Organic reactive intermediate:

Reactive intermediate or an intermediate is a short-lived, high-energy, highly reactive molecule. When generated in a chemical reaction, it will **quickly convert into a more stable molecule**. Only in **exceptional cases** can these compounds be **isolated** and **stored**, **this usually involves changing reaction conditions such as low temperature or concentration and applying the techniques of chemical kinetics, chemical thermodynamics, or spectroscopy**. When their existence is indicated, **reactive intermediates can help explain how a chemical reaction** takes place. **Reactive intermediates based on carbon are** free **radicals**, **carbenes**, **carbocations**, **carbanions**, **nitrenes**, and **benzynes**.

Common features of intermediate:

Reactive intermediates **have several** features in common:

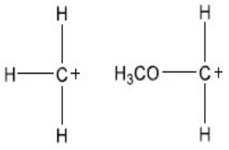
1. **Low concentration** concerning the reaction substrate and the final reaction product.
2. Often **generated** by the **chemical decomposition** of a chemical compound.
3. It is often **possible to prove** the existence of this species by **spectroscopi**c means.
4. Often **stabilization** by **conjugation** or **resonance**.
5. Often **difficult to distinguish** from a **transition state**.
6. **Prove existence** using **chemical trapping**.

A carbocation: is molecule having a carbon atom bearing three bonds and a positive formal charge. It is **sp^2 hybridized** with a planar structure and bond angles of about 120°, such as methenium **CH_3^+ which contans the vacant unhybridized p orbital lies perpendicular to the plane of C—H bonds**, and ethanium $C_2H_7^+$. **Carbocations** are generally **unstable because they do not have eight electrons to satisfy the octet rule**.

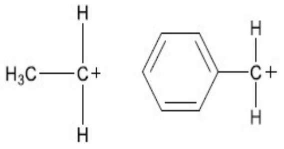
Carbocation Classification:

To understand carbocations, we need to learn some basic carbocation nomenclature concerning the **number of carbon groups bonded to the open valence shell carbon**. A **carbocation in which the open valence shell carbon is not bonded to any carbon groups is termed a methyl carbocation**, the **methyl group** is so **unstable** it is **only observed** in the **gas phase**. A **primary carbocation (1^o carbocation) is one in which there is one carbon group attached to the carbon bearing the positive charge**. A **secondary** (**2^o**) carbocation is one in which there are **two carbons attached to the carbon bearing the positive charge**. Likewise, a **tertiary (3^o) carbocation is one in which there are three carbons attached to the carbon bearing the positive charge**.

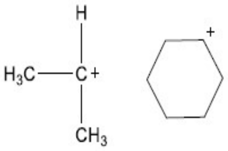
Examples:



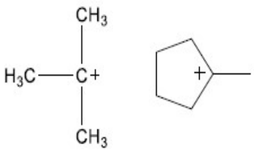
Methyl carbocations
No C–C$^+$ bonds



Primary (1^o) carbocations
One C–C$^+$ bond



Secondary (2^o) carbocations
Two C–C$^+$ bonds



Tertiary (3^o) carbocations
Three C–C$^+$ bonds

Carbocations are often the target of **nucleophilic attack by nucleophiles** such as water or halide ions. **Carbocations** typically undergo **rearrangement reactions from less stable structures to equally stable or more stable ones**.

A **carbocation** may be **stabilized** by **resonance** by a **carbon-carbon double bond** next to the **ionized carbon**. Such cations as **allyl** cation ($CH_2=CH–CH_2^+$) and **benzyl** cation **($C_6H_5–CH_2^+$)** are **more stable than most other carbocations**. Molecules that can form **allyl or benzyl** carbocations are **especially reactive**. These carbocations where the **C$^+$ is adjacent to another carbon atom that has a double or triple bond have extra stability because of the overlap of the empty p orbital of the carbocation with the p orbital's of the π bond. This overlap of the orbital's allows the charge to be shared between multiple atoms delocalization of the charge and, therefore, stabilizes the carbocation**. Carbocations are the **key intermediates** in several reactions and particularly in **nucleophilic substitution** reactions.

