

Fundamentals of Chemistry, Module III: Organic Chemistry

Semester-1, CCF-2022 (NEP)

Course: CHEM-H-CC-2-2-TH

Course taught by: Kaushik Basu, Department of Chemistry, SPCMC, Kolkata

email: chiralkaushik@gmail.com



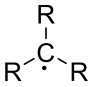

Recommended texts:

1. Study Guide to Organic Chemistry, Volume 1, Second Ed., by Saha, Chakraborty, Saha & Basu, Techno World, ISBN 978-8192669564,
2. Organic Chemistry, Second Ed. by Clayden, Greeves & Warren, OUP, ISBN 978-0198728719

Reactive Intermediates in Organic Chemistry:

Reactive intermediates (RI/I): A molecular entity / chemical species with a lifetime appreciably longer than a molecular vibration (which typically takes $\sim 10^{-10}$ s) that is formed (directly or indirectly) from the reactants and reacts further to give (either directly or indirectly) the products of a chemical reaction.

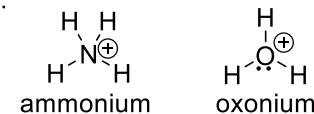
A typical RI in organic chemistry involves a carbon which either does not have the requisite four bonds or the full complement of eight electrons. The most common RIs are of four types: Carbocations, Carbanions, Free radicals and Carbenes. These are represented as:

				
	carbocation	carbanion	free radical	carbene
No. of electrons around carbon:	6	8	7	6
Nature:	electrophilic	nucleophilic	nucleophilic / electrophilic (depends on R)	nucleophilic / electrophilic (depends on R)

Let us one by one discuss the structural features, relative stabilities, ways of generation and some common reaction pathways of these RIs.

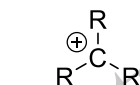
Carbocations: Earlier, the positively charged intermediate which we now refer to as carbocation was called the "carbonium ion".

It is a misnomer, as "-onium" generally refers to a covalence higher than that of the neutral atom. For example, in ammonium ion the nitrogen atom is quadravalent and has a complete octet while, in general, N is trivalent. Similarly we have oxonium ions.

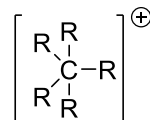


In this sense, carbonium should be R_5C^{\oplus}

These species are found, although very rarely. Much more common is another variation where C has valency 3, instead of general quadravalency. For example, the R_3C^+ , as drawn above. The trivalent, e^- -deficient carbocation is called the *carbenium ion*. In general, when we refer to carbocation, we mean this more common R_3C^+ species.



carbenium ion,
central C is tricoordinated and hypovalent,
has 6 valence electrons around it
structure can adequately be described by
two-electron two-centre bonds only.



carbonium ion,
central C is pentacoordinated and hypervalent,
has 8 valence electrons around it
structure cannot adequately be described by
two-electron two-centre bonds only.

Reactive Intermediates in Organic Chemistry:

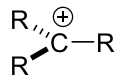
Structure and classification of carbocations:



Sextet of electrons
with three attached
groups

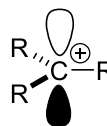
implies:

electrophilic nature



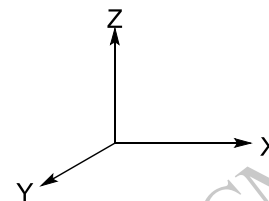
Trigonal planar
geometry

sp^2 hybridisation



sp^2 hybridised

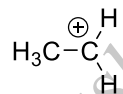
p_z orbital is vacant
 σ -bonds formed using the
 sp^2 hybrid AOs in XY plane



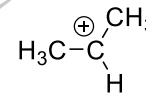
A] Classification depending upon the number of carbons attached to the positively charged carbon:



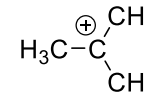
Methyl carbocation
No C-C⁺ Bond



1^o carbocation
One C-C⁺ Bond
(ethyl cation,
primary)



2^o carbocation
Two C-C⁺ Bond
(isopropyl cation,
secondary)



3^o carbocation
Three C-C⁺ Bond
(*tert*-butyl cation,
tertiary)

No. of carbons attached
to +vely charged C:

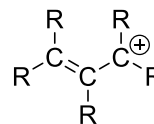
0

1

2

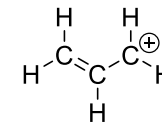
3

B] If the carbon bearing the positive charge is immediately adjacent to a carbon-carbon double bond, the carbocation is called an allylic carbocation. The simplest case (when all R = H) is known as the allyl carbocation:



allylic carbocation

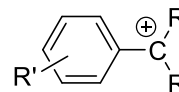
This is also a tertiary carbocation.



allyl carbocation

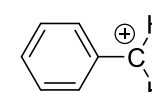
This is also a primary carbocation.

C] If the cationic carbon is immediately adjacent to a benzene ring, the carbocation is termed as benzylic carbocation. The simplest case is the benzyl carbocation.



benzylic carbocation

This is also a tertiary carbocation.



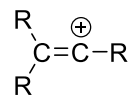
benzyl carbocation

This is also a primary carbocation.

Reactive Intermediates in Organic Chemistry:

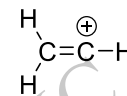
Structure and classification of carbocations:

D] If the carbon bearing the positive charge is part of an alkene, the carbocation is a vinylic carbocation. The simplest case is the vinyl carbocation.



vinylic carbocation

This is also a secondary carbocation.



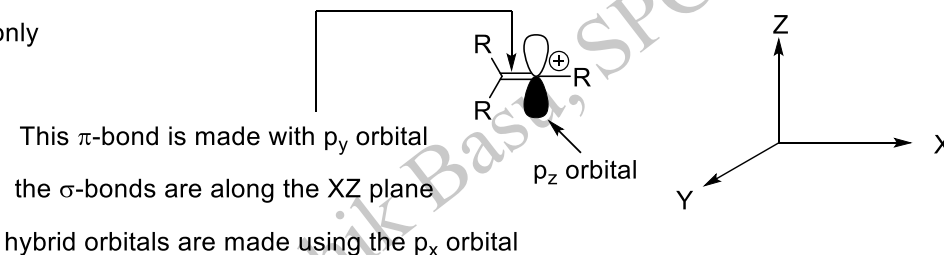
vinyl carbocation

This is also a primary carbocation.

Note that in this case the positively charged carbon atom has only two groups attached to it and is linear in shape.

This indicates an sp hybridization.

The carbon has one vacant p orbital.



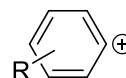
This π -bond is made with p_y orbital
the σ -bonds are along the XZ plane

The sp hybrid orbitals are made using the p_x orbital

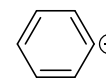
E] If the carbon bearing the positive charge is part of a benzene ring, the carbocation is termed as an aryl carbocation. The simplest case is called the phenyl carbocation.

The positively charged carbon is sp^2 hybridised and one of the sp^2 hybrid orbitals is vacant. The p_z orbital is used to form the π -bond with the adjacent ring carbon.

These two orbitals are orthogonal, so they do not overlap with each other.



