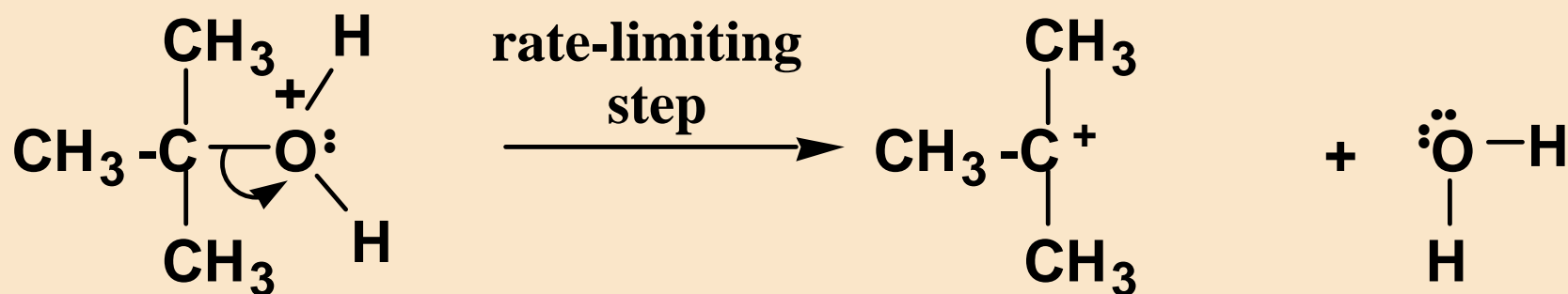
9 Reaction with HX - S_N1

Step 1: rapid, reversible proton transfer to the OH group



9 Reaction with HX - S_N1

Step 2: loss of H₂O to give a carbocation intermediate



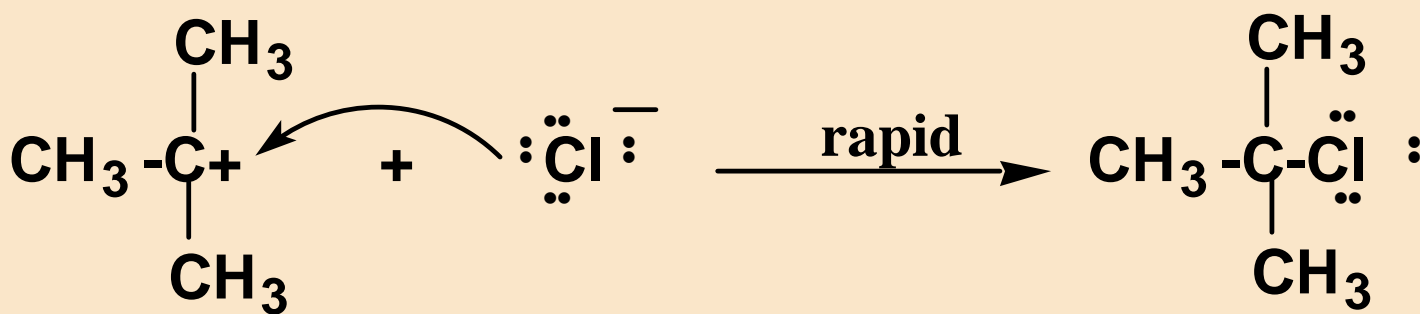
An oxonium ion

A 3° carbocation
intermediate

- the role of the acid is to transform OH, a poor leaving group, into HOH, a good leaving group

9 Reaction with HX - S_N1

Step 3: reaction of the carbocation intermediate (a Lewis acid) with halide ion (a Lewis base)

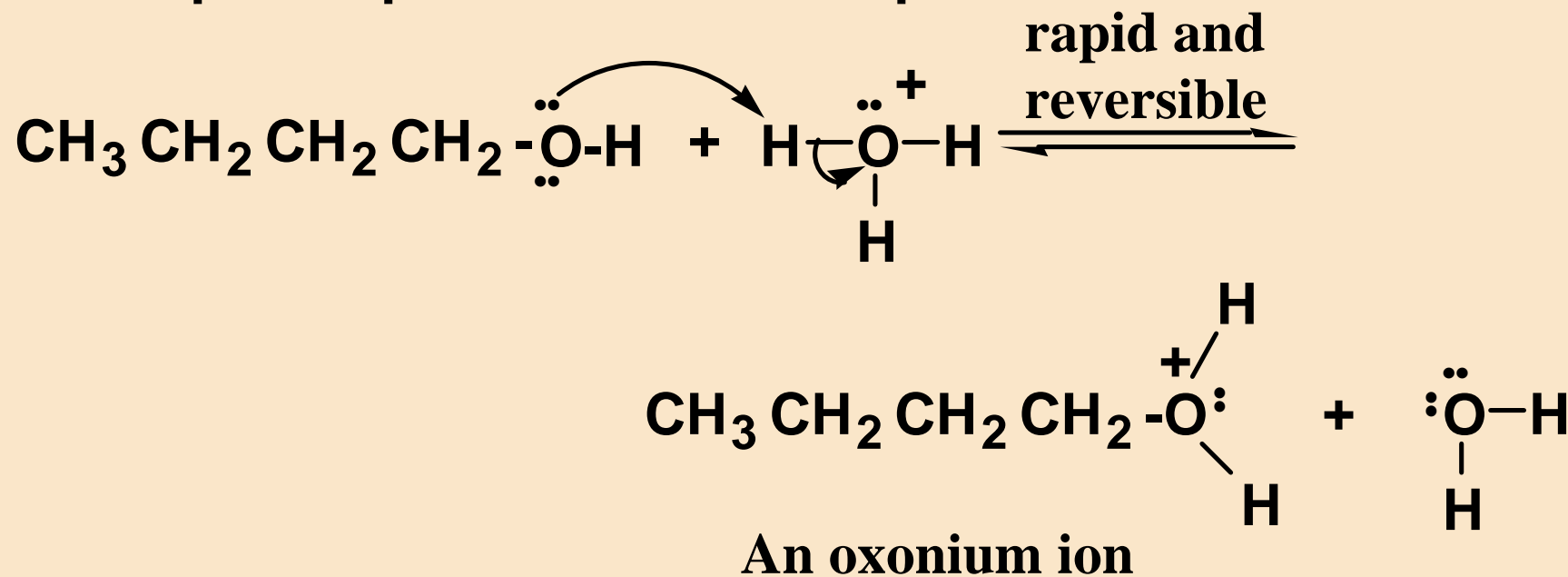


2-Chloro-2-methylpropane
(tert-Butyl chloride)

9 Reaction with HX - S_N2

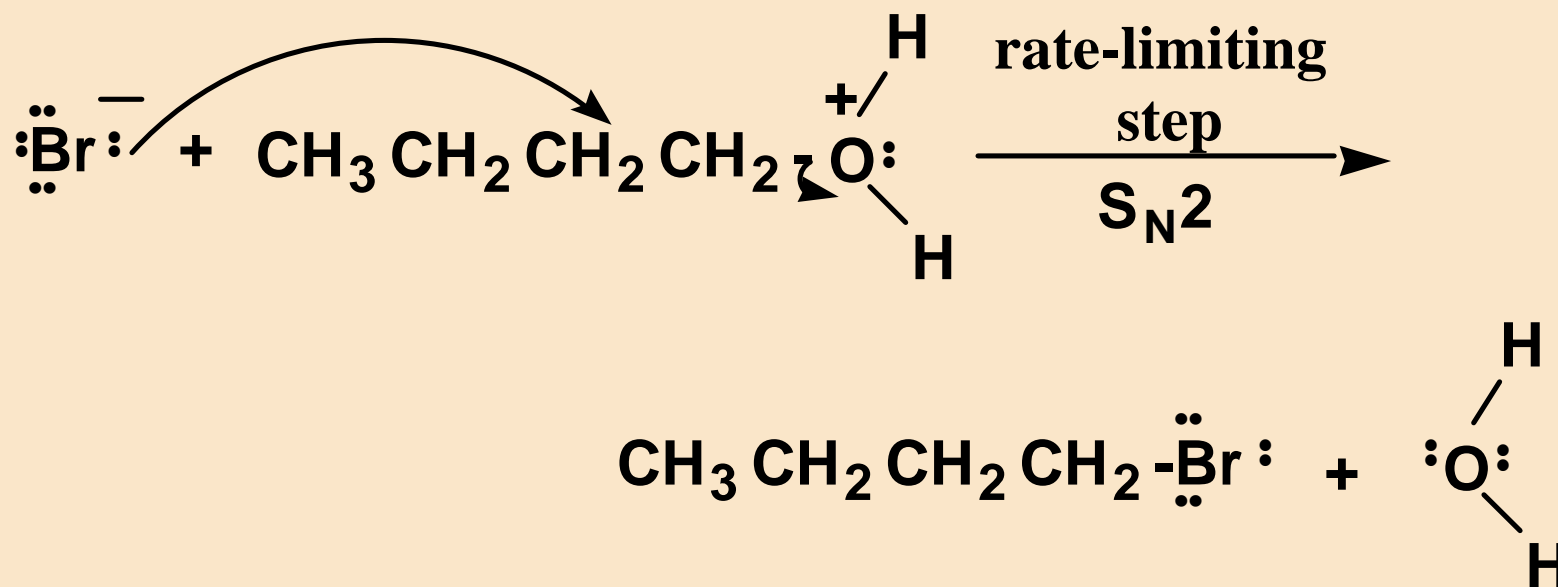
u 1° alcohols react with HX by an S_N2 mechanism

Step 1: rapid and reversible proton transfer



9 Reaction with HX - S_N2

Step 2: displacement of HOH by halide ion

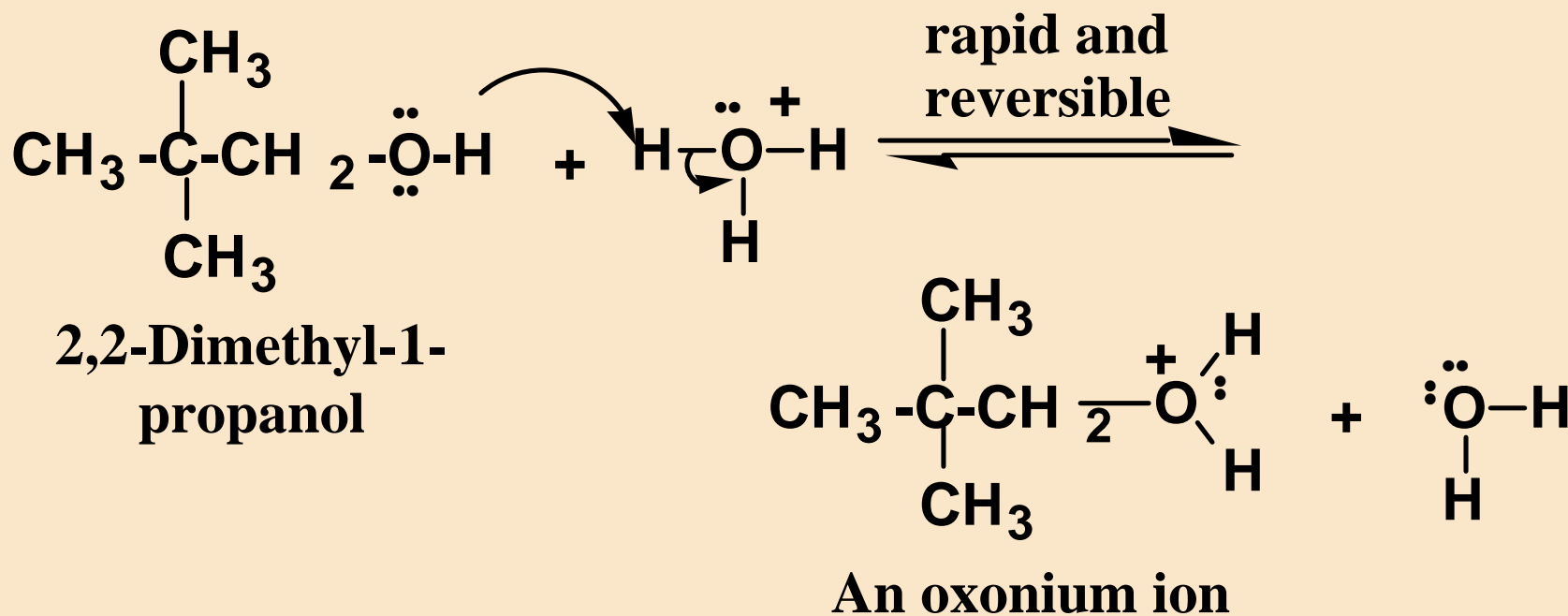


9 Reaction with HX-Rearr

- u For 1° alcohols with extensive β -branching
 - S_N1 not possible because this pathway would require a 1° carbocation
 - S_N2 not possible because of steric hindrance created by the β -branching
- u These alcohols react by a concerted loss of HOH and migration of an alkyl group

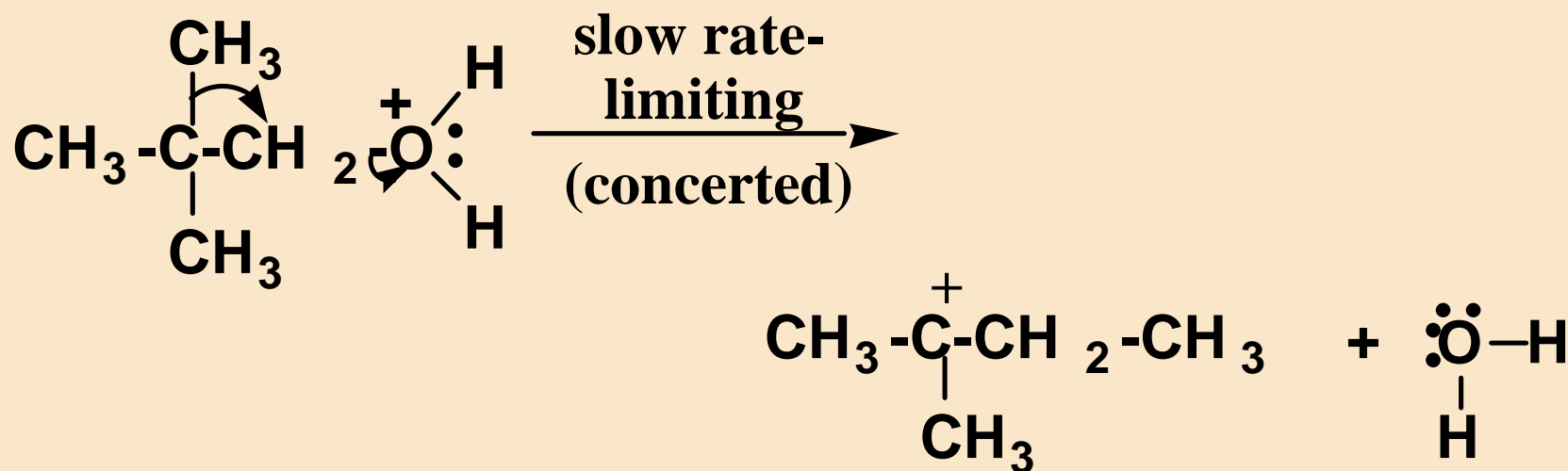
9 Reaction with HX-Rearr

Step 1: proton transfer to form an oxonium ion



9 Reaction with HX-Rearr

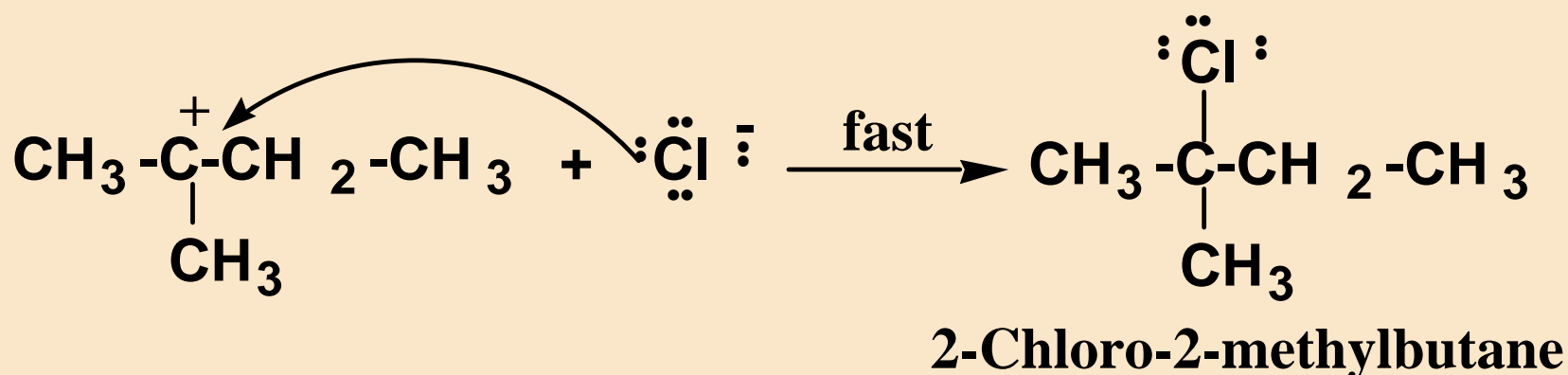
Step 2: concerted elimination of HOH and migration of a methyl group to give a 3° carbocation