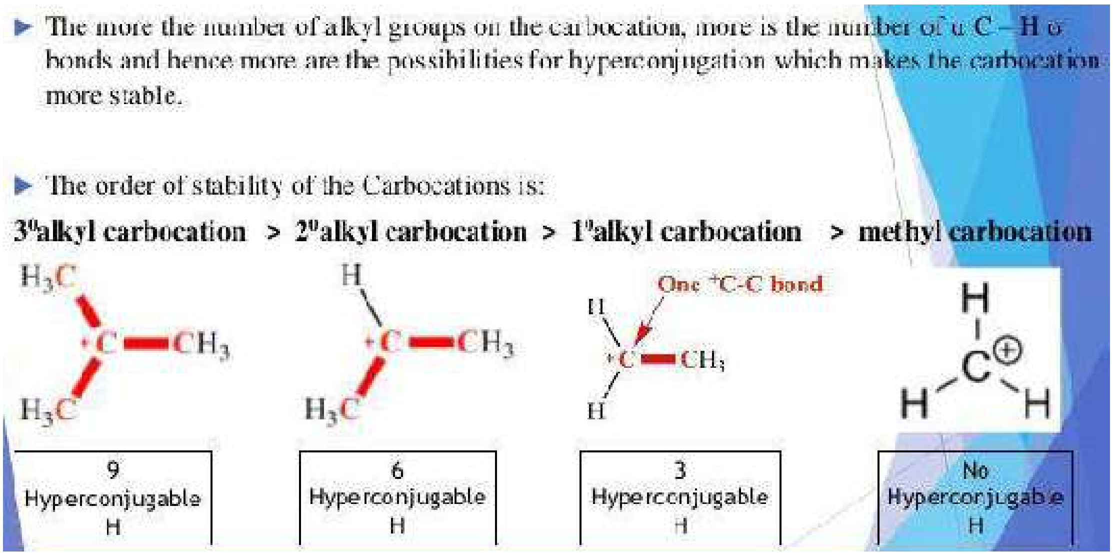
Stability of carbocation:

The stability order of carbocations bearing only **alkyl groups** is:

$$3^o > 2^o > 1^o > CH_3$$

Cation stability is influenced by four factors:

1. **Hyperconjugation** **Increasing the number of alkyl substituents increases the stability of the carbocation**. This is **due to the orbital overlap between the σ bond and the empty p orbital on the sp^2 carbon. Any structural feature which tends to reduce the electron deficiency at the tricoordinate carbon stabilizes the carbocation.**



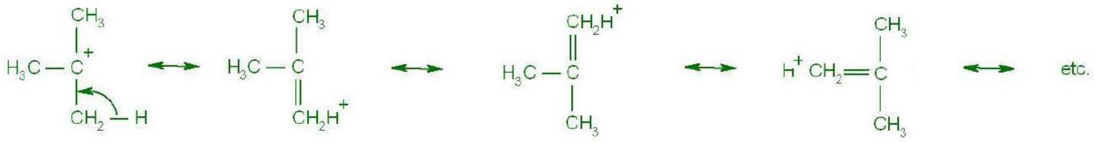
- The more the number of alkyl groups on the carbocation, more is the number of α C—H σ bonds and hence more are the possibilities for hyperconjugation which makes the carbocation more stable.

- The order of stability of the Carbocations is:

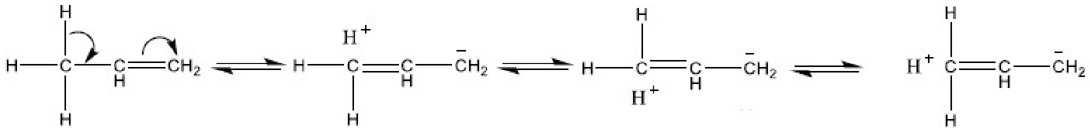
3°alkyl carbocation > 2°alkyl carbocation > 1°alkyl carbocation > methyl carbocation

9 Hyperconjugable H	6 Hyperconjugable H	3 Hyperconjugable H	No Hyperconjugable H

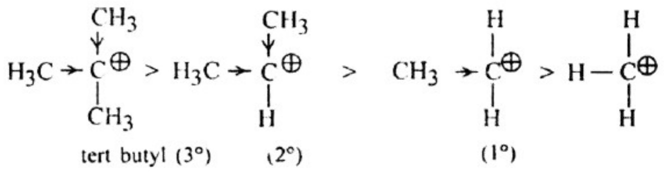
- **Tertiary carbocation is more stable than secondary.**



When an **alkyl group is attached to an unsaturated system such as a double bond or a benzene ring, the order of inductive effect is reversed**.

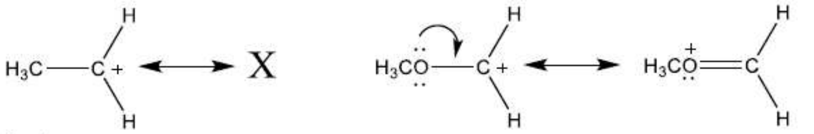


2. **Inductive Effects** **Neighbouring alkyl groups contain polarizable electrons and these can shift towards the positive charge**. (**Small Hydrogen substituent's cannot do this**).