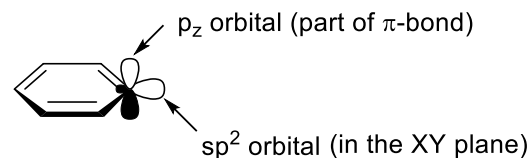
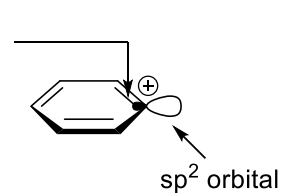
aryl carbocation



phenyl carbocation

both secondary carbocations

π -bond formed
b/w p_z orbitals



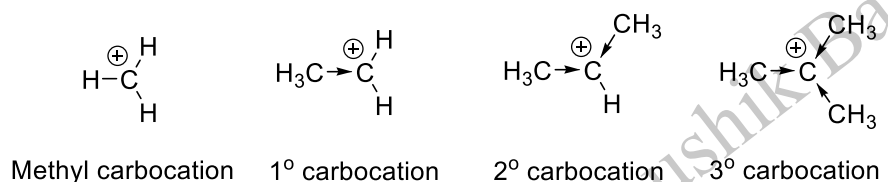
Reactive Intermediates in Organic Chemistry:

Stability of carbocations: Factors responsible:

A] Inductive and field effect:

Among the simple alkyl carbocations, the order of stability is: $\xrightarrow{\text{3}^\circ \text{ carbocation, 2}^\circ \text{ carbocation, 1}^\circ \text{ carbocation}}$
stability decreases

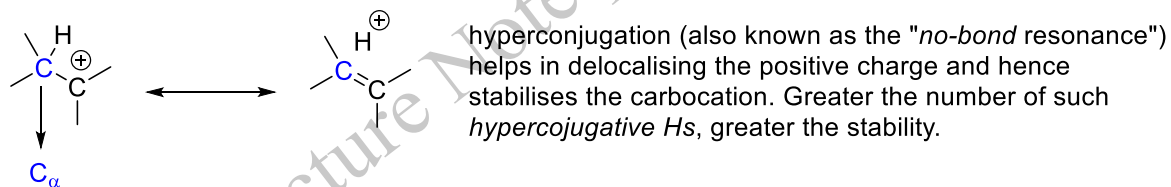
The increasing stability with increase in the number of alkyl substituents can be explained on the basis of inductive and field effect. Recall that inductive effect is the electron displacement mechanism operating through sigma bond while field effect operates through space. Alkyl groups are inductively ER in nature (+I effect) and at the same time they are quite polarisable which helps in stabilizing a neighbouring charge.



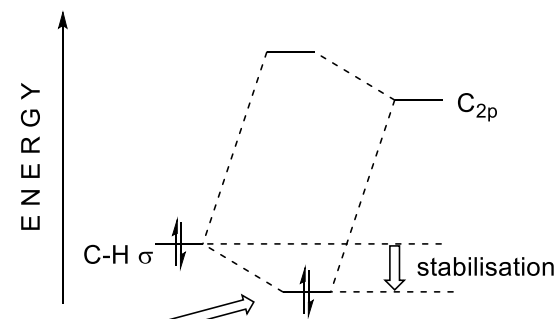
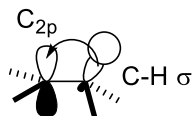
with the increasing number of alkyl groups electron-donating inductive and field effect increases, i.e. stability increases; delocalisation of positive charge will stabilise the carbocation; greater the delocalisation, greater is the stability

B] Hyperconjugation:

If the positively charged carbon centre of a carbocation has an adjacent saturated carbon (C_α) with C-H bond(s), it can delocalize its charge through hyperconjugation. In resonance description, we have the following canonical forms:

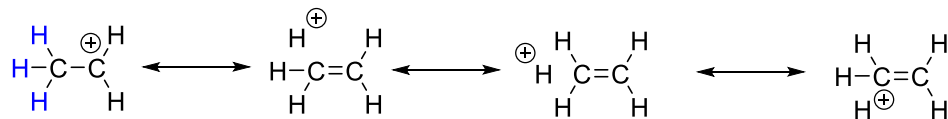


In MO terms, this is transfer of e density from the C_α -H sigma MO into the adjacent vacant p orbital:

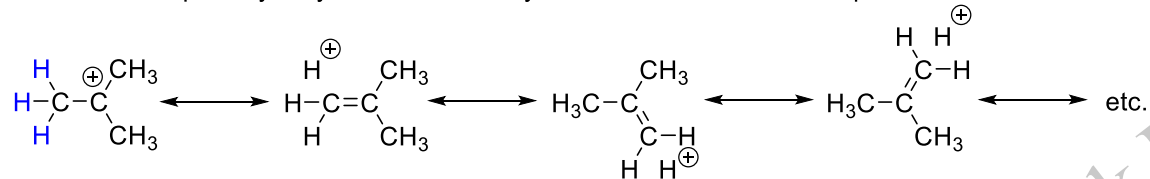


e-pair is lowered in energy, overlap is stabilising in nature

Stability of carbocations: Factors responsible:

 B) Hyperconjugation (contd.): Greater the number of such *hyperconjugative Hs*, greater the stability.


For primary ethyl carbocation only three canonical forms are possible


 For *tertiary*-butyl carbocation nine canonical forms are possible

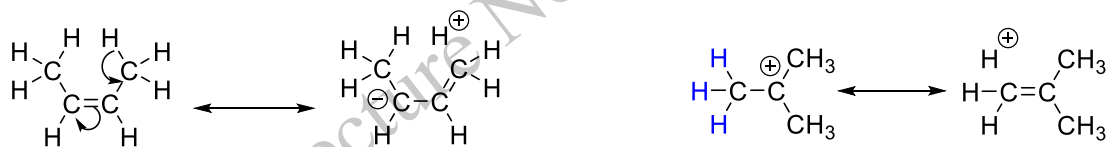
For a secondary carbocation like isopropyl cation, six canonical forms are possible. (try!)

Based upon this analysis done above, we can say:

	methyl cation	primary	secondary	tertiary
No. of hyperconjugative H:	0	3	6	9
	—————→ stability increases			

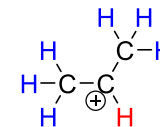
This is the same trend as observed when we discussed inductive effect.

Recall that we've already seen hyperconjugation in alkenes:


 This is an example of 'heterovalent' or 'sacrificial hyperconjugation', so named because the contributing structures contains one two-electron bond *less* than the normal Lewis formula

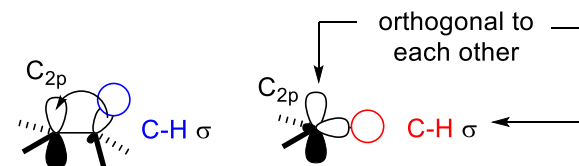
 In contrast, the hyperconjugation seen in carbocations is called *isovalent* hyperconjugation.

What is a hyperconjugative H?

 H on the carbon that is adjacent to the positively charged carbon. Any H that is directly attached to the carbon carrying the positive charge is *not* the hyperconjugative H.