A 3° carbocation
intermediate

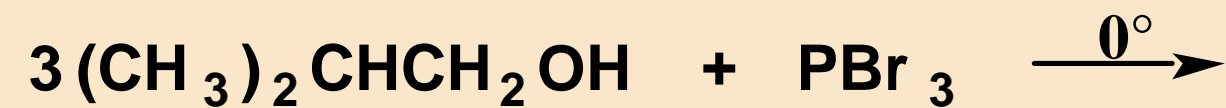
9 Reaction with HX-Rearr

Step 3: reaction of the carbocation intermediate (a Lewis acid) with halide ion (a Lewis base)



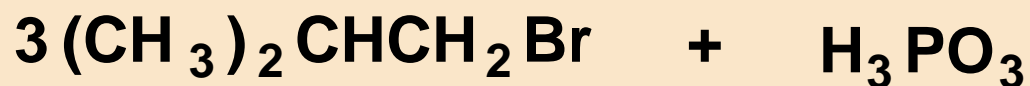
9 Reaction with PBr_3

- u An alternative method for the synthesis of 1° and 2° alkyl bromides is reaction of an alcohol with phosphorus tribromide
 - gives less rearrangement than with HBr



2-Methyl-1-propanol
(Isobutyl alcohol)

Phosphorus
tribromide

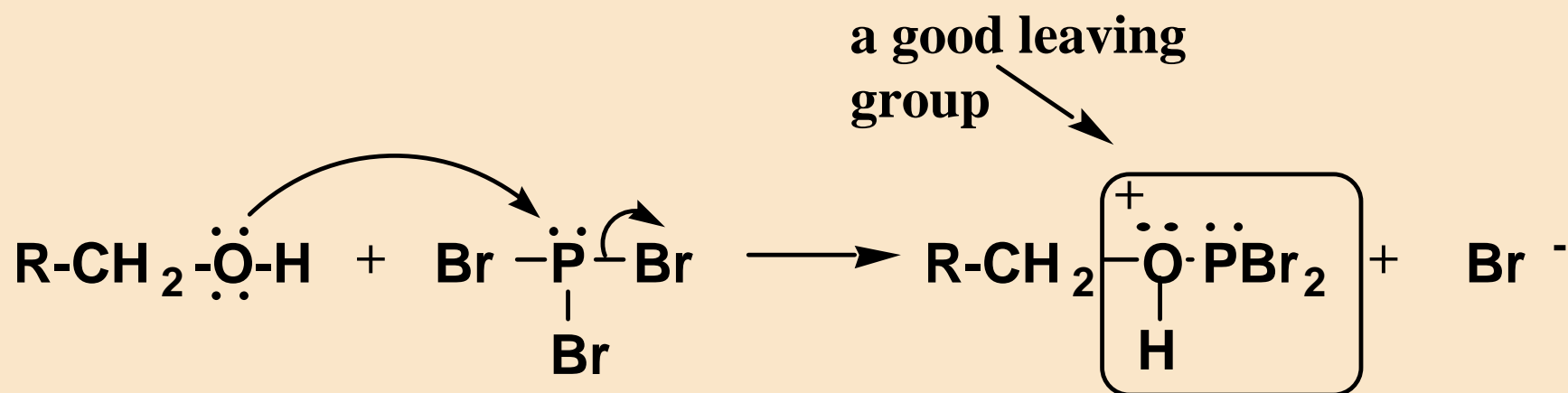


1-Bromo-2-methylpropane
(Isobutyl bromide)

Phosphorous
acid

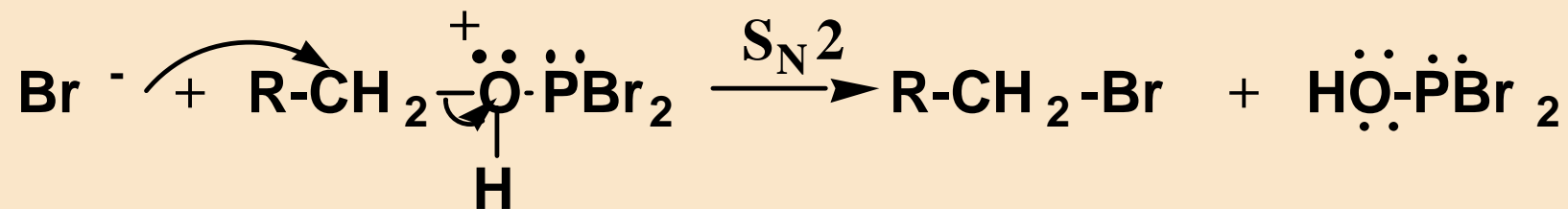
9 Reaction with PBr_3

Step 1: formation of an protonated dibromophosphite, which converts OH, a poor leaving group, to a good leaving group



9 Reaction with PBr_3

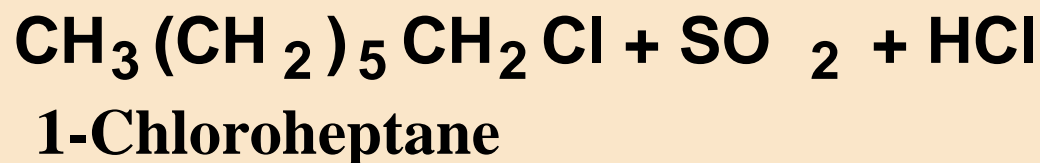
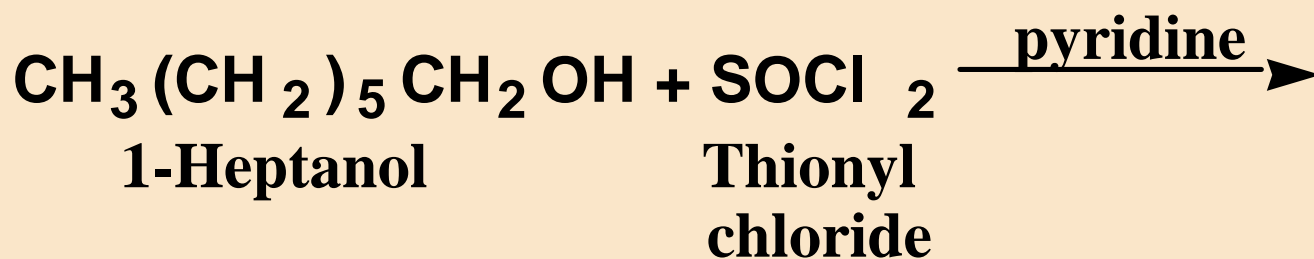
Step 2: displacement of the leaving group by bromide ion



9 Reaction with SOCl_2

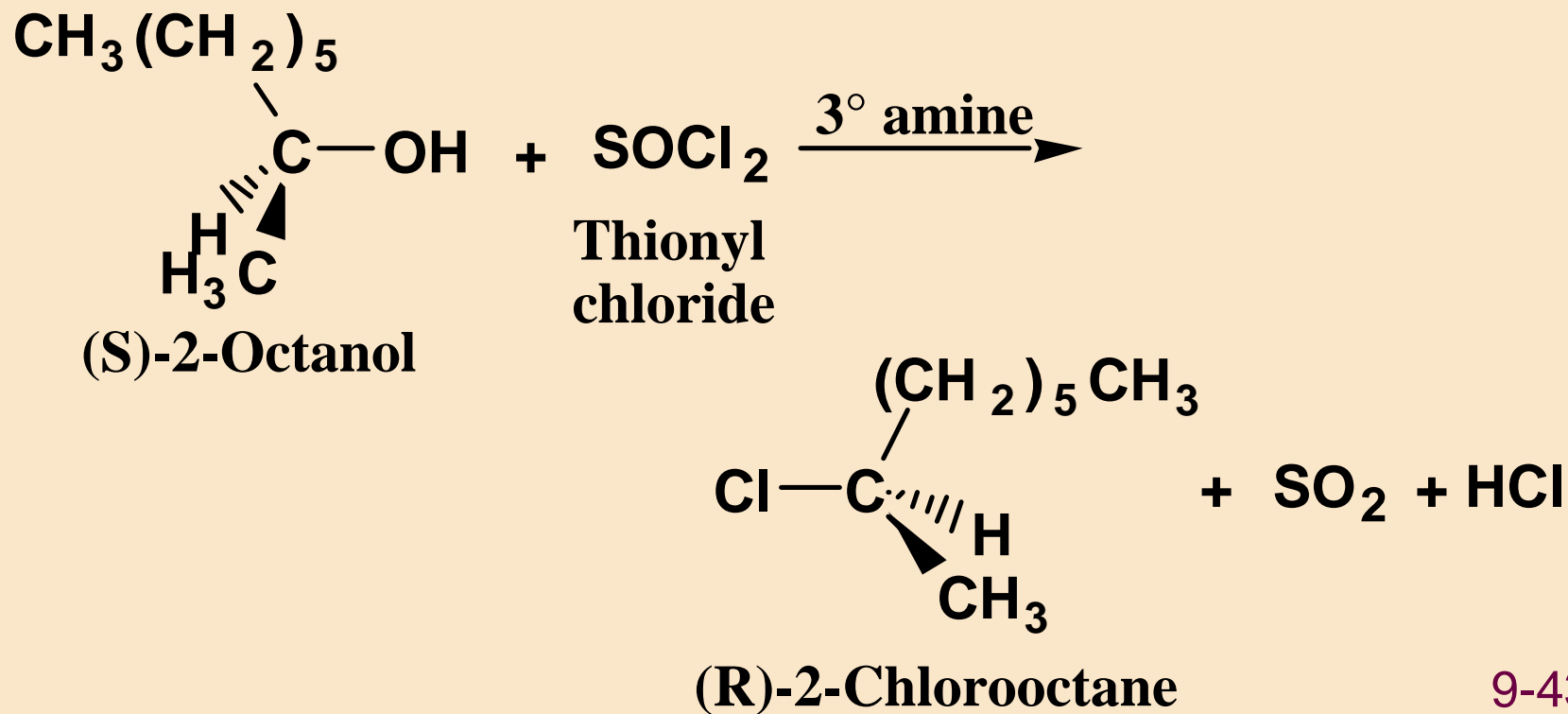
u Thionyl chloride is the most widely used reagent for the conversion of 1° and 2° alcohols to alkyl chlorides

- a base, most commonly pyridine or triethylamine, is added to neutralize the HCl



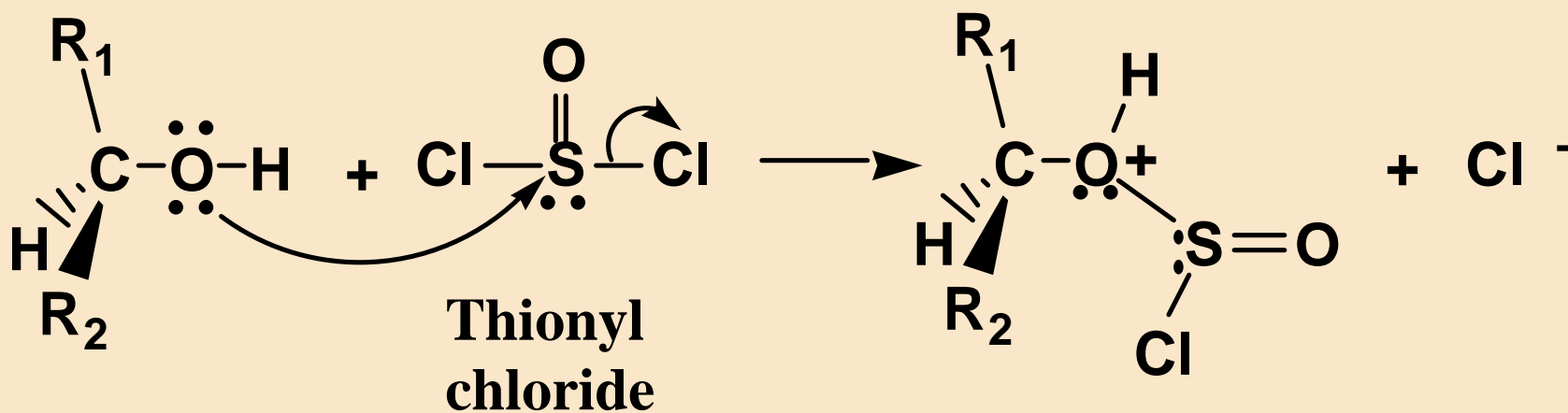
9 Reaction with SOCl_2

- u Reaction of an alcohol with SOCl_2 in the presence of a 3° amine is stereoselective; proceeds with inversion of configuration



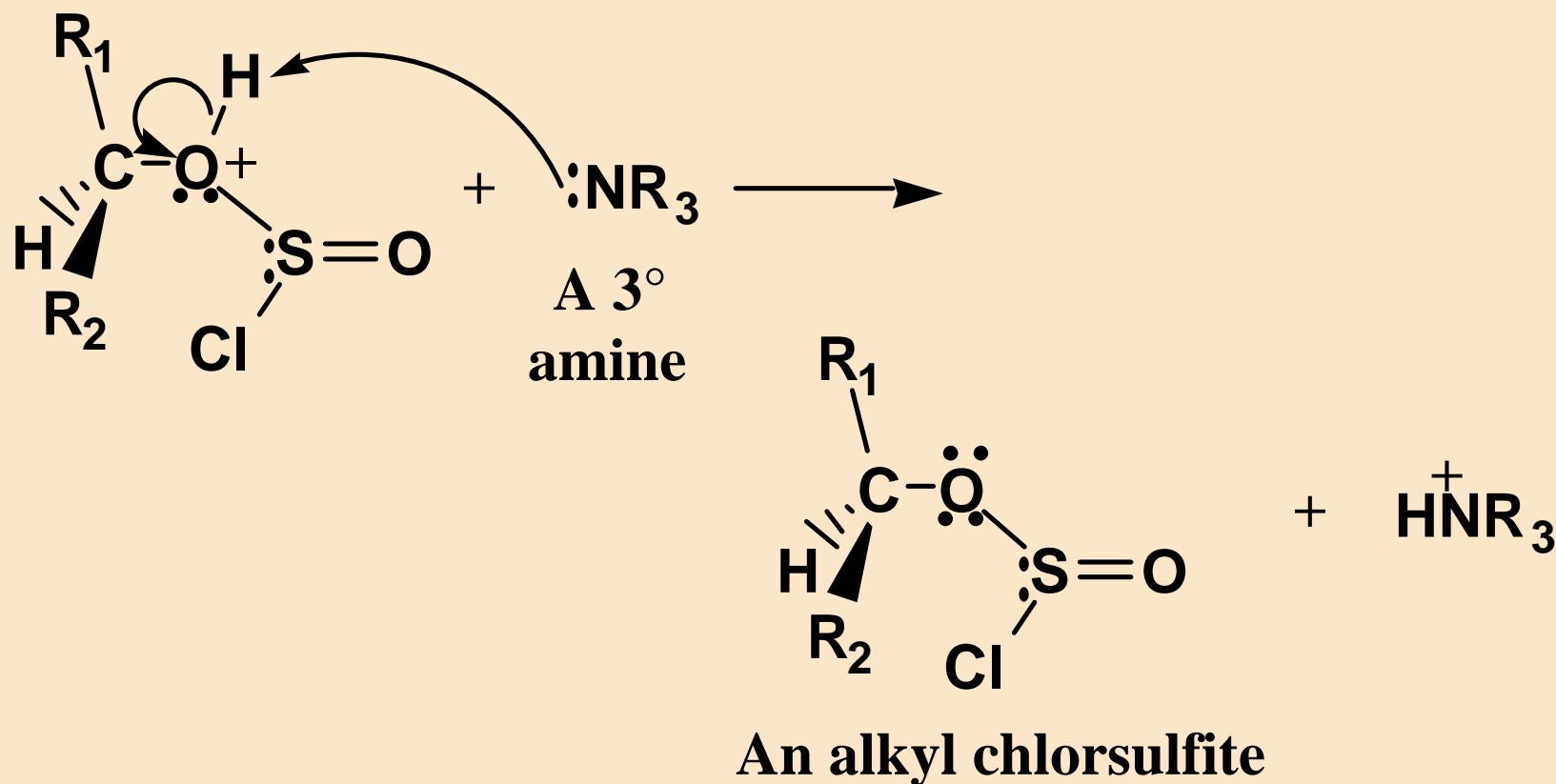
9 Reaction with SOCl_2

Step 1: nucleophilic displacement of chlorine by oxygen



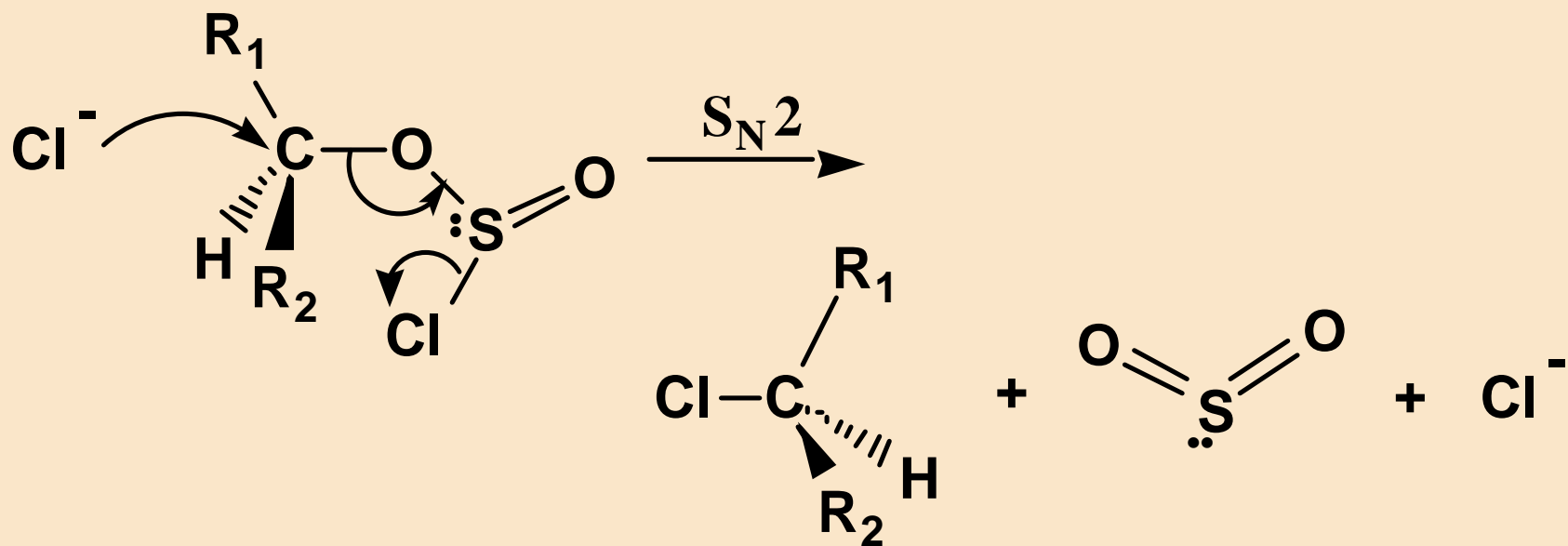
9 Reaction with SOCl_2

Step 2: proton transfer to the 3° amine to form an alkyl chlorosulfite



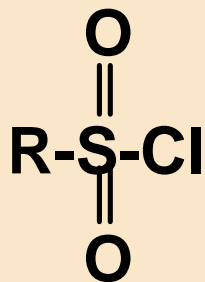
9 Reaction with SOCl_2

Step 3: backside displacement by chloride ion and decomposition of the chlorosulfite