3. **Resonance Effects** **Conjugation with multiple bonds or lone pairs of electrons increases the stability of a carbocation**. Therefore, allylic and benzylic systems are more stable than their saturated counterparts.

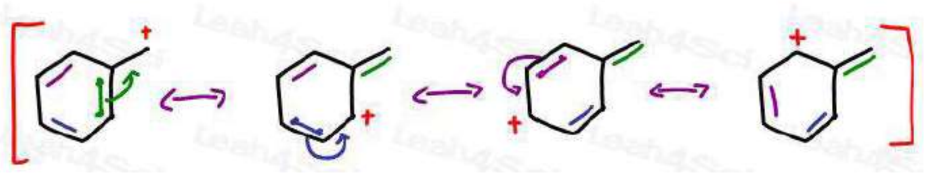
Be aware of the **potential for heteroatom's to stabilize carbocations (since they can have lone pairs)**.



Lacks resonance.
A less stable carbocation.

Has resonance delocalization of the open valence shell. A more stable carbocation.

an allylic carbocation



Benzylic carbocation

When the **positive carbon is in conjugation with a double bond**, the **stability is more**. This is so, **because due to resonance the positive charge is spread over two atoms instead of being concentrated on only one**. This explains the **stability associated with the allylic cation**. The **benzylic cations are stable**, since one can draw canonical forms as for allylic cations.

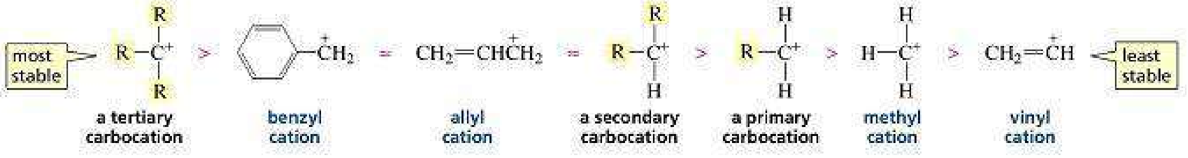
- **Electron donating p-methoxy and p-amino groups stabilize the carbocation by 14 and 26 kcal/mole, respectively. The electron withdrawing groups like p-nitro destabilize by 20 kcal/mol. A hetero atom with an unshared pair of electrons when present adjacent to the cationic centre strongly stabilizes the carbocation.**

4. **<u>Hybridization</u>** also influences cation stability. **The more s character in an orbital, the less stable the cation**. Therefore, **sp hybrid cations are very unstable**.

Due to the **resonance stabilization, a primary allylic or benzylic carbocation is almost as stable as a secondary alkyl carbocation and a secondary allylic or benzylic carbocation is about as stable as a tertiary alkyl carbocation.**

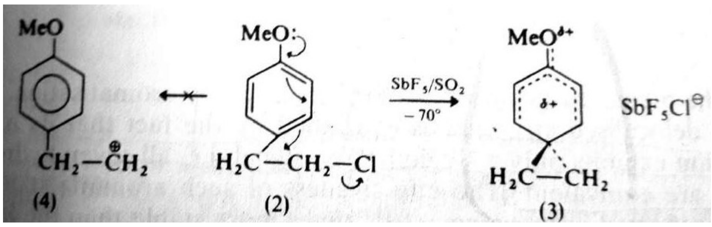
Cyclopropylmethyl cations are **even more stable** than the **benzyl** cations. This **special stability is a result of conjugation between the bent orbitals of the cyclopropyl ring and the vacant p orbital of the cationic carbon**. That the **carbocations are planar** is shown by the fact that these are **difficult or impossible to form at bridgeheads**, where they **cannot be planar**. The stability order of carbocation is explained by hyperconjugation. In vinyl cations ($CH_2 = C^+H$), resonance stability lacks completely and these therefore are very much less stable.