 The **blue** Hs can take part in hyperconjugation

 The **red** H cannot take part in hyperconjugation

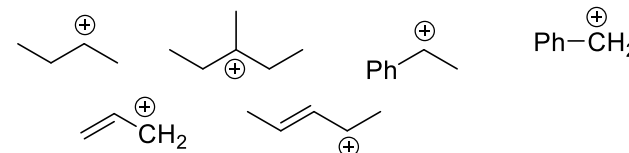
Methyl cation does not have any H that can take part in hyperconjugation:


 C-H σ and C_{2p} orbitals parallel - overlap possible

No overlap possible b/w orbitals shown

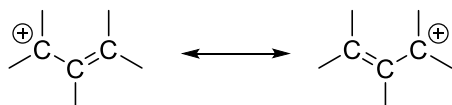
Homework:

Identify the following carbocations as primary/secondary/tertiary and count the number of hyperconjugative Hs

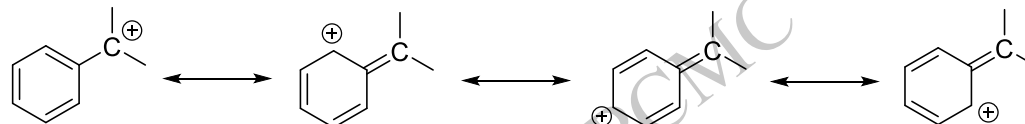


Stability of carbocations: Factors responsible:

C] Resonance / conjugation: Delocalization of positive charge is very effective when it is in conjugation with an olefinic double bond. Case in point is the allylic and benzylic carbocation:

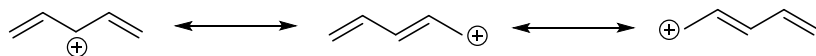


Positive charge is delocalised over three atoms instead of being localized over one

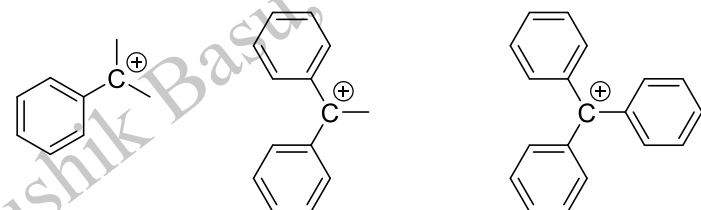


Positive charge is delocalised over the benzene ring

Greater the conjugation, higher is the stability:



divinylmethyl carbocation



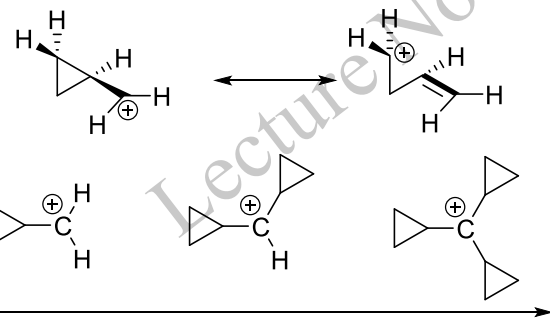
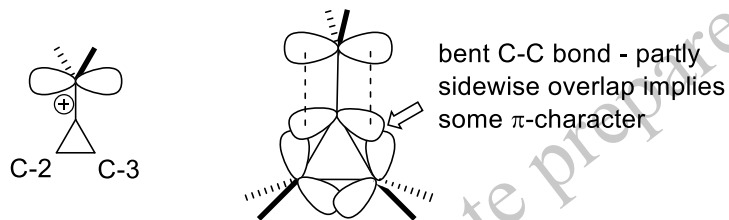
aryl cation

diarylmethyl cation

triarylmethyl cation

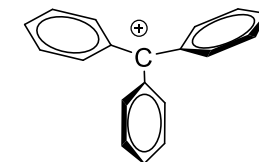
Stability increases

As discussed earlier, a cyclopropyl group adjacent to a positively charged carbon can delocalise the charge, by conjugation using the bent C-C bond orbitals:

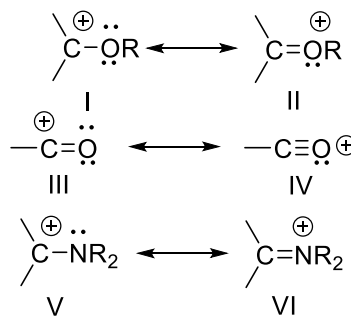


stability increases

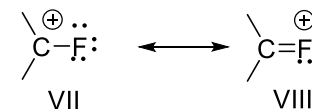
To minimize the steric congestion among the phenyl groups, triphenylmethyl cation (aka the trityl cation) develops a propeller-twist, This twisted shape implies loss of conjugation to some extent.



The other structural feature which stabilizes a carbocation is the presence of a heteroatom with unshared pair of electrons adjacent to the carbon bearing the positive charge.



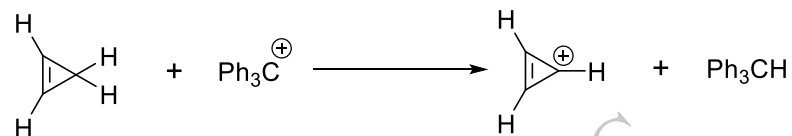
Canonical forms II, IV, VI and VIII, inspite of having a positive charge on the electronegative oxygen atom, is more stable because in this canonical each element has an octet.



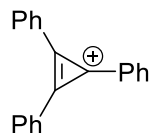
Reactive Intermediates in Organic Chemistry:

Stability of carbocations: Factors responsible:

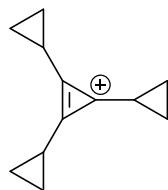
D] Aromaticity: Cyclopropene is reported to undergo facile hydride exchange with triphenylmethyl cation:



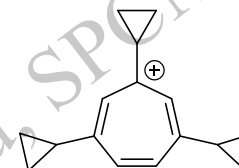
The cyclopropenyl cation is more stable than the trityl cation. This unusually high stability of cyclopropenyl cation is a result of its aromaticity, i.e. its bonding MOs being completely occupied.



The triphenyl derivative of cyclopropenyl cation has also been synthesized and is found to be relatively stable.



tricyclopropylcyclopropenyl cation among the most stable carbocations known, capable of existence even in water.

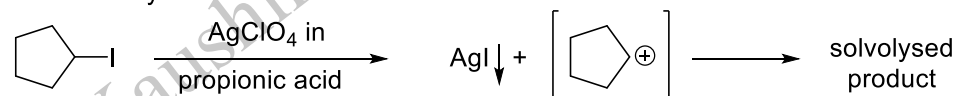


tricyclopropyl dev. of tropylium cation - which is itself aromatic.

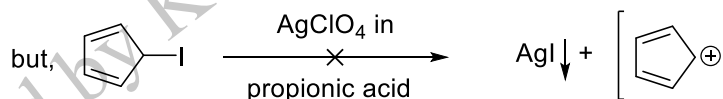
On the other hand, the cyclopentadienyl cation contains 4π -electrons:



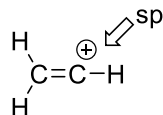
Proof of instability:



This is antiaromatic and hence very difficult to form.

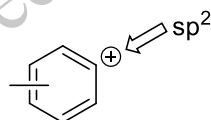
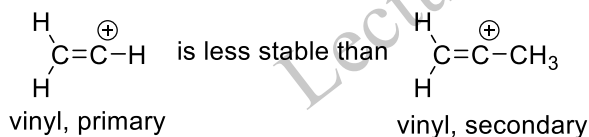


E] The two rather unstable carbocations:



vinyl cation

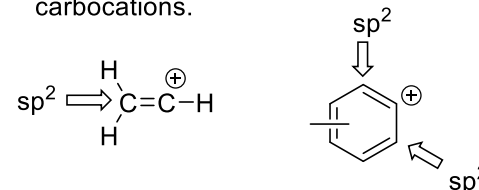
the e-deficient, positively charged carbon is sp hybridised; recall that sp carbon is more electronegative than sp^2 ones, and less able to support the positive charge



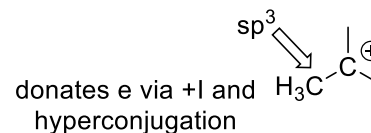
aryl cation

the e-deficient, positively charged carbon is sp^2 hybridised; but the vacant orbital is one sp^2 , unlike the p-orbital common to trigonal planar carbocations. It is better for a cation to have a vacant p orbital rather a vacant sp^2 orbital as the latter has 33% s-character.