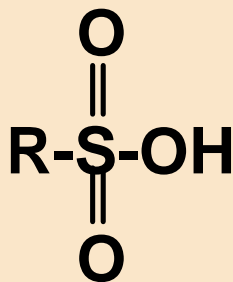


9 Alkyl Sulfonates

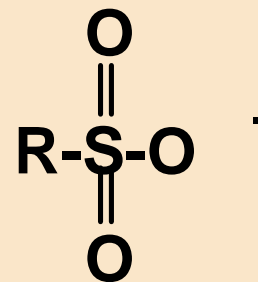
- u **Sulfonyl chlorides are derived from sulfonic acids, acids as strong as sulfuric acid**



**A sulfonyl
chloride**



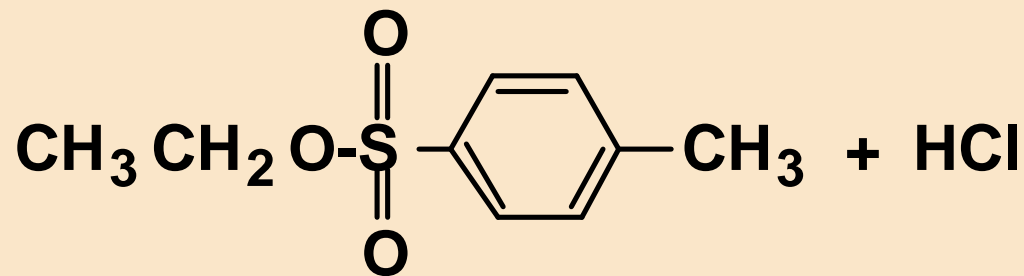
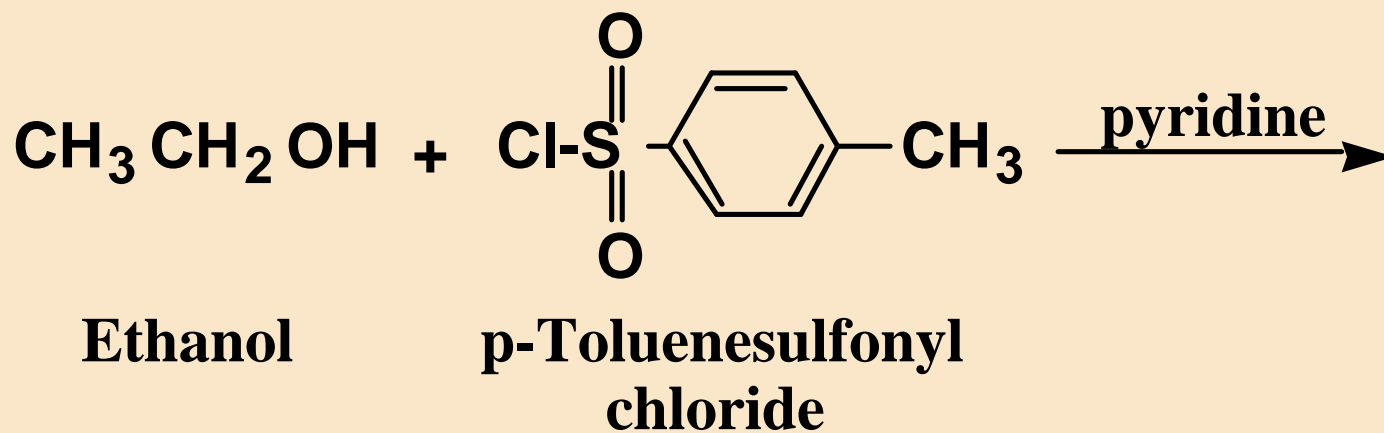
**A sulfonic acid
(a very strong acid)**



**A sulfonate anion
(a very weak base and
good leaving group)**

9 Alkyl Sulfonates

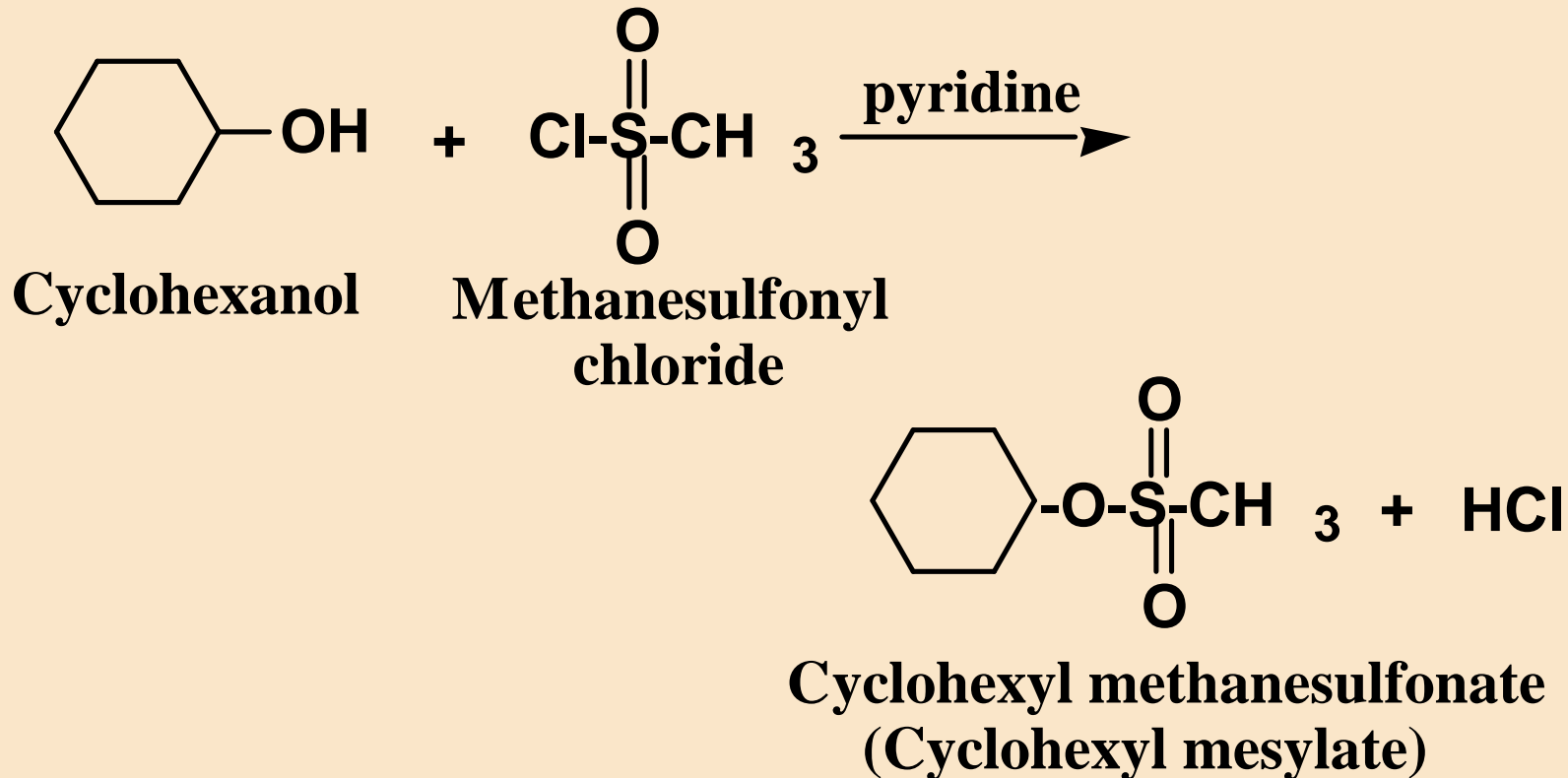
u A commonly used sulfonyl chloride is p-toluenesulfonyl chloride (Ts-Cl)



Ethyl p-toluenesulfonate
(Ethyl tosylate)

9 Alkyl Sulfonates

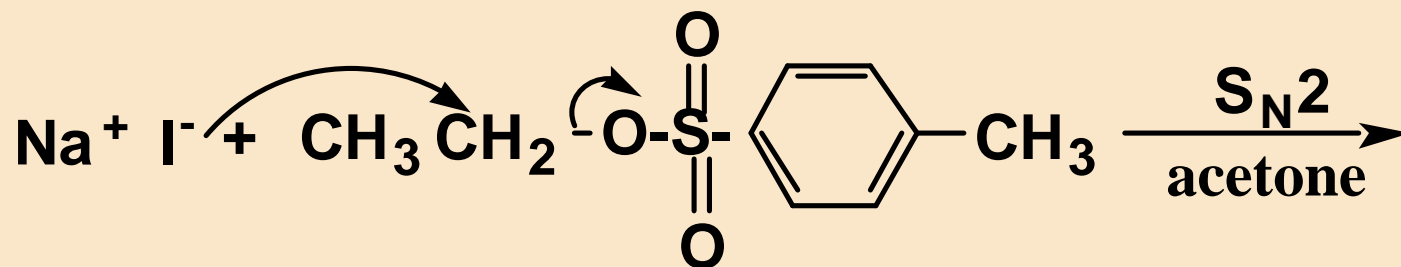
u Another commonly used sulfonyl chloride is methanesulfonyl chloride (Ms-Cl)



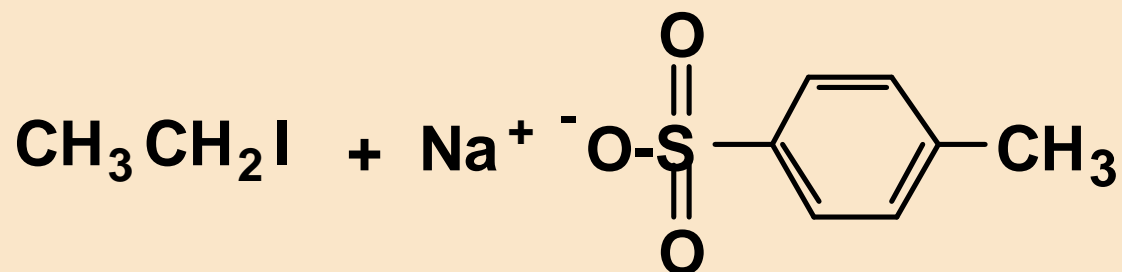
9 Alkyl Sulfonates

- u Sulfonate anions are very weak bases (the conjugate base of a strong acid) and are very good leaving groups for S_N2 reactions
- u Conversion of an alcohol to a sulfonate ester converts OH, a very poor leaving group, into a sulfonic ester, a very good leaving group

9 Alkyl Sulfonates



Ethyl p-toluenesulfonate

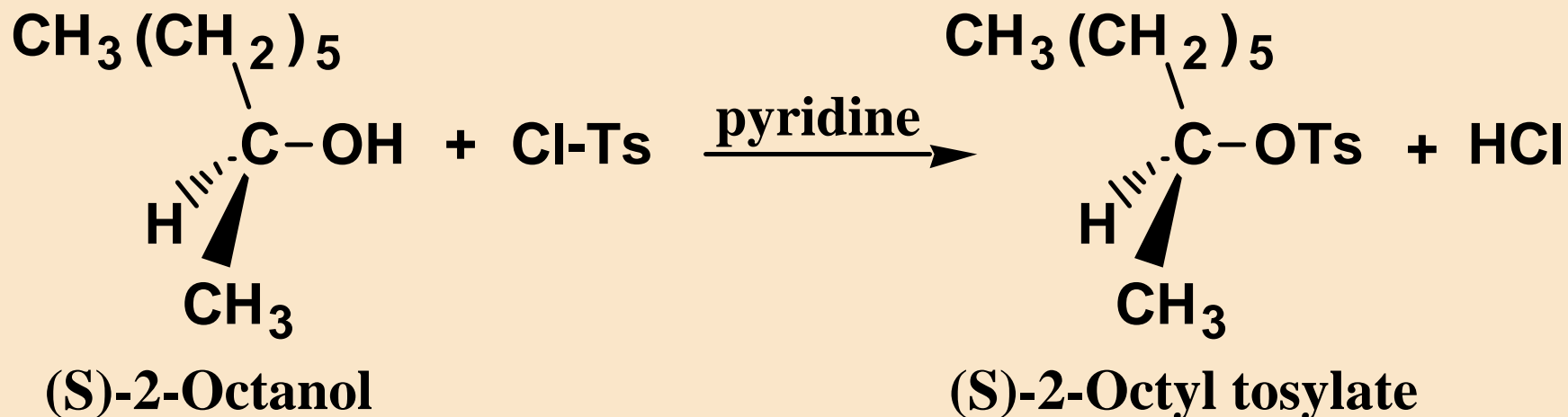


p-Toluenesulfonate anion
(a good leaving group)

9 Alkyl Sulfonates

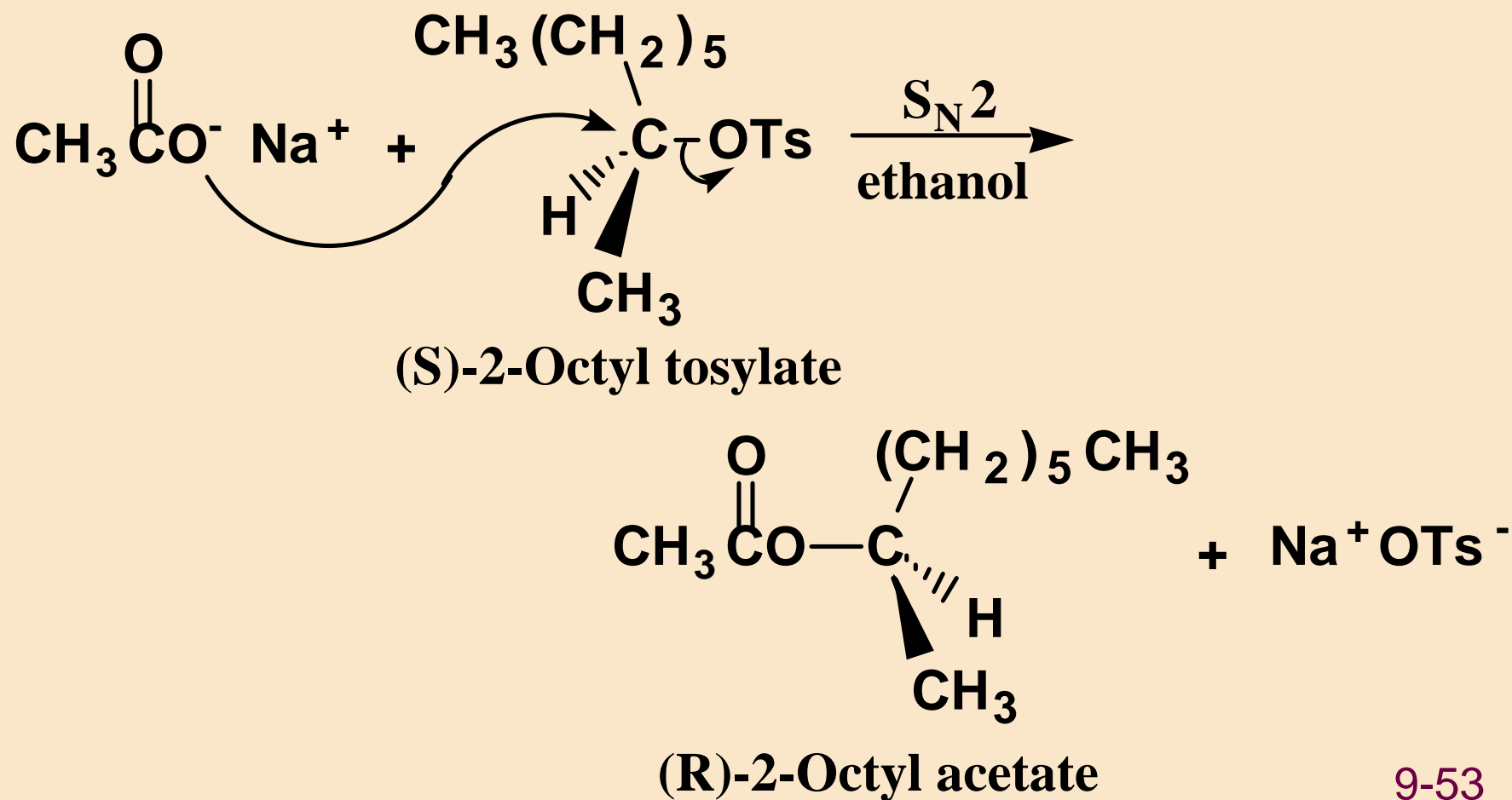
- u This two-step procedure converts (S)-2-octanol to (R)-2-octyl acetate