In addition, the positive charge bearing carbon in a vinyl and in an aryl cation is attached to one and two sp^2 carbons respectively. These sp^2 carbons are more electronegative than sp^3 . The inductive EW effect of these further destabilise the vinylic and aryl carbocations.



Compare these with:

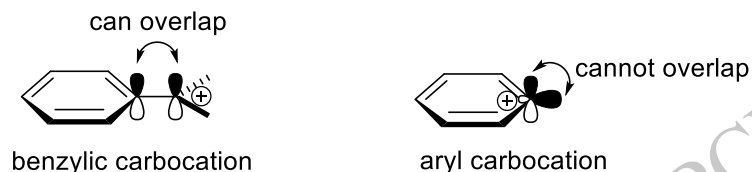


Reactive Intermediates in Organic Chemistry:

Stability of carbocations: Factors responsible:

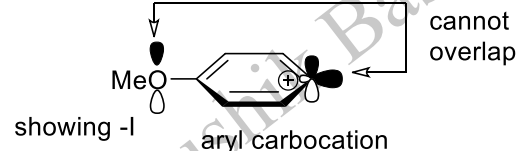
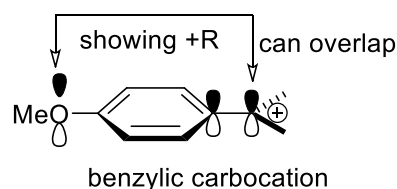
E] Aryl carbocation versus benzylic carbocation (contd.):

Note carefully, aryl cation cannot enjoy any resonance stabilisation from the aryl ring, unlike the benzylic carbocation:

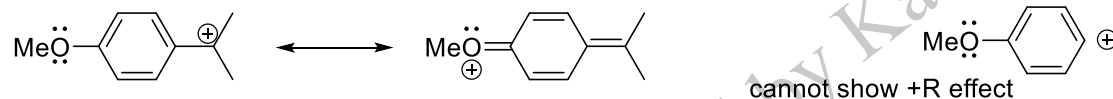


Any heteroatom-based substituent that we put on the aryl ring, it can act as a +R ER group for benzylic cation if placed at the appropriate position, but for the aryl cation it will always act as an -I EW group as it cannot show its +R effect.

The OMe can operate through both the sigma and the pi network of the benzene ring; through the sigma network it is -I but through pi it is +R. OMe has a stabilising influence here

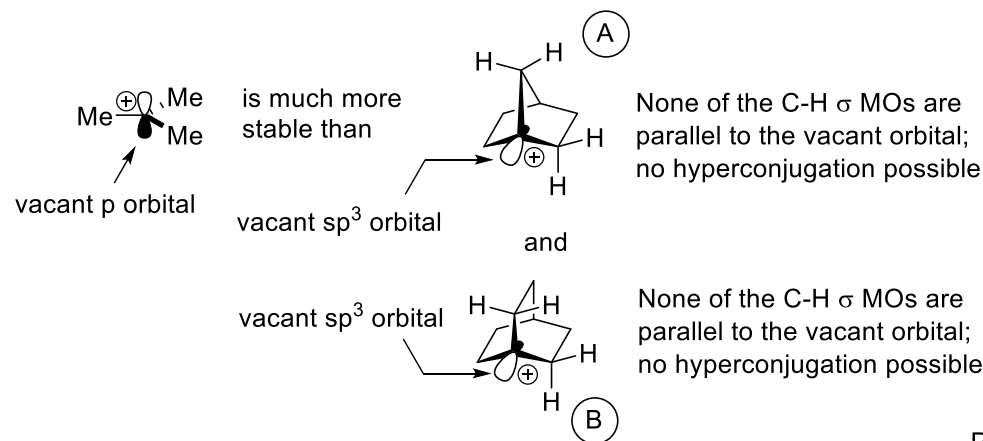
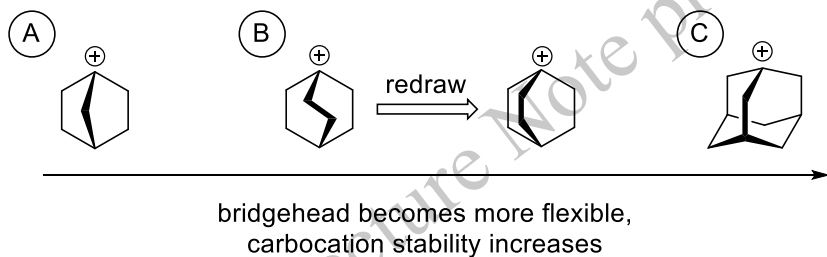


The OMe can operate only through the sigma network of the benzene ring and shows only the -I effect. OMe has a destabilising influence here



F] Carbocation at the bridgehead: Strain

Tricoordinated, positively charged carbon in the carbocation has to be planar. This is difficult to achieve in the bridgehead positions in the following systems. As the system becomes more flexible, the carbocations at the bridgehead becomes somewhat more stable (relative to more rigid bridgehead cations)



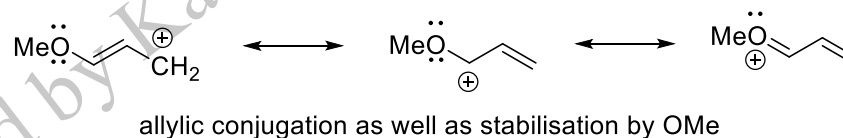
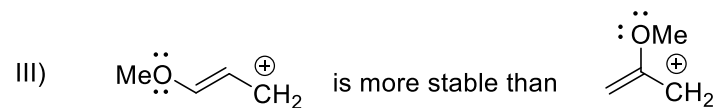
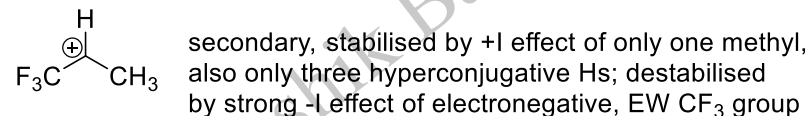
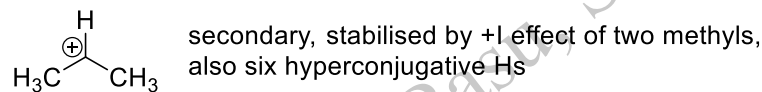
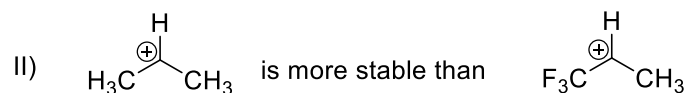
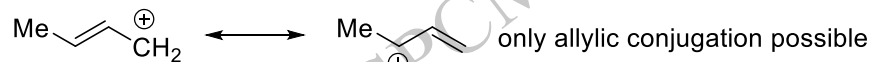
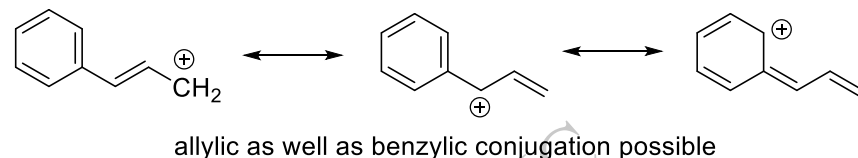
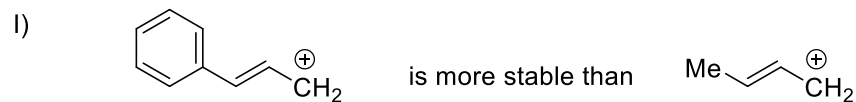
None of the C-H σ MOs are parallel to the vacant orbital; no hyperconjugation possible

None of the C-H σ MOs are parallel to the vacant orbital; no hyperconjugation possible

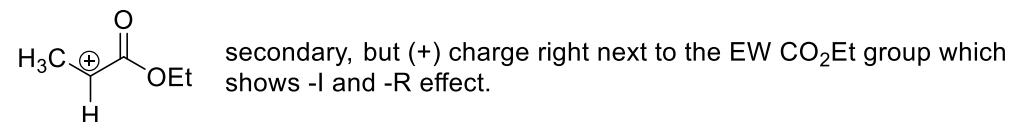
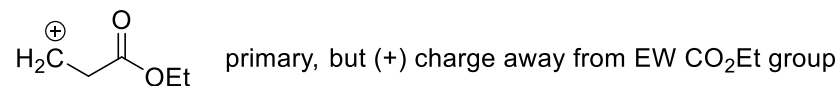
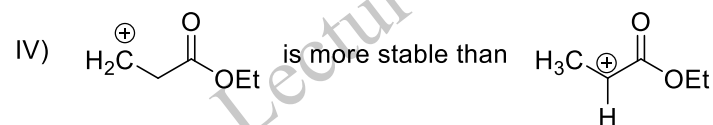
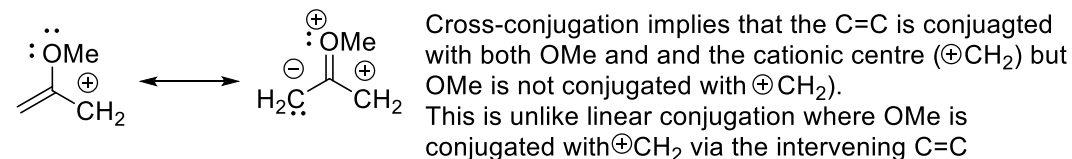
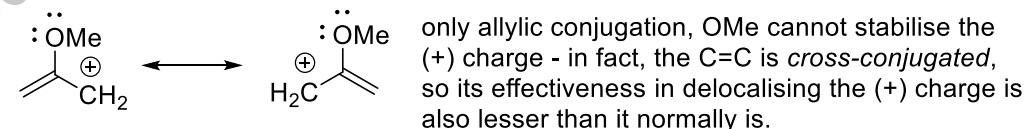
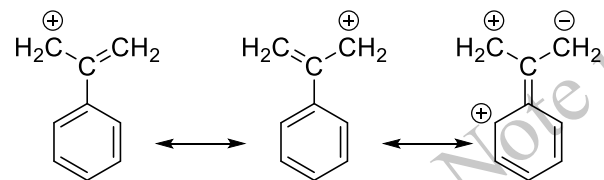
As the rings become more flexible (less rigid) the bridgehead carbon can become a little bit flatter. Consequently, it can handle the positive charge a little bit better. Note that all carbocations are tertiary but their stability differs widely.

Reactive Intermediates in Organic Chemistry:

Stability of carbocations: Comparing the relative stability - a few case studies

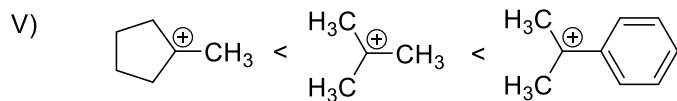


Example of another cross-conjugated system:
2-phenylallyl

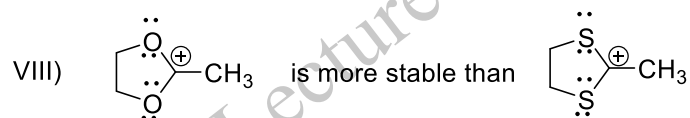
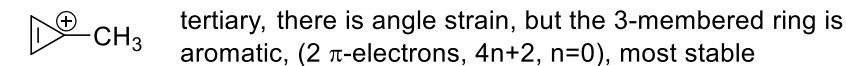
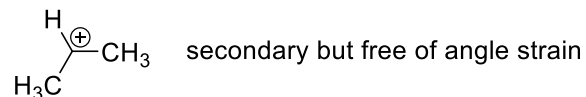
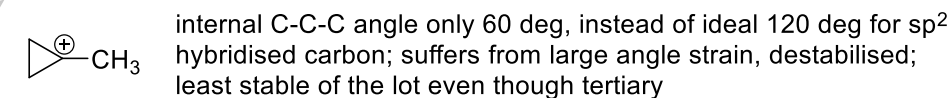
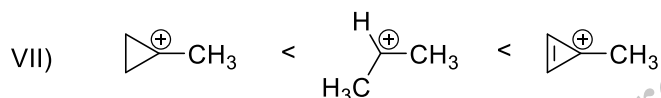
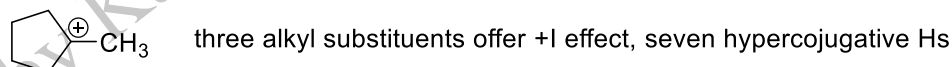
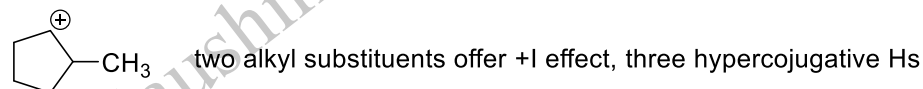
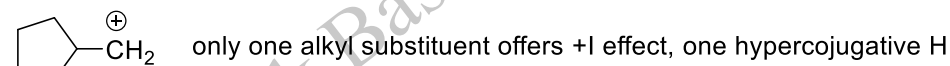
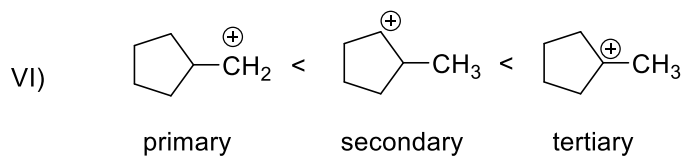
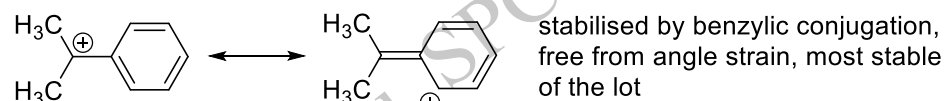
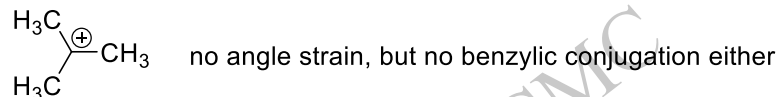
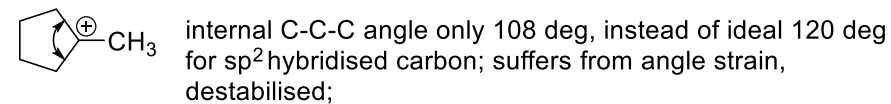


Reactive Intermediates in Organic Chemistry:

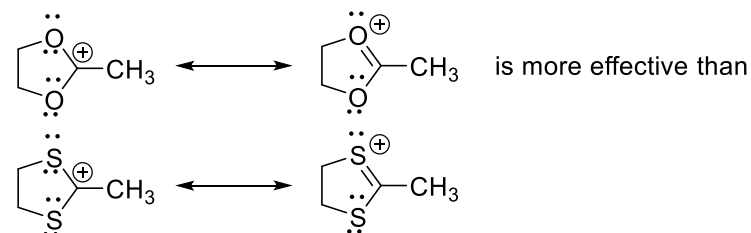
Stability of carbocations: Comparing the relative stability - a few case studies



All tertiary carbocations, yet stability different

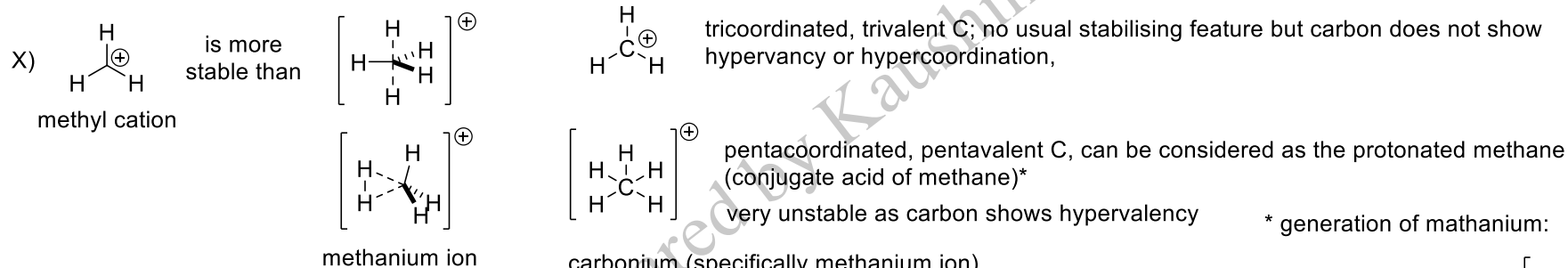
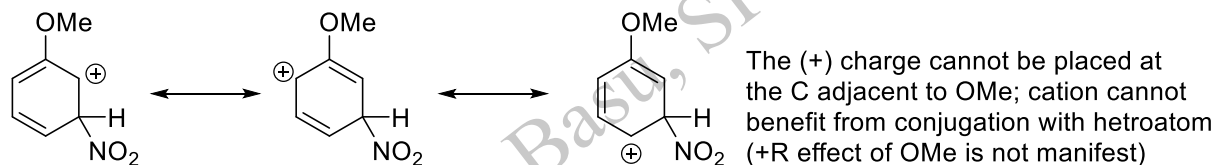
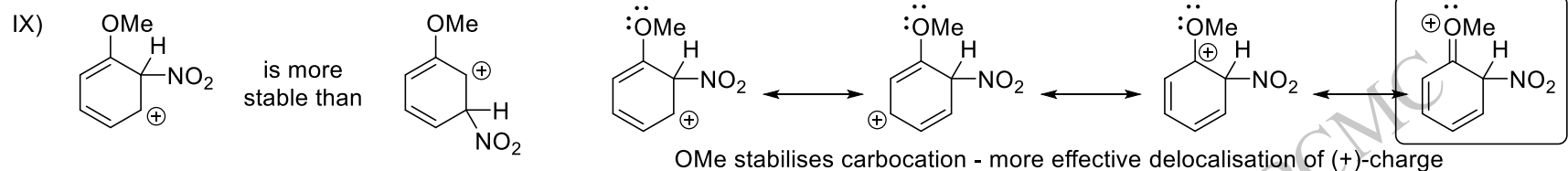


Both carbocations benefit from heteroatom conjugation, but conjugation between C(2p) and O(2p) is more effective than between C(2p) and S(3p) - due to orbital size mismatch in the latter case



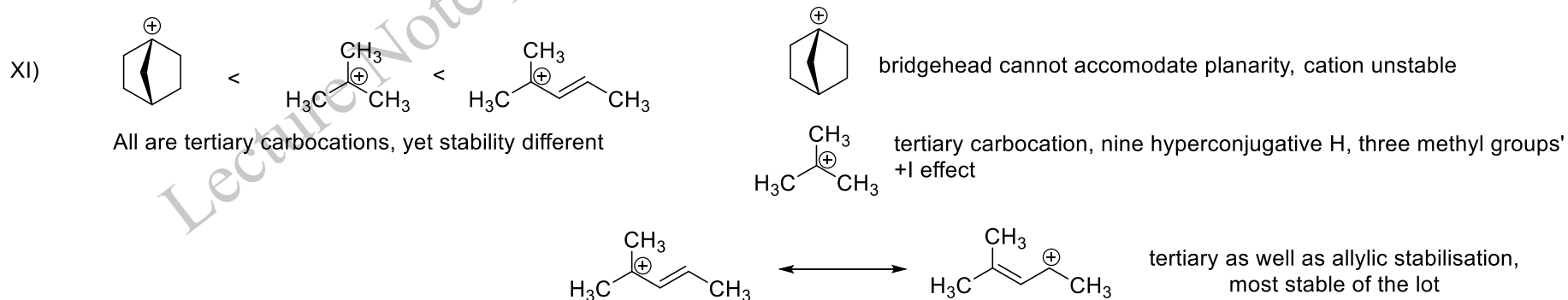
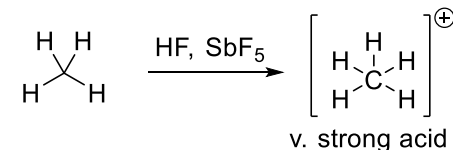
Reactive Intermediates in Organic Chemistry:

Stability of carbocations: Comparing the relative stability - a few case studies



carbonium (specifically methanium ion) - a non-classical carbocation, complete description using only 2c-2e bond not possible.

* generation of mathanium:



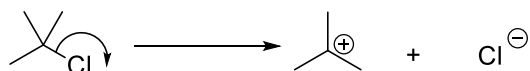
Reactive Intermediates in Organic Chemistry:

Generation and fate of carbocations:

Generation:

A] via heterolysis of carbon-heteroatom bond:

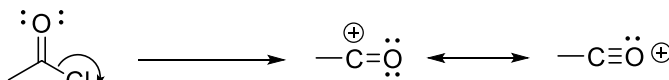
from alkyl halides:



carbocation formation is facilitated by polar, ionising solvent

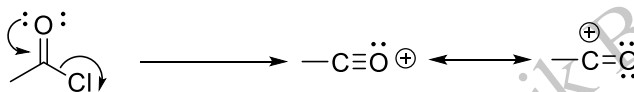
This is the first step of unimolecular nucleophilic substitution and elimination (S_N1 and E1) reactions

from acyl halides:

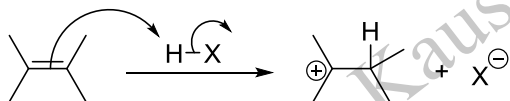


an acylium ion - carbocation stabilised by oxygen lone pair

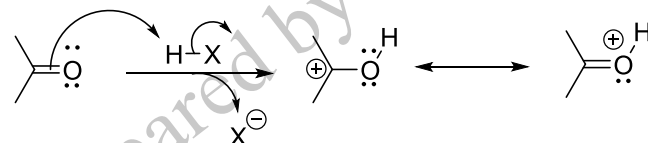
alternative representation:



B] via protonation of carbon-carbon and /or carbon-heteroatom multiple bond:

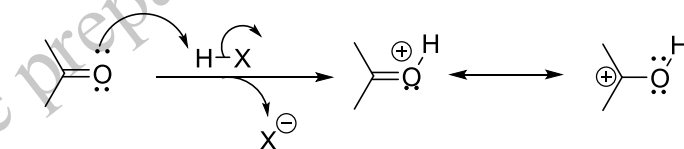


first step of electrophilic addition to C=C

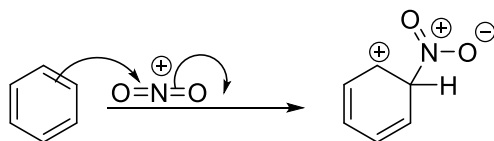


an oxocarbenium ion - carbocation stabilised by oxygen lone pair

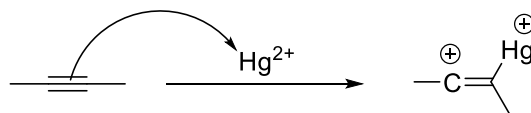
alternative representation:



C] via reaction of carbon-carbon multiple bond with an electrophile:



nitronium ion is the electrophile here
first step of aromatic electrophilic substitution



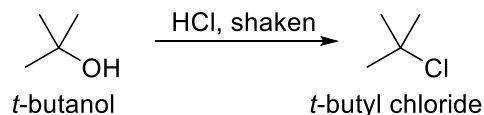
Hg(II) ion is the electrophile here

Reactive Intermediates in Organic Chemistry:

Generation and fate of carbocations:

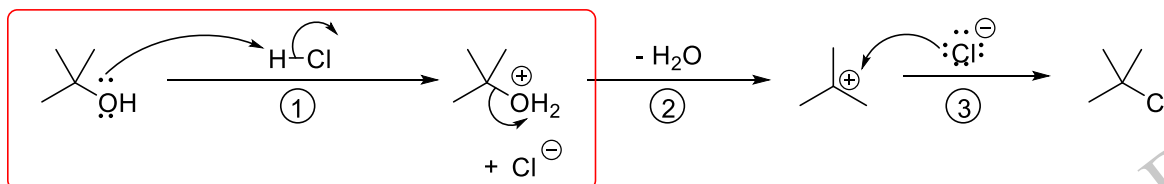
Fate:

A] Capture by a nucleophile: Example-1



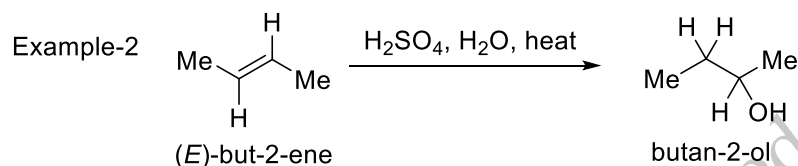
This is a *nucleophilic substitution* reaction, OH is the displaced by chloride. More exactly, S_N1 reaction, substitution, nucleophilic, unimolecular

The reaction is believed to proceed in the following way:

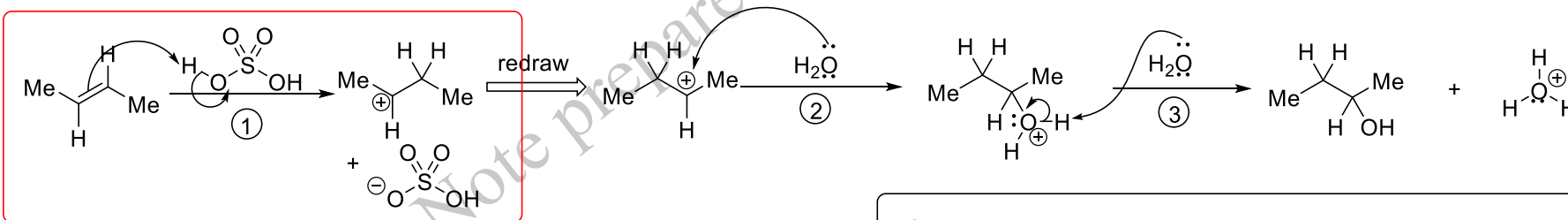


- ① protonation, t-butanol acting as a base
- ② loss of water, generation of carbocation; C-O bond breaks
- ③ nucleophilic capture of the carbocation, chloride ion as nucleophile; C-Cl bond forms

Questions: Why does the OH not leave directly? Why do we need to protonate it?
Answers will be found later.



This is an *addition reaction*, the elements of water (H, OH from H-OH) are added across the C=C, we get an alcohol. This the hydration (adding the components of water into a molecule) of alkene to an alcohol.



- ① protonation, the alkene acting as a base, generation of carbocation; C=C bond breaks, O-H bond breaks, C-H bond forms
- ② nucleophilic capture of the carbocation, water as nucleophile; C-O bond forms
- ③ deprotonation, water acting as a base; one O-H bond breaks, other O-H bond forms

The reaction starts with an addition of a proton to one of the olefinic carbon. As proton can be considered to be an electrophile, we can say that this addition starts off by adding an electrophile (proton) to the C=C. So we call this addition reaction an *electrophilic addition*. Note that if the proton is considered as an electrophile, the C=C is the nucleophile in the first step.

Reactive Intermediates in Organic Chemistry:

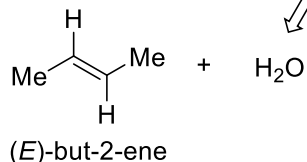
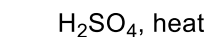
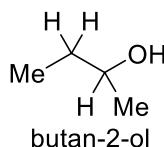
Generation and fate of carbocations:

Fate:

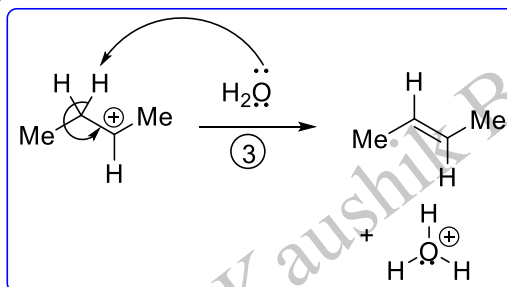
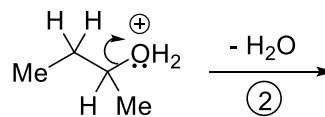
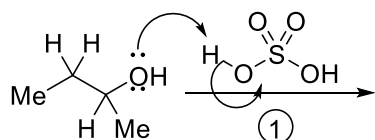
B] Loss of a proton from adjacent carbon to form a C=C:

Gets protonated in presence of strong acid, but let us for now assume that it remains as H₂O

Example-1

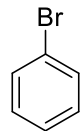
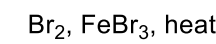
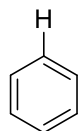


This is a an *elimination* reaction, H and OH (H₂O) is eliminated to form a C=C. More exactly, E₁ reaction, elimination, unimolecular. This is dehydration of alcohol to an alkene.