Step 1: formation of a p-toluenesulfonate (Ts) ester



9 Alkyl Sulfonates

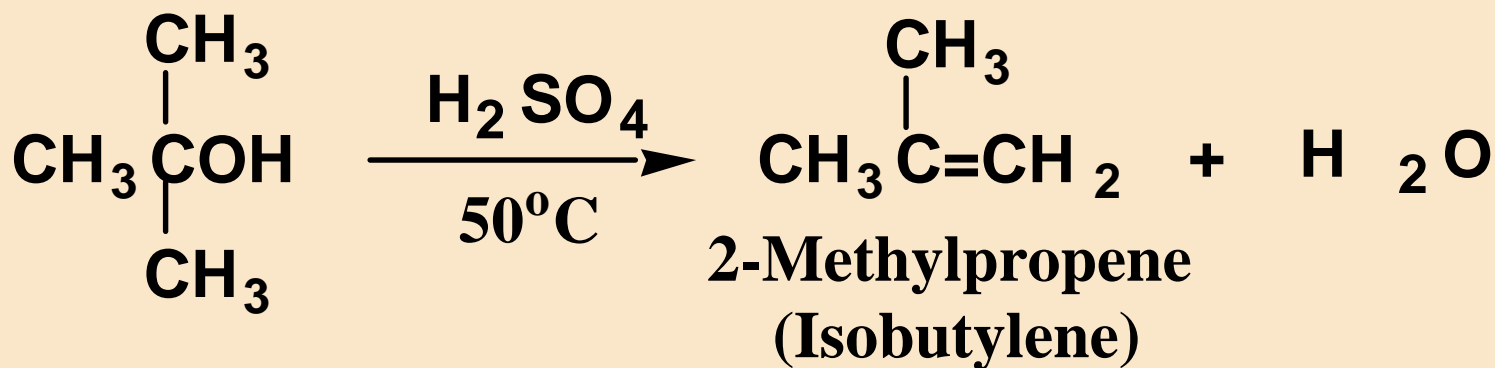
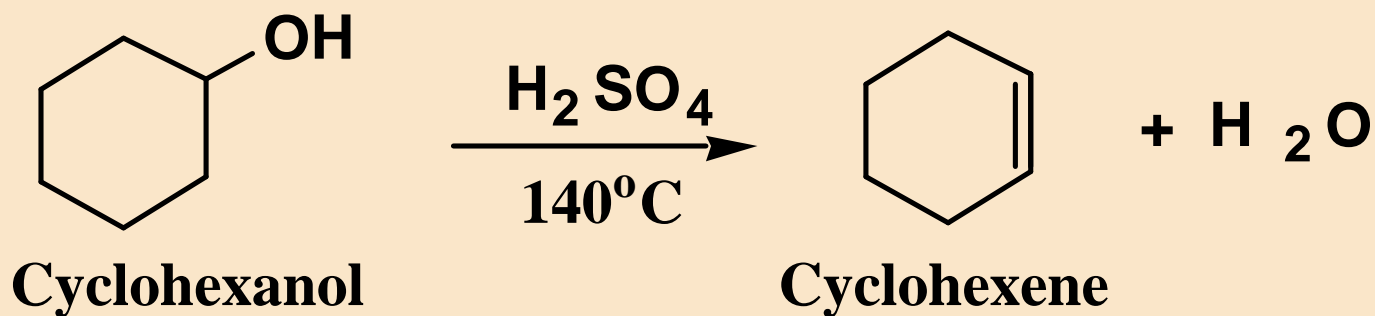
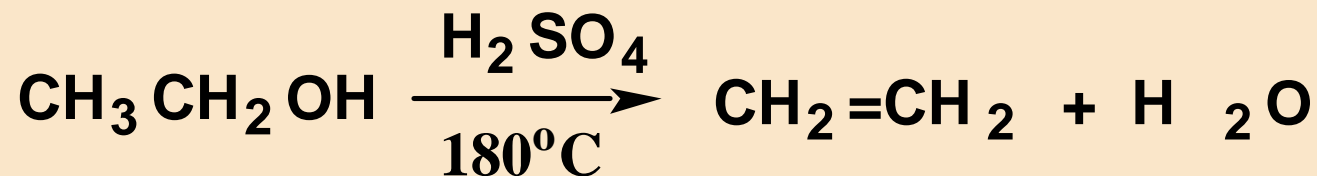
Step 2: nucleophilic displacement of tosylate



9 Dehydration of ROH

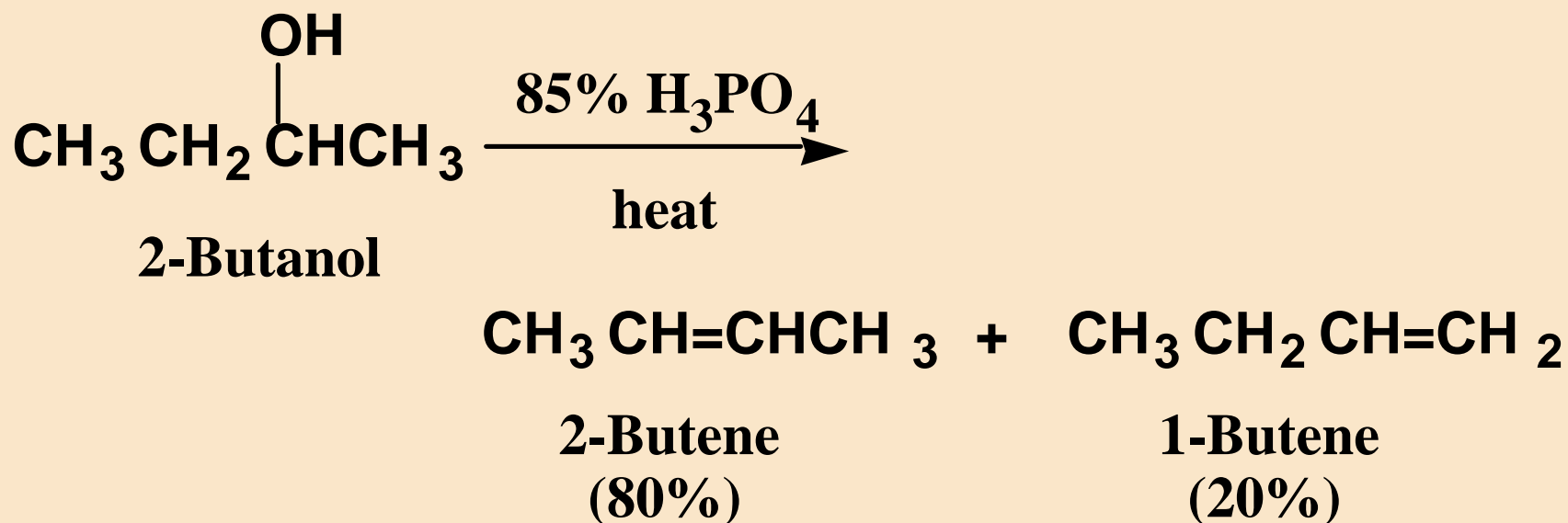
- u An alcohol can be converted to an alkene by elimination of H and OH from adjacent carbons (a β -elimination)
 - 1° alcohols must be heated at high temperature in the presence of an acid catalyst, such as H_2SO_4 or H_3PO_4
 - 2° alcohols undergo dehydration at somewhat lower temperatures
 - 3° alcohols often require temperatures at or slightly above room temperature

9 Dehydration of ROH



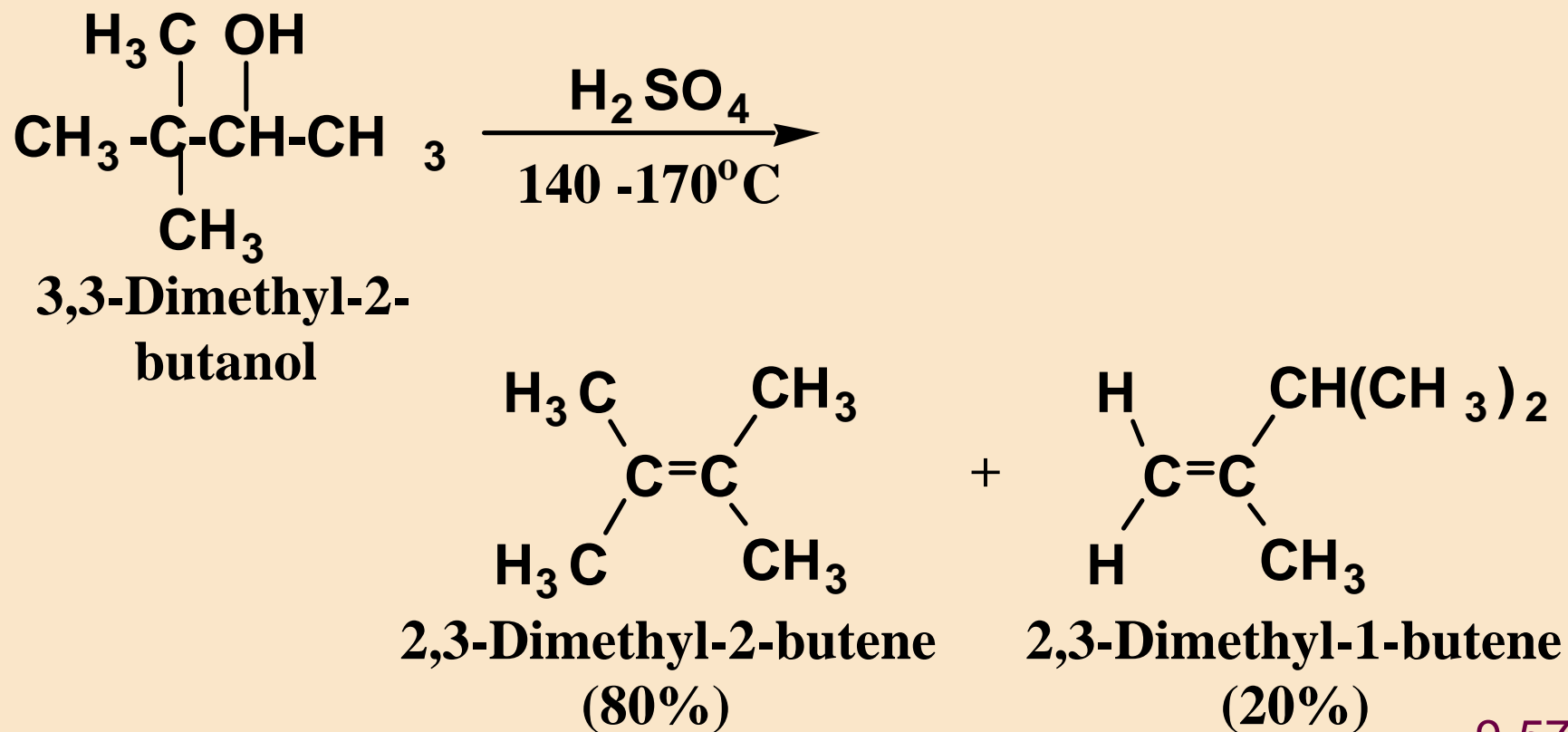
9 Dehydration of ROH

- u Where isomeric alkenes are possible, the alkene having the greater number of substituents on the double bond usually predominates (Zaitsev rule)



9 Dehydration of ROH

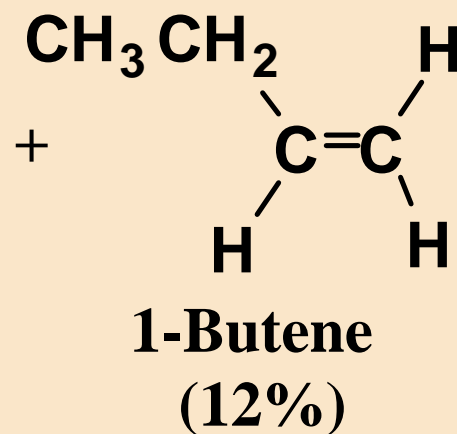
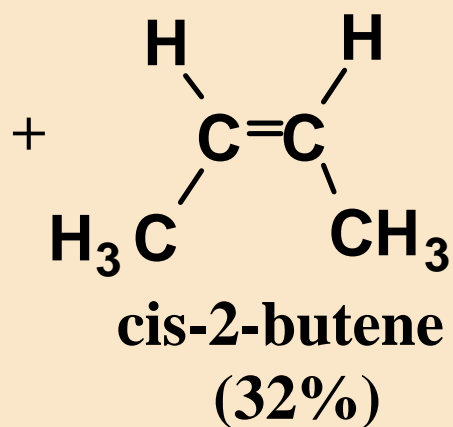
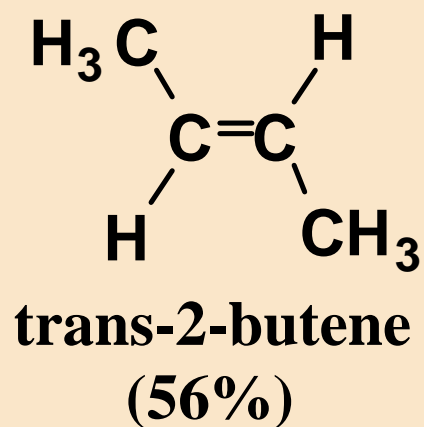
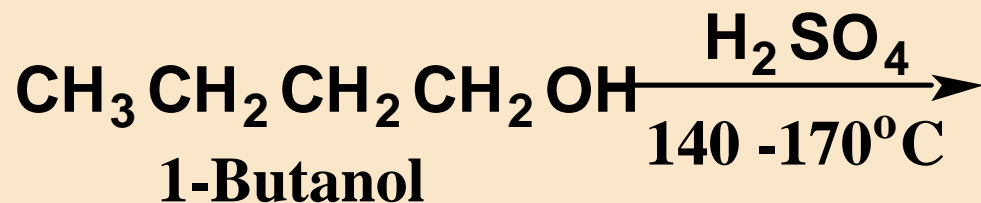
u Dehydration of 1° and 2° alcohols is often accompanied by rearrangement



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9 Dehydration of ROH

u Acid-catalyzed dehydration of 1-butanol gives a mixture of three alkenes



9 Dehydration of ROH

u Based on evidence of

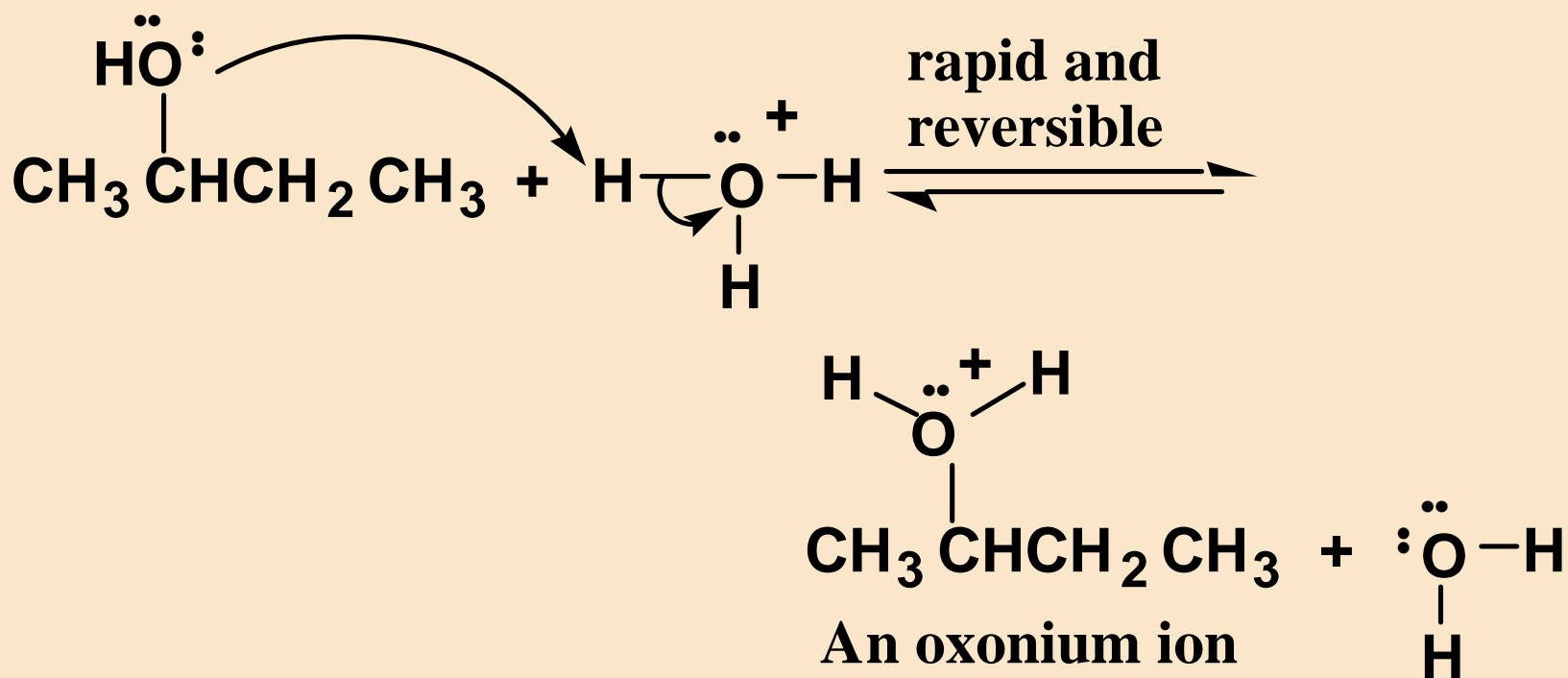
- ease of dehydration ($3^\circ > 2^\circ > 1^\circ$)
- prevalence of rearrangements

u chemists propose a three-step mechanism for the dehydration of 2° and 3° alcohols