- ① protonation, the alcohol acting as a base; which bond breaks? which bond forms?
- ② loss of water, formation of the carbocation; which bond breaks?
- ③ deprotonation, water acting as a base, C-H bond breaks; proton loss leads to formation of a C=C bond

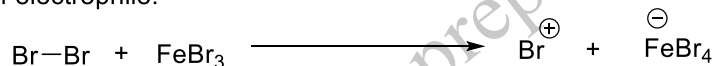
Example-2



This is a an *electrophilic substitution reaction* (on aromatic ring), in short, we call this aromatic electrophilic substitution (S_EAr)

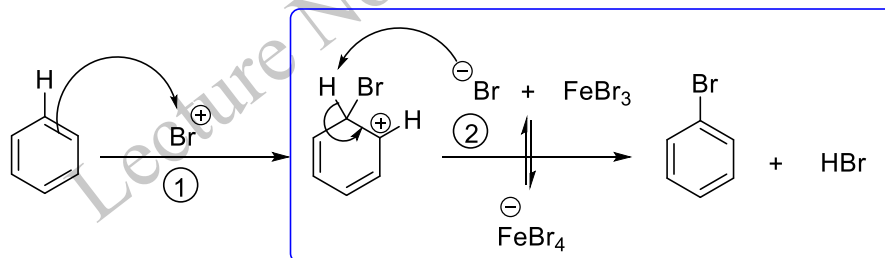
Proton is being replaced by Br⁺.
This is bromination of benzene ring.

Generation of electrophile:



Br⁺ is the electrophile

Reaction of the electrophile with aromatic ring:



- ① addition of electrophile, generation of carbocation; C=C bond breaks, C-Br bond forms
- ② deprotonation, bromide acting as the base; which bond breaks? which bond forms?

Notice how the aromaticity of the ring is lost in the first step, but is regained immediately in the second step.

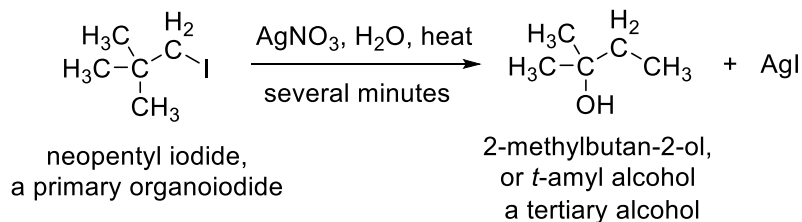
Reactive Intermediates in Organic Chemistry:

Generation and fate of carbocations:

Fate:

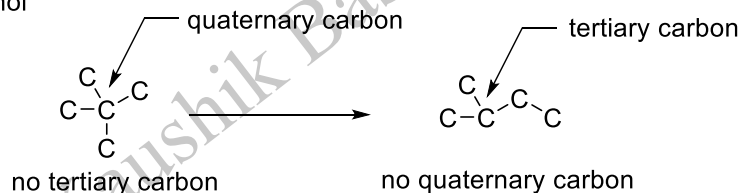
C] Rearrangement to another carbocation:

Example-1

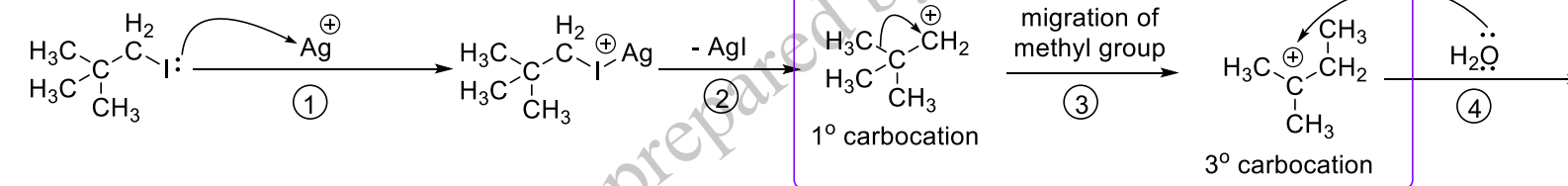


This is a nucleophilic substitution reaction, OH replaces iodide. More exactly, S_N1 reaction, substitution, nucleophilic, unimolecular.

Clearly, there has occurred a *rearrangement of the carbon skeleton* from the reactant to the product here:



The reaction is believed to proceed in the following way:



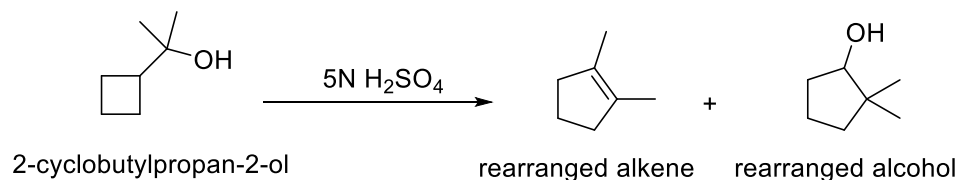
Recall that a tertiary carbocation is *generally* more stable than a secondary carbocation.

Generation and fate of carbocations:

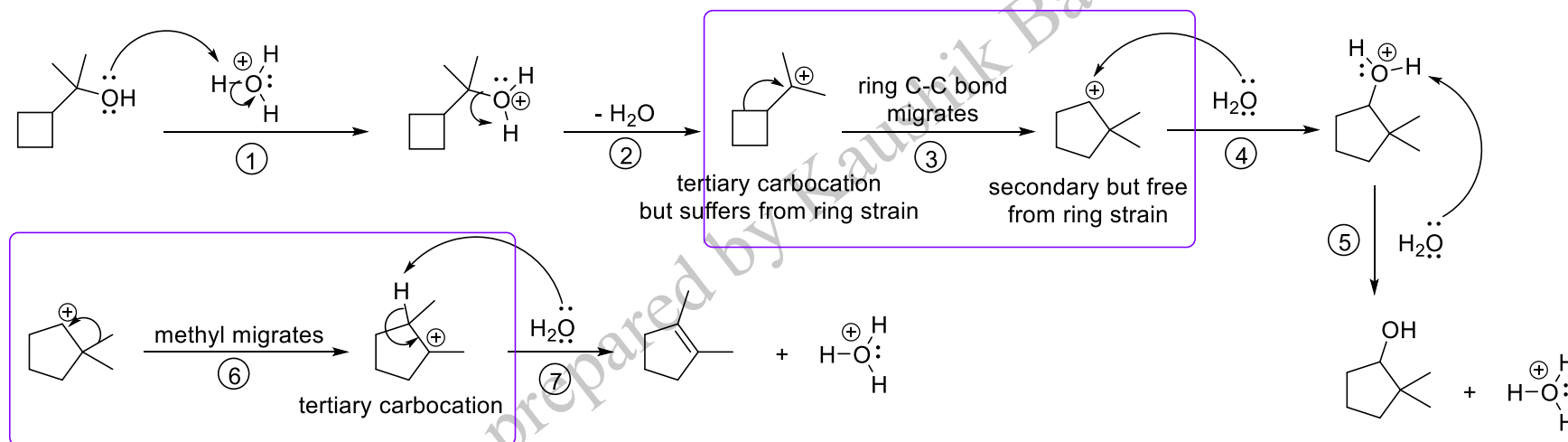
Fate:

C] Rearrangement to another carbocation:

Example-2



The reaction is believed to proceed in the following way:



- ① protonation of OH
- ② loss of water, formation of the carbocation
- ③ carbocation rearrangement by ring expansion, from less stable to more stable RI
- ④ nucleophilic capture of carbocation by water
- ⑤ deprotonation, water acting as a base, alcohol formed

- ⑥ carbocation rearrangement by methyl shift, from less stable to more stable RI
- ⑦ loss of proton, water acting as a base, alkene formed

Take home lesson: carbocations rearrange by shifting alkyl groups or hydrogens to generate even more stable carbocations.

Think which bonds are being broken and formed in each of the steps.