- because this mechanism involves formation of a carbocation intermediate in the rate-limiting step, it is classified as E1

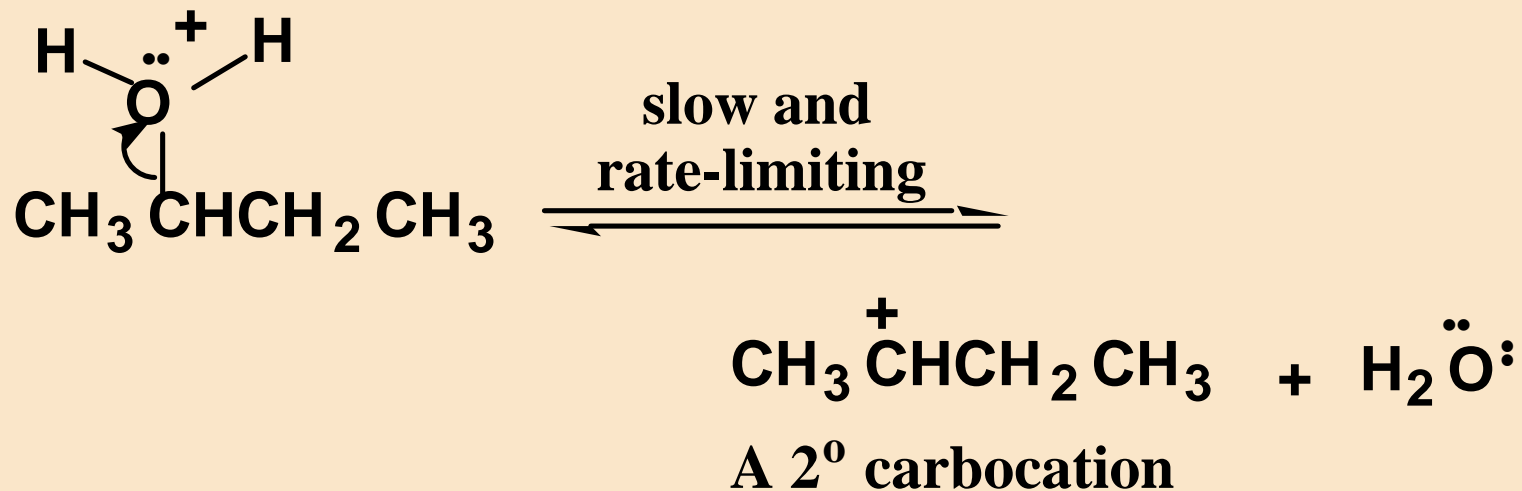
9 Dehydration of ROH

Step 1: proton transfer from H_3O^+ to the $-\text{OH}$ group to form an oxonium ion



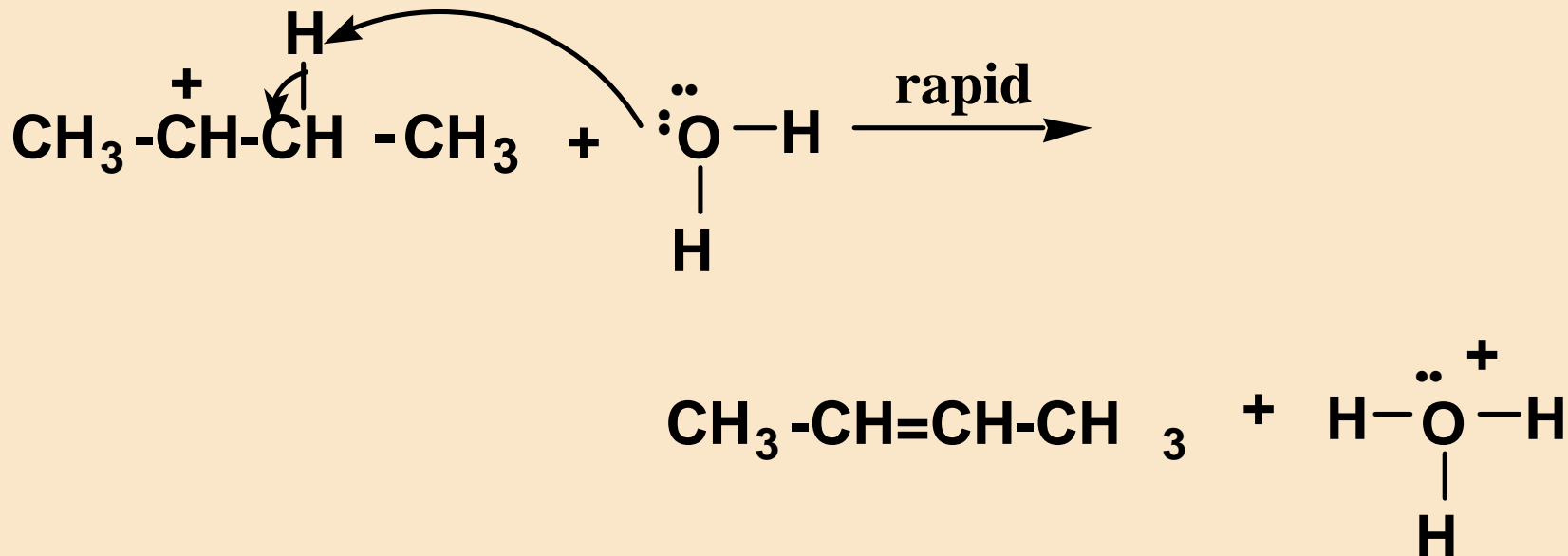
9 Dehydration of ROH

Step 2: the C-O bond is broken and water is lost, giving a carbocation intermediate



9 Dehydration of ROH

Step 3: proton transfer of H⁺ from a carbon adjacent to the positively charged carbon to water. The sigma electrons of the C-H bond become the pi electrons of the carbon-carbon double bond

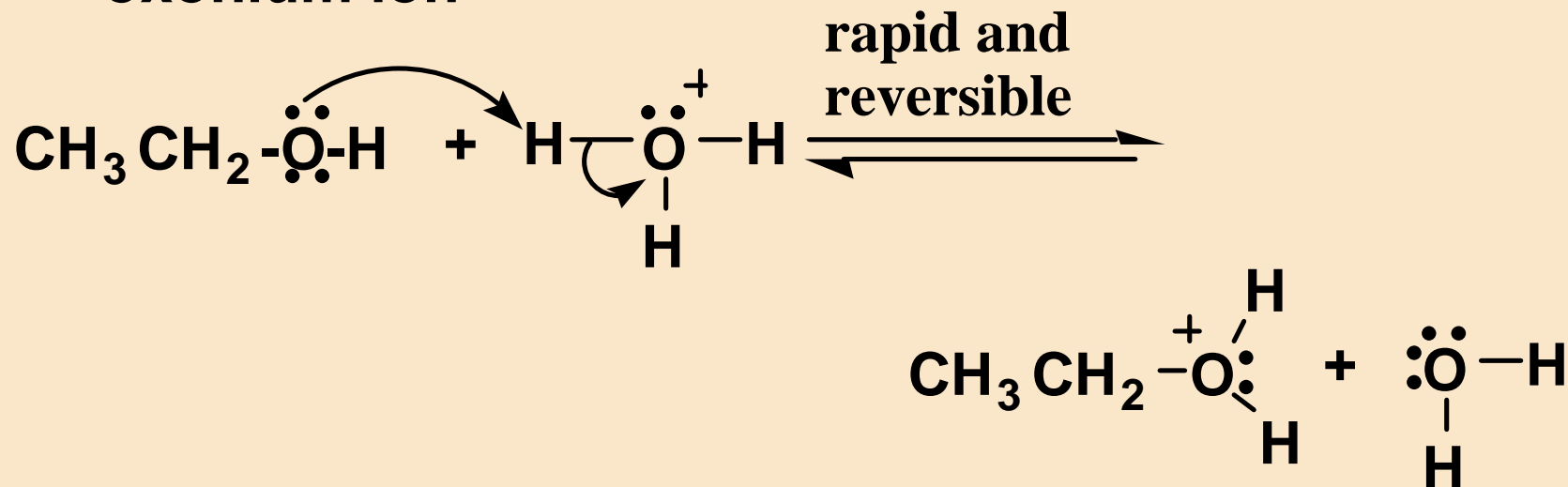


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9 • Dehydration of ROH

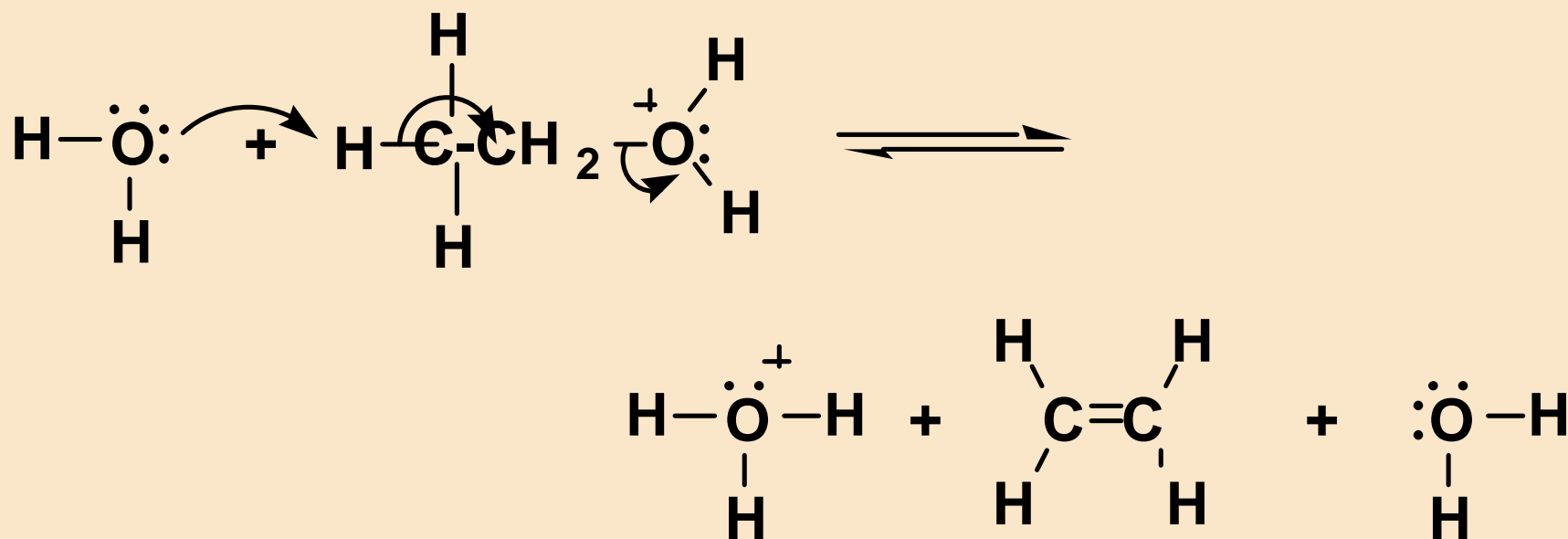
1° alcohols with little β -branching follow an E2 mechanism

Step 1: proton transfer from H_3O^+ to OH to form an oxonium ion



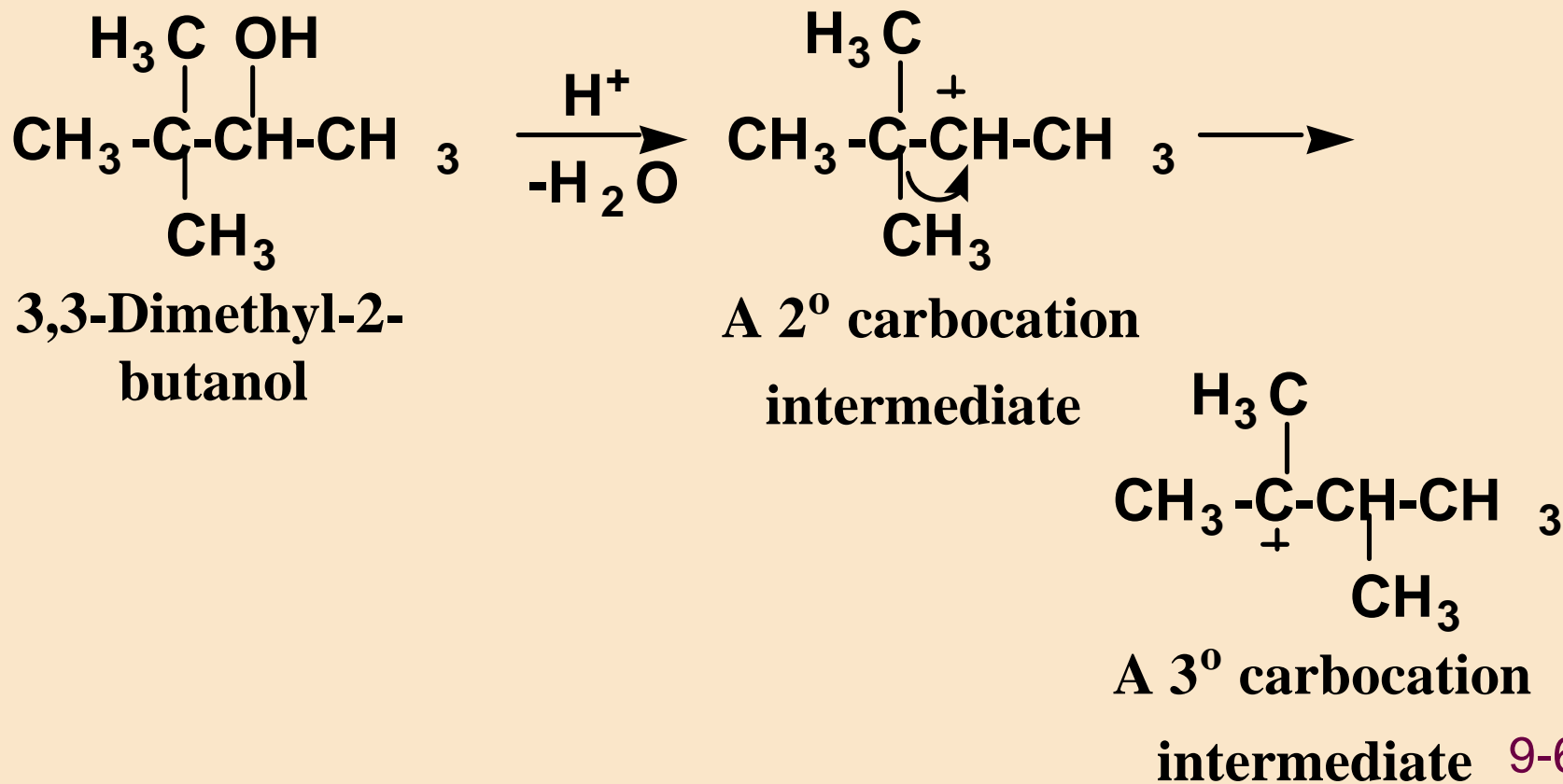
9 Dehydration of ROH

Step 2: Simultaneous loss of H from the β -carbon and OH_2 from the α -carbon

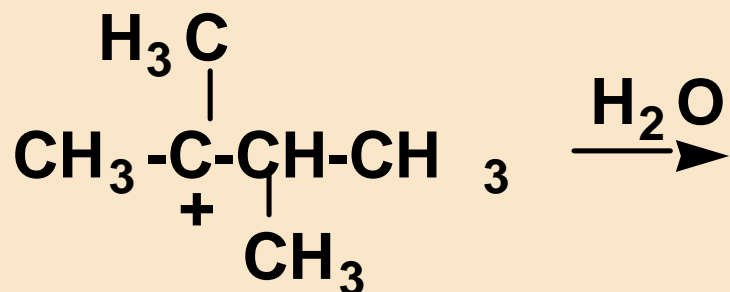


9 Dehydration of ROH

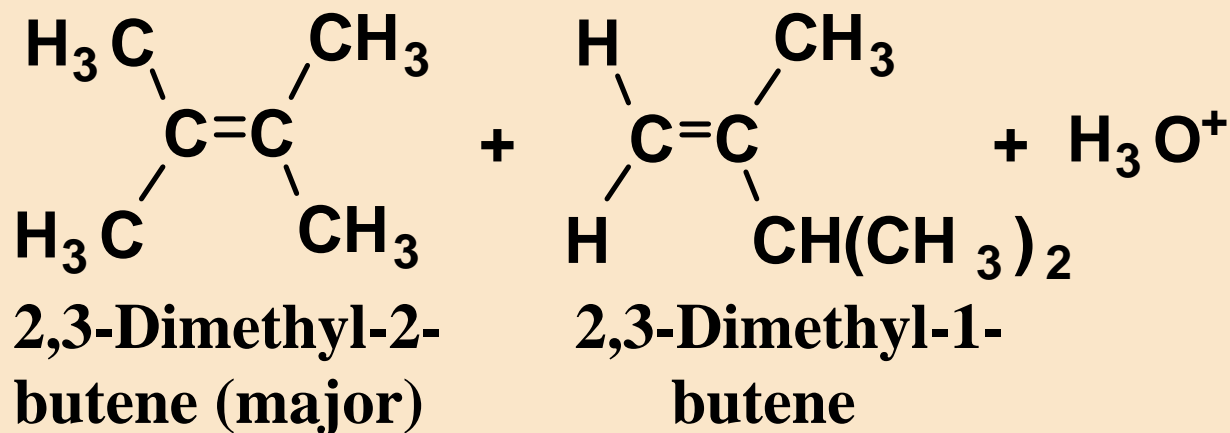
u Dehydration with rearrangement occurs by a carbocation rearrangement



9 Dehydration of ROH

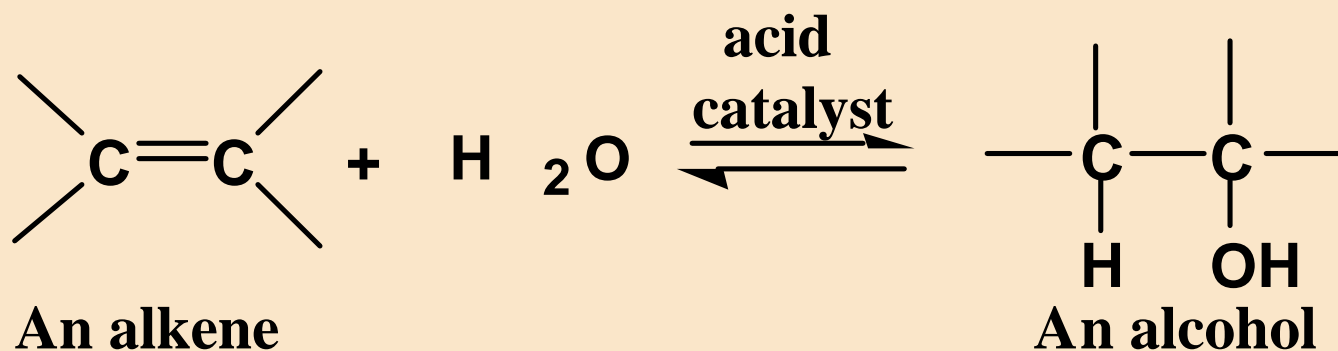


A 3^o carbocation
intermediate



9 Dehydration of ROH

- u Acid-catalyzed alcohol dehydration and alkene hydration are competing processes

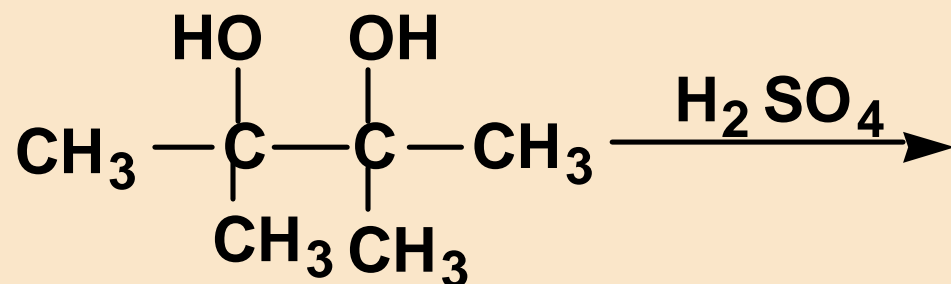


- u **Principle of microscopic reversibility:** the sequence of transition states and reactive intermediates in the mechanism of a reversible reaction must be the same, but in reverse order, for the backward reaction as for the forward reaction

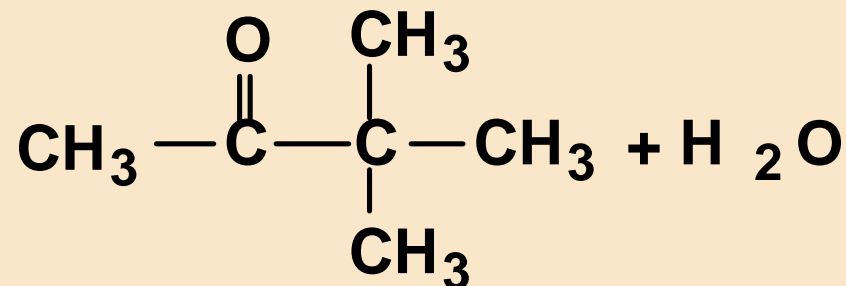
9-67

9 Pinacol Rearrangement

- u The products of acid-catalyzed dehydration of a glycol are different from those of alcohols



2,3-Dimethyl-2,3-butanediol
(Pinacol)

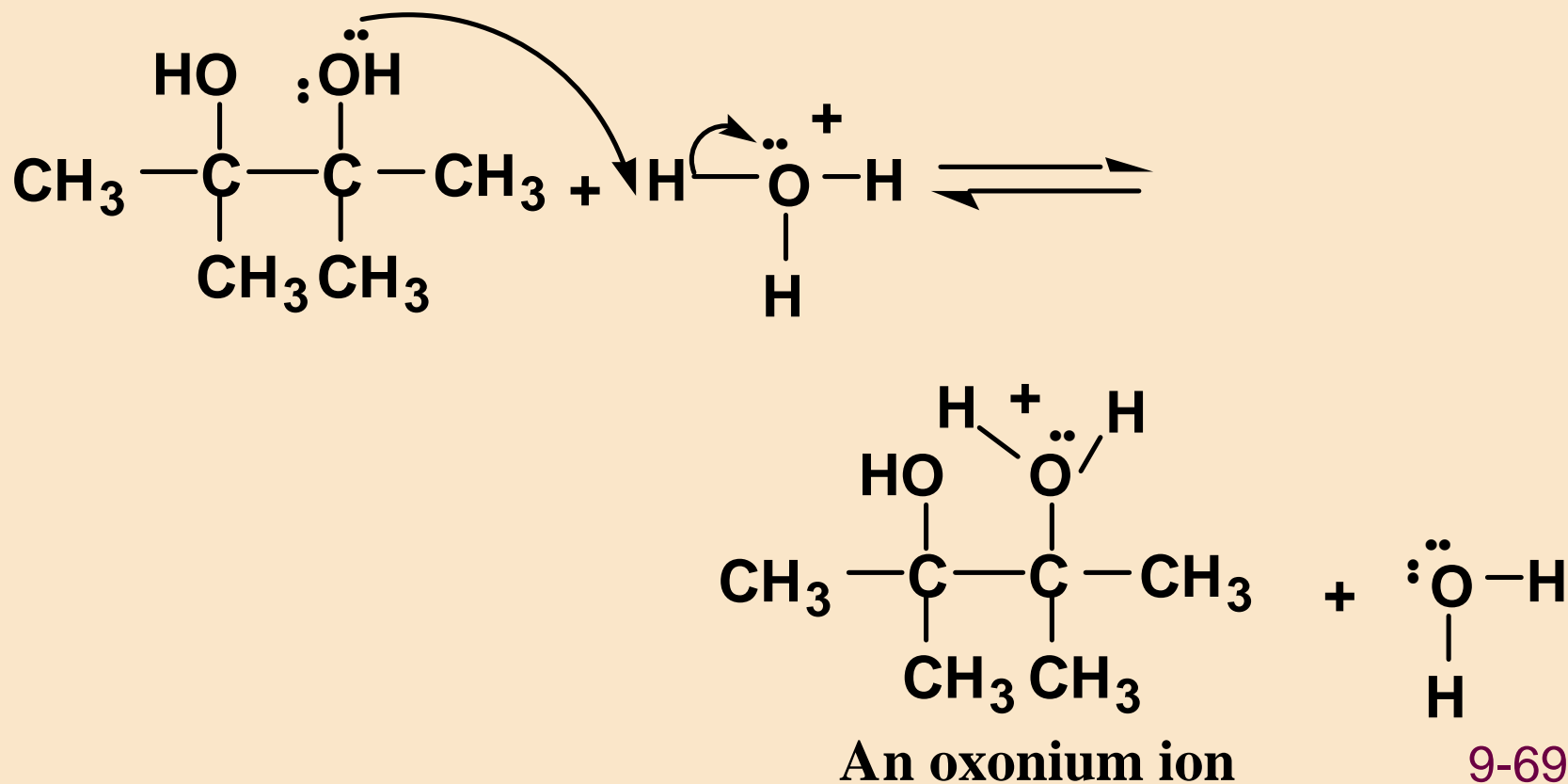


3,3-Dimethyl-2-butanone
(Pinacolone)

9-68

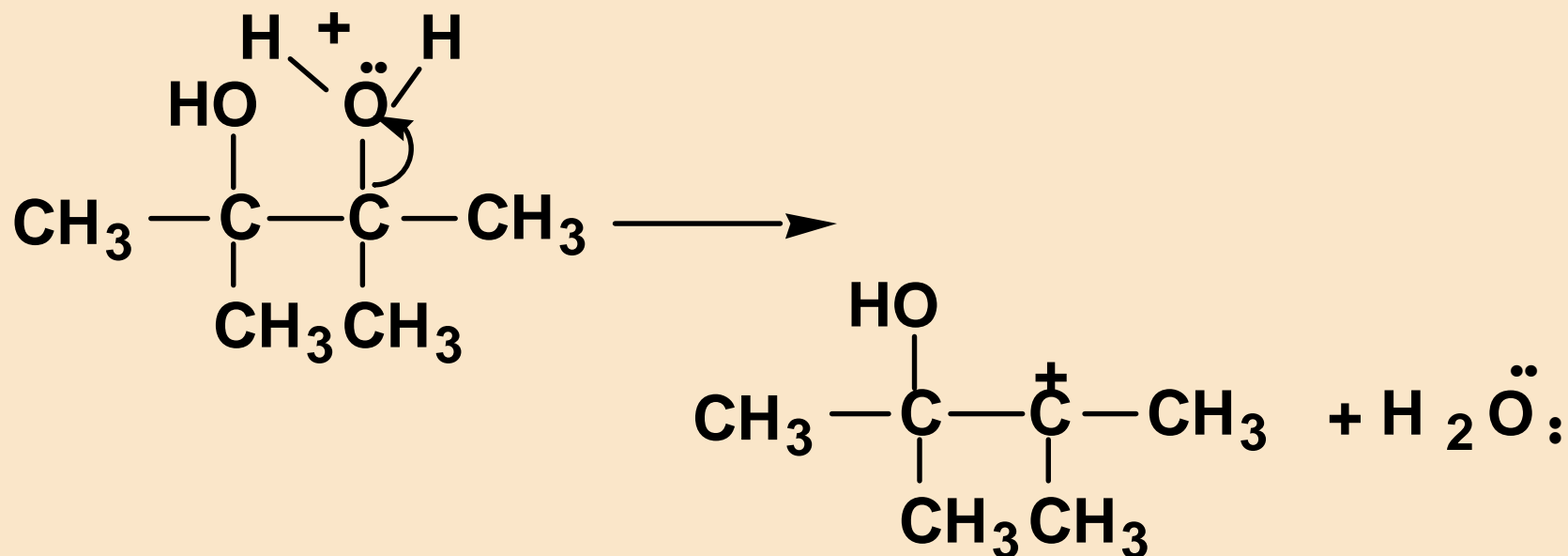
9 Pinacol Rearrangement

Step 1: proton transfer to an OH, a poor leaving group, converts it to a better leaving group



9 Pinacol Rearrangement

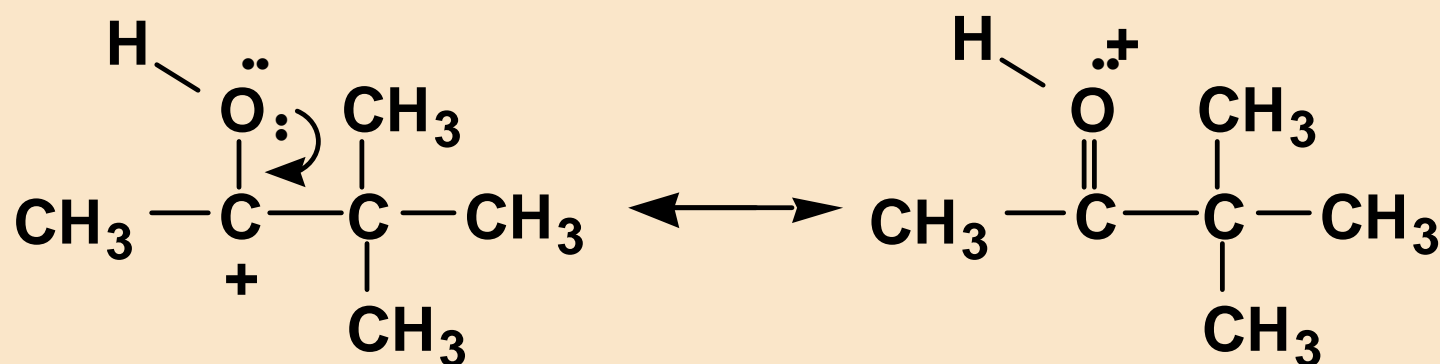
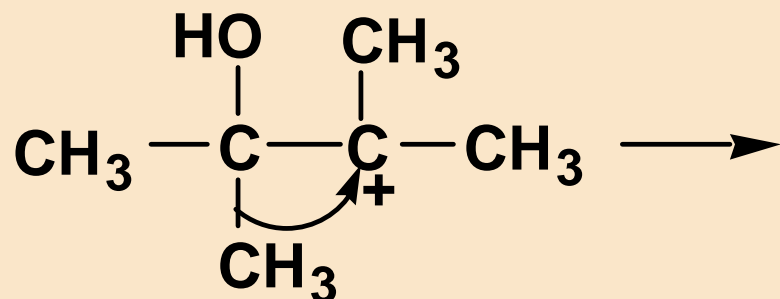
Step 2: Loss of water to form a carbocation intermediate



A 3° carbocation
intermediate

9 Pinacol Rearrangement

Step 3: migration of an adjacent group, with its bonding electrons, leaves a more stable carbocation

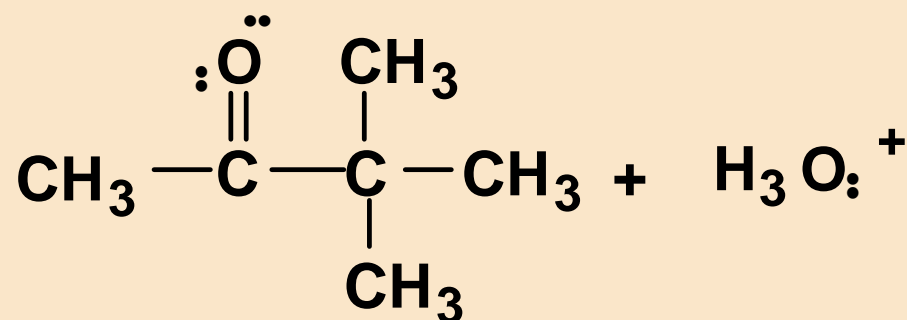
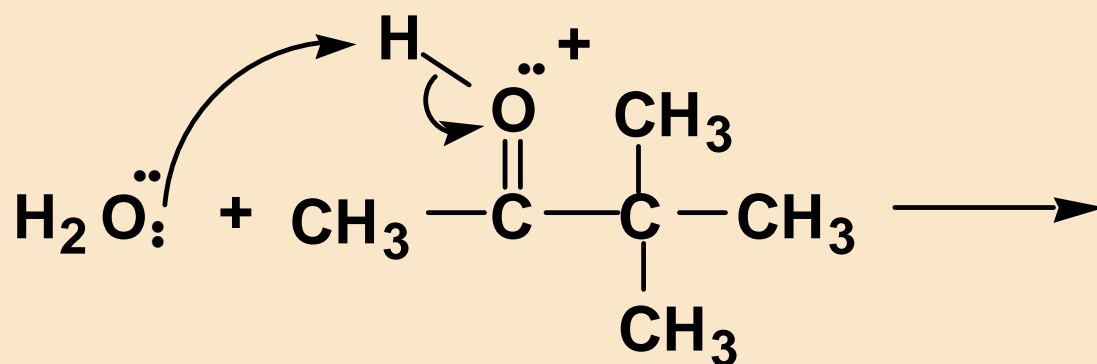


A resonance-stabilized cation intermediate

9-71

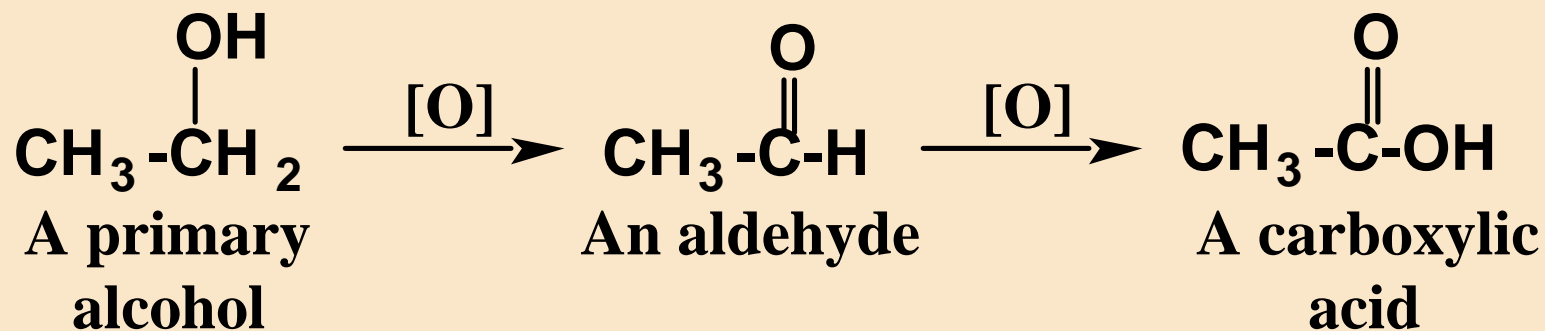
9 Pinacol Rearrangement

Step 4: proton transfer to solvent



9 Oxidation: 1° ROH

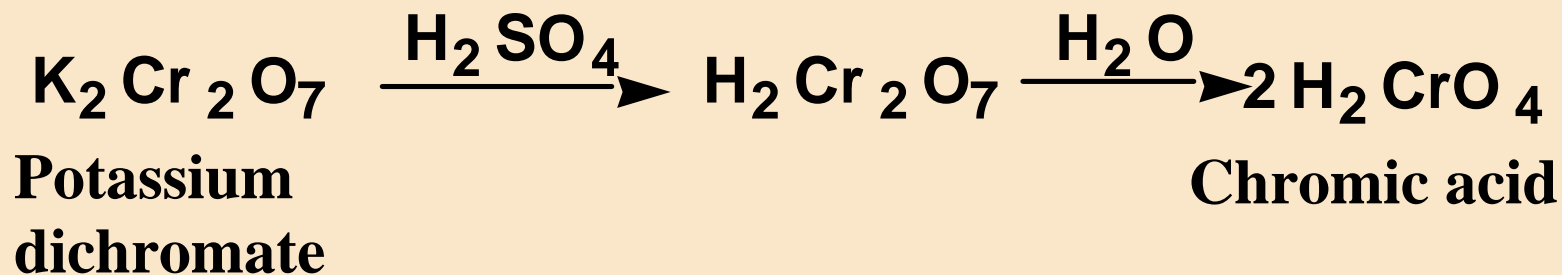
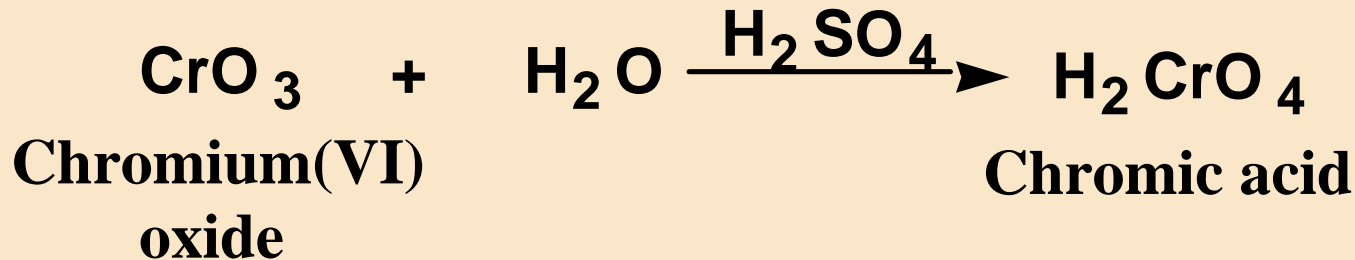
- u A primary alcohol can be oxidized to an aldehyde or a carboxylic acid, depending on the experimental conditions



- to an aldehyde is a two-electron oxidation
- to a carboxylic acid is a four-electron oxidation

9 Oxidation: 1° ROH

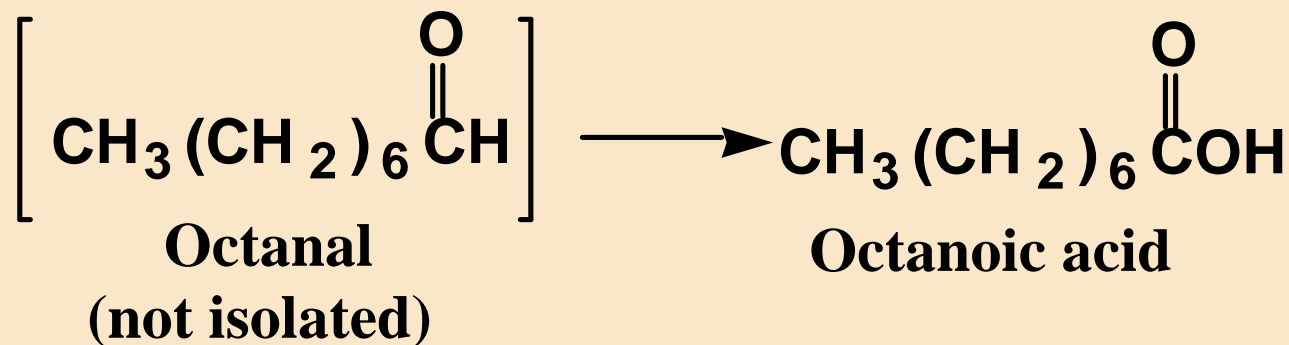
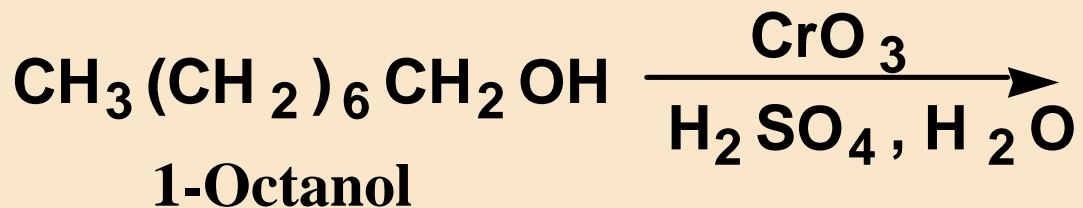
- u A common oxidizing agent for this purpose is chromic acid, prepared by dissolving chromium(VI) oxide or potassium dichromate in aqueous sulfuric acid



9 Oxidation: 1° ROH

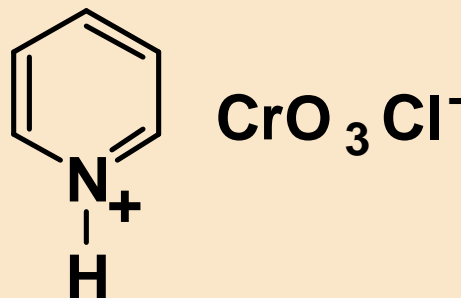
u Oxidation of 1-octanol gives octanoic acid

- the aldehyde intermediate is not isolated



9 Oxidation: 1° ROH

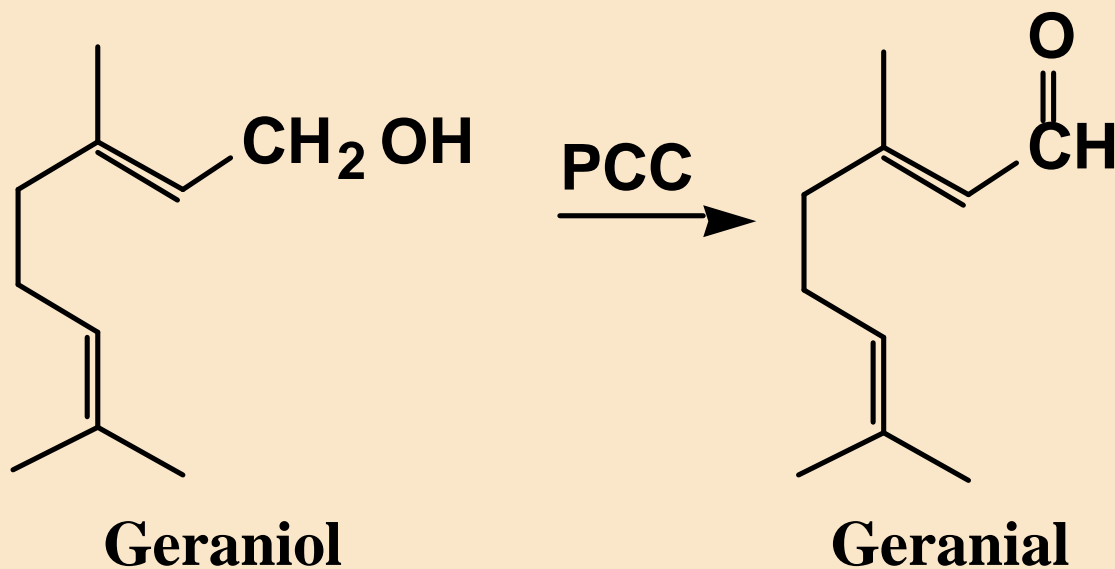
- u **Pyridinium chlorochromate (PCC):** a form of Cr(VI) prepared by dissolving CrO₃ in aqueous HCl and adding pyridine to precipitate PCC



- PCC is selective for the oxidation of 1° alcohols to aldehydes; it does not oxidize aldehydes further to carboxylic acids

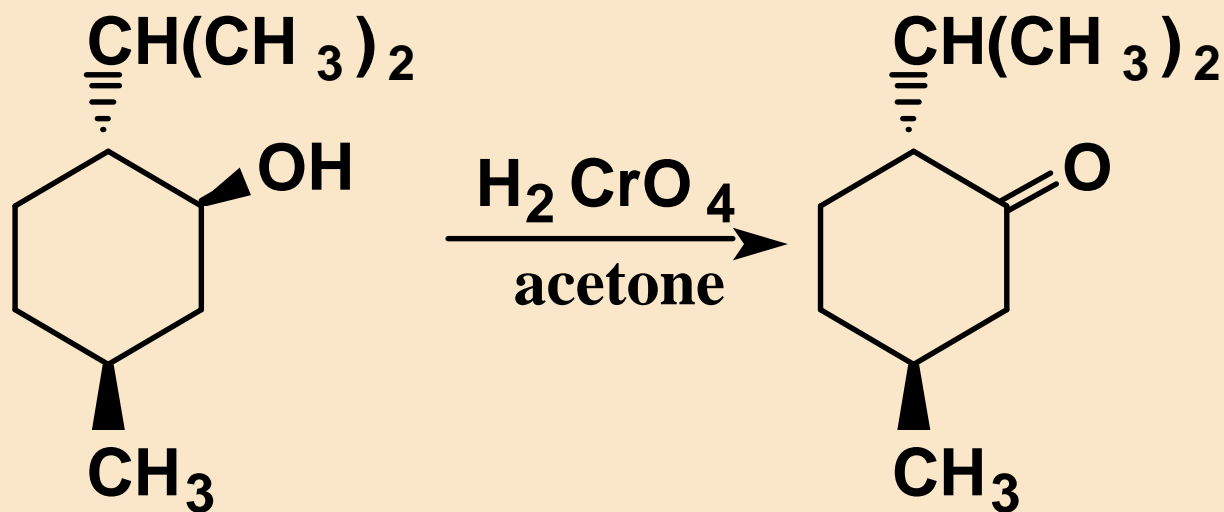
9 Oxidation: 1° ROH

u PCC oxidation of a 1° alcohol to an aldehyde



9 Oxidation: 2° ROH

- u 2° alcohols are oxidized to ketones by both PCC and chromic acid



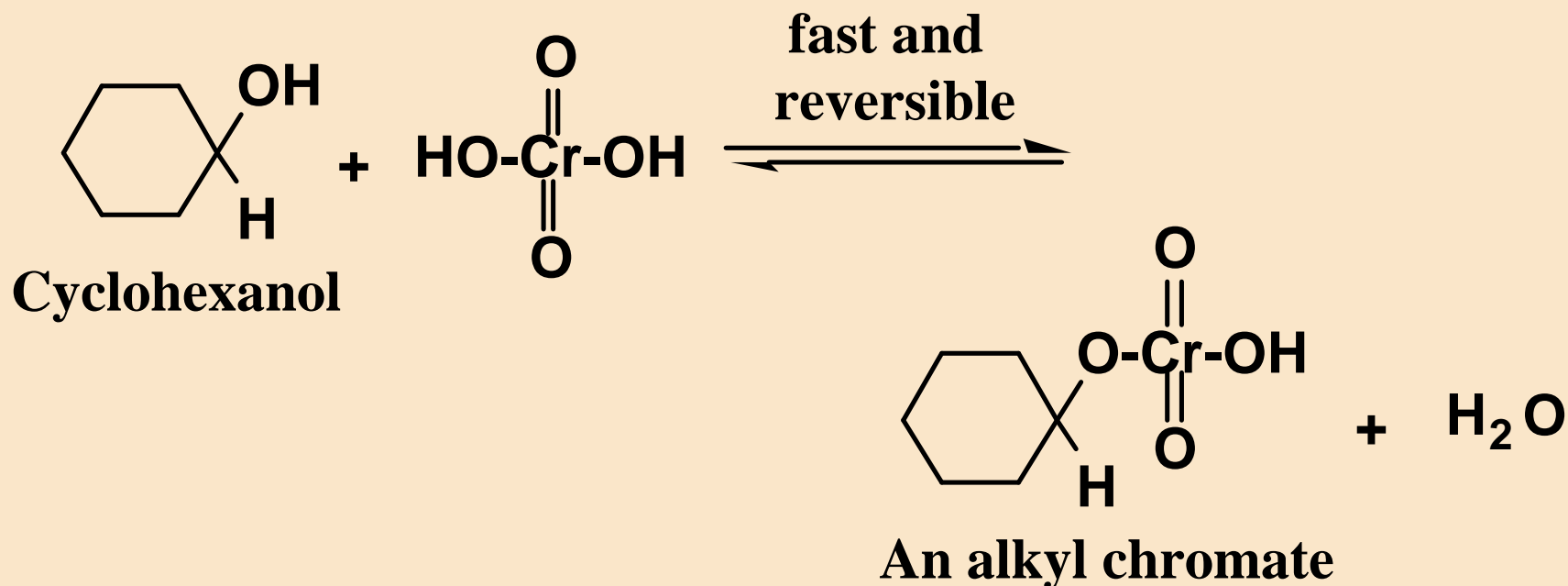
2-Isopropyl-5-methyl-
cyclohexanol
(Menthol)

2-Isopropyl-5-methyl-
cyclohexanone
(Menthone)

9 Oxidation: 1° & 2° ROH

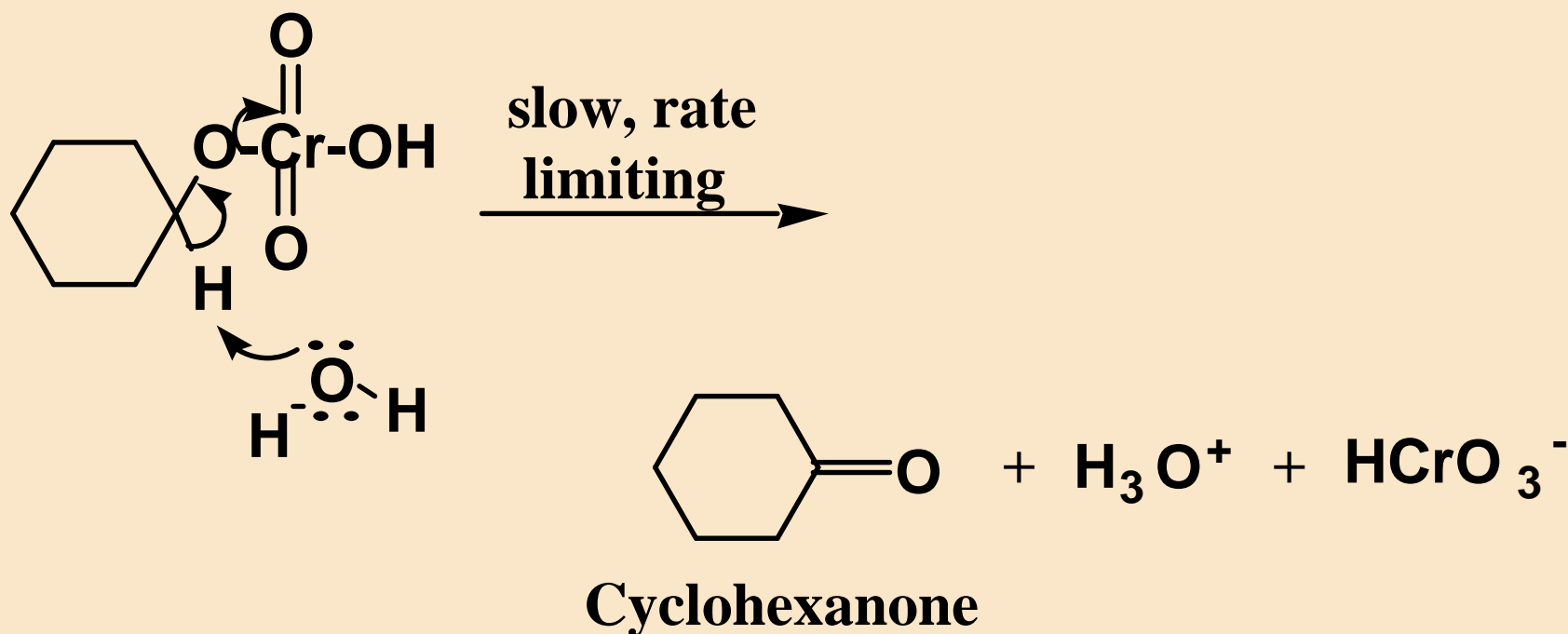
u The mechanism of chromic acid oxidation of an alcohol involves two steps

Step 1: formation of an alkyl chromate ester



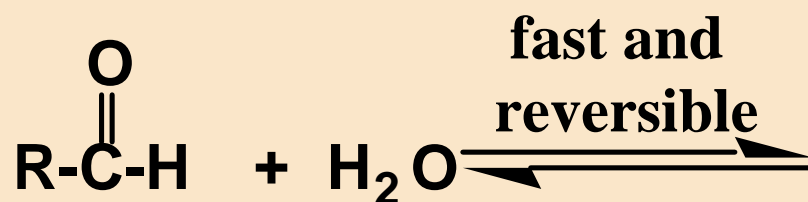
9 Oxidation: 1° & 2° ROH

Step 2: proton transfer to solvent and decomposition of the alkyl chromate ester

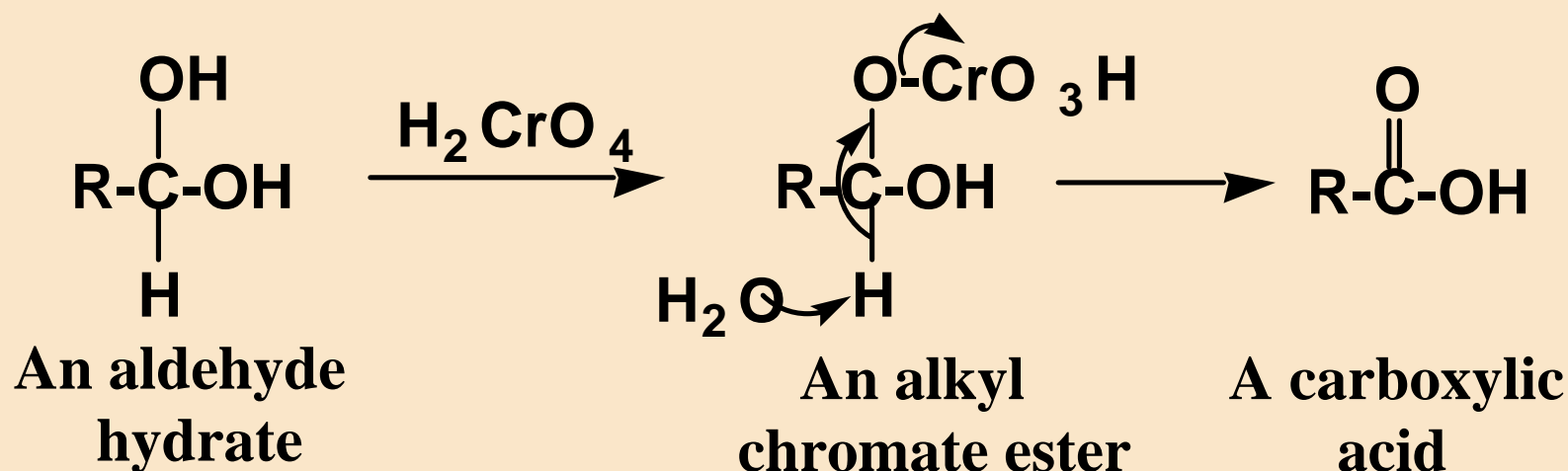


9 Oxidation: 1° & 2° ROH

- u In chromic acid oxidation of a CHO group, it is the hydrated form that is oxidized



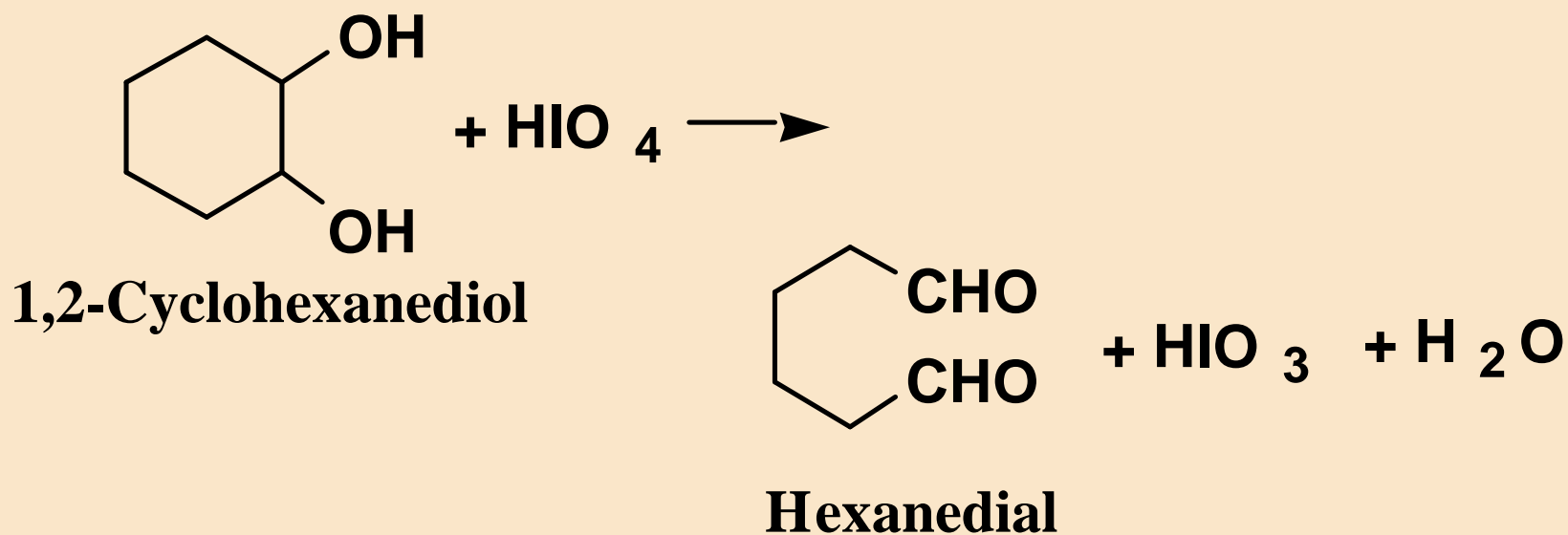
An aldehyde



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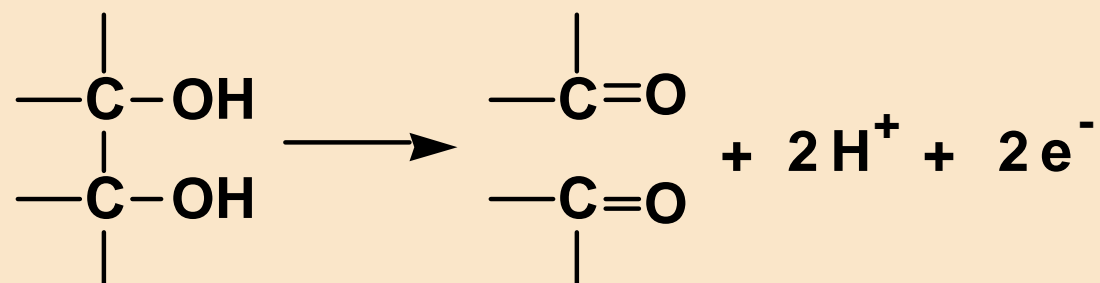
9 Oxidation of Glycols

- u Glycols are cleaved by oxidation with periodic acid, H_5IO_6 (or, alternatively $\text{HIO}_4 \cdot 2\text{H}_2\text{O}$)

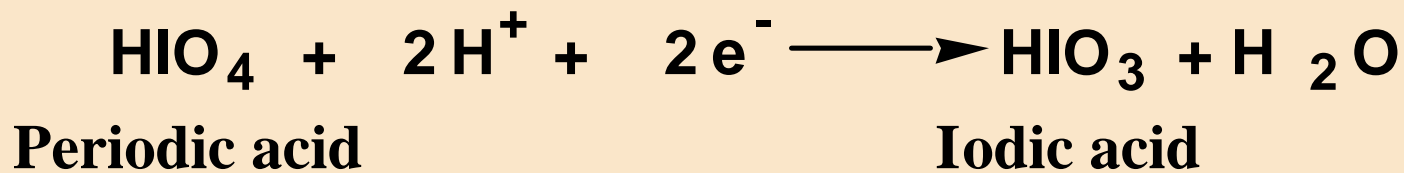


9 Oxidation of Glycols

- the glycol undergoes a two-electron oxidation



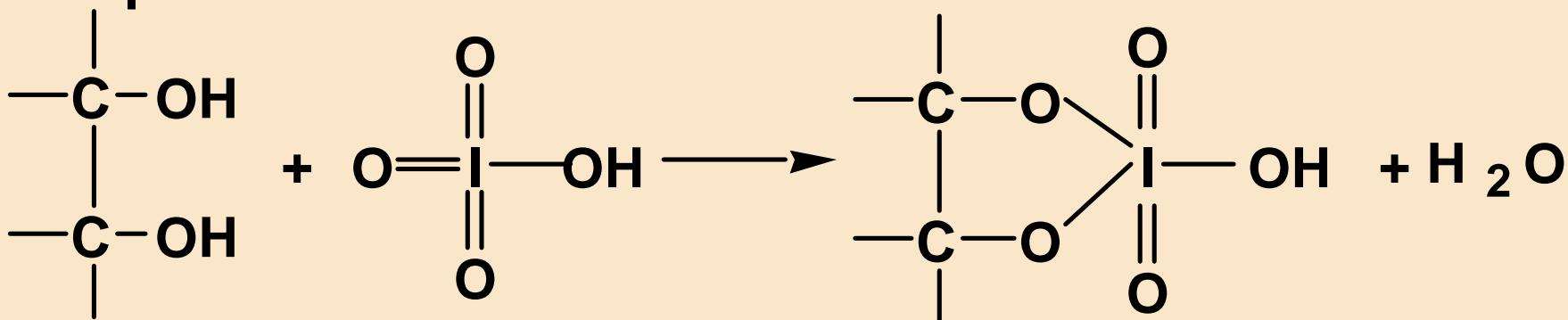
- periodic acid undergoes a two-electron reduction



9 Oxidation of Glycols

- u The mechanism of periodic acid oxidation of a glycol is divided into two steps

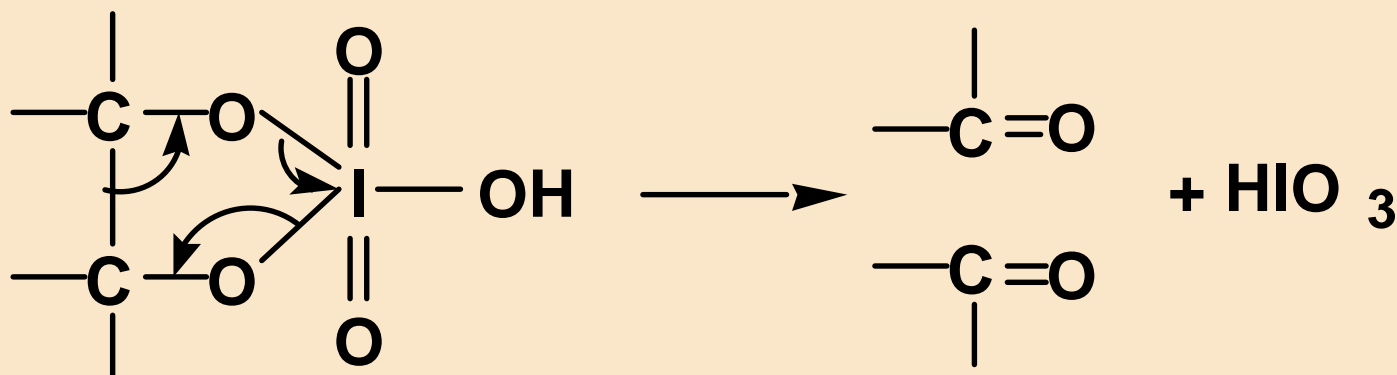
Step 1: formation of a five-membered cyclic periodic ester



A cyclic periodic ester

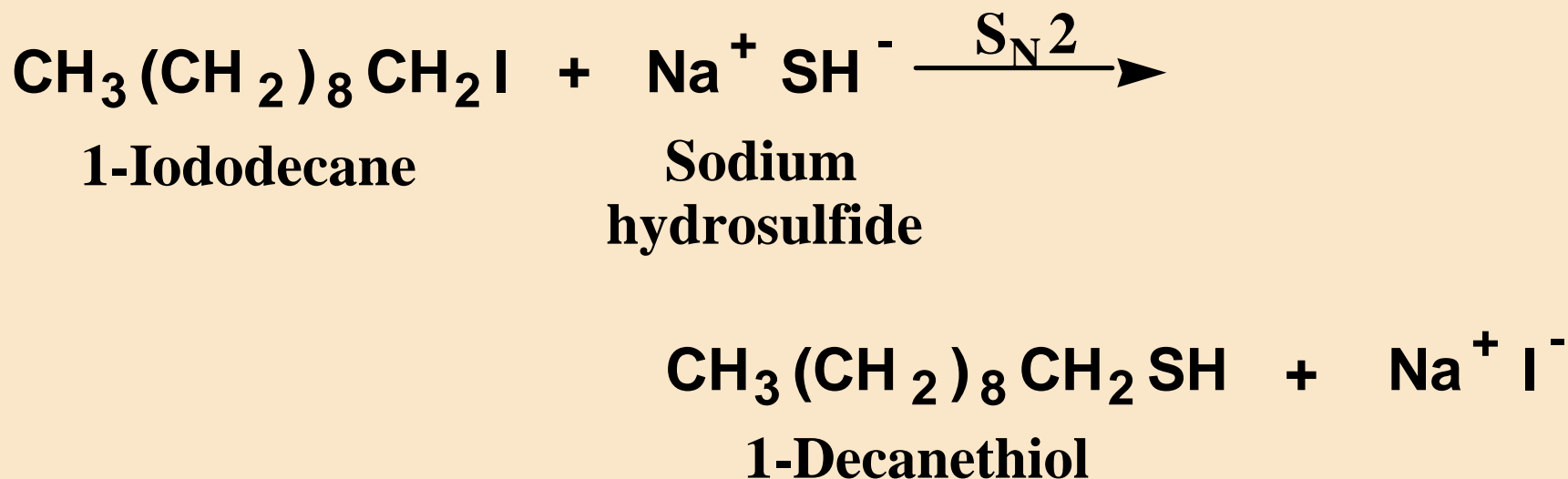
9 Oxidation of Glycols

Step 2: redistribution of electrons within the five-membered ring to give iodic acid and two carbonyl groups



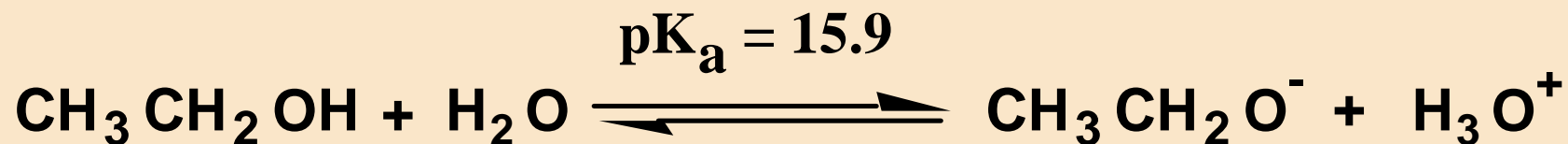
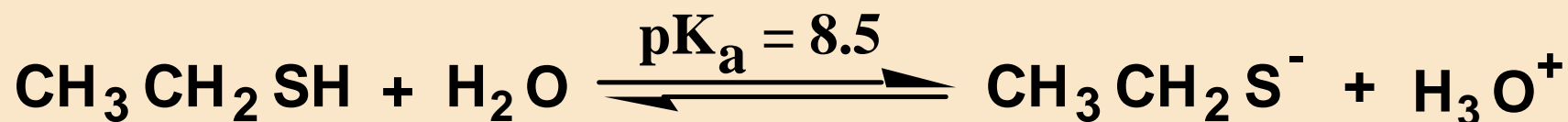
9 Thiols

- u The most common preparation of thiols, RSH, depends on the very high nucleophilicity of hydrosulfide ion, HS⁻



9 Thiols

u Thiols are stronger acids than alcohols



9 Thiols

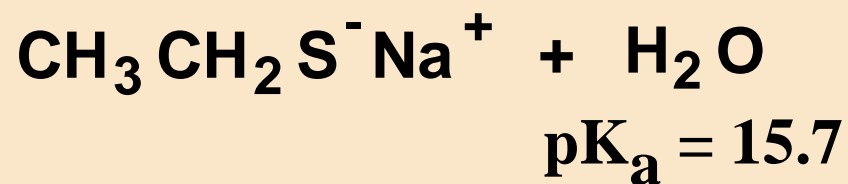
- u When dissolved in an aqueous NaOH, they are converted completely to alkylsulfide salts



$$\text{pK}_a = 8.5$$

Stronger
acid

Stronger
base

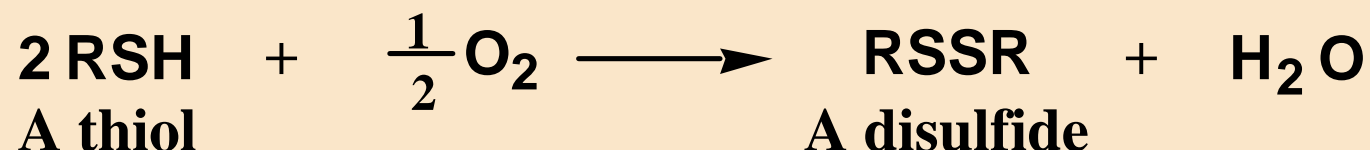


Weaker base

Weaker
acid

9 Thiols

- u Thiols are oxidized to disulfides by a variety of oxidizing agents, including O_2 . They are so susceptible to this oxidation that they must be protected from air during storage



- u The most common reaction of thiols in biological systems is interconversion between thiols and disulfides, -S-S-

9

Alcohols and Thiols

End of Chapter 9

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