relative stabilities of carbocations



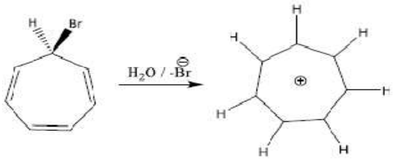
<u>Delocalization Stability:</u>

Bridged carbocation formation: for example: **bridged phenonium ion**

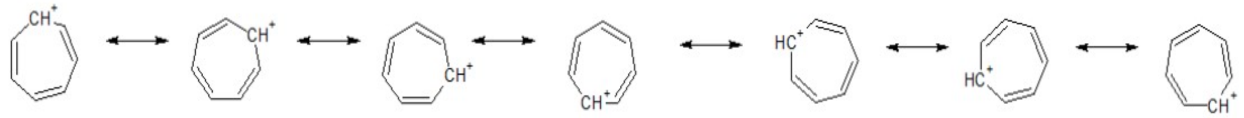


<u>The Stability by Aromatization:</u>

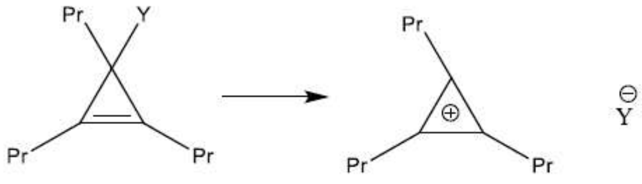
Carbocation from tropylium bromide compound:



Tropylium cation

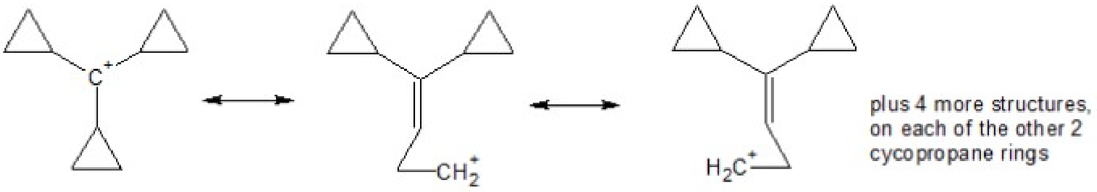


7 resonance structures for the tropylium carbocation



1,2,3- Tripropylcyclopropene

Cyclopropenyl cation

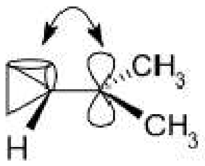


7 resonance structures for the tricyclopropyl carbocation

Due to the **overlapping of cyclopropyl ring's bond to vacant p-orbital** at **carbocation**.

It is a **very special and important case of organic chemistry**. **They are stable due to binding bond conjugation**. So, cyclopropane donates electrons to methyl carbocation and stabilizes it.

The **bent bonds of the cyclopropane ring can overlap with the empty p orbital without steric hindrance**.



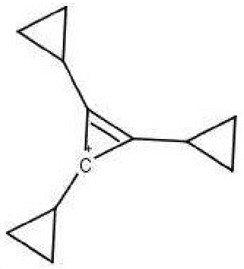
The **positive charge on the carbon of triphenylmethyl carbocation is distributed uniformly over several structures. The aromaticity (you can move the pi bonds around) of the phenyl groups allows for many possible resonance structures, and thus more potential for delocalization of the positive charge**.

The **triphenylmethyl cation, $(C_6H_5)_3C^+$ is stable because it has many resonance structures**.

However, **the resonance overlap of the π orbitals is not perfect because steric hindrance forces the ion to have a propeller shape**.

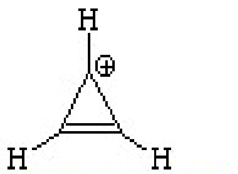
The most stable carbocation:

Add the conjugation with cyclopropyl rings, and the **most stable carbocation** prepared to date is probably the **tricyclopropylcyclopropenium** cation.

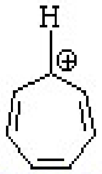


Arenium ions:

Nothing beats the stability of aromatic cations like **cyclopropenium and cycloheptatrienylium (tropylium)** cations.



cyclopropenium ion



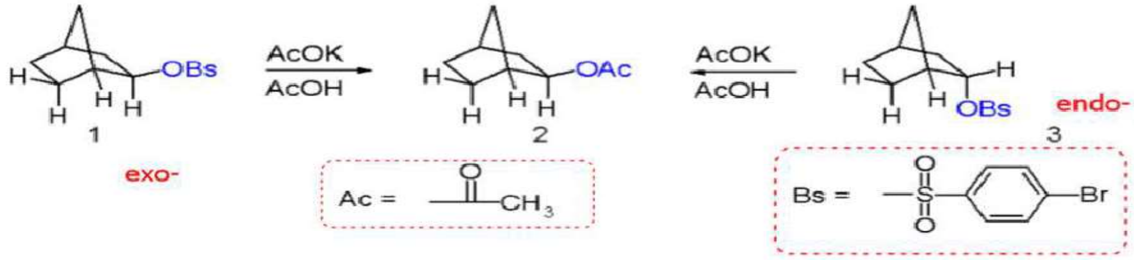
cycloheptatrienyl ion

tropylium is highly stable due to conjugated system, that being, it is **resonance stabilized and the number of canonical** forms of tropylium is **more**.

Non-classical carbocations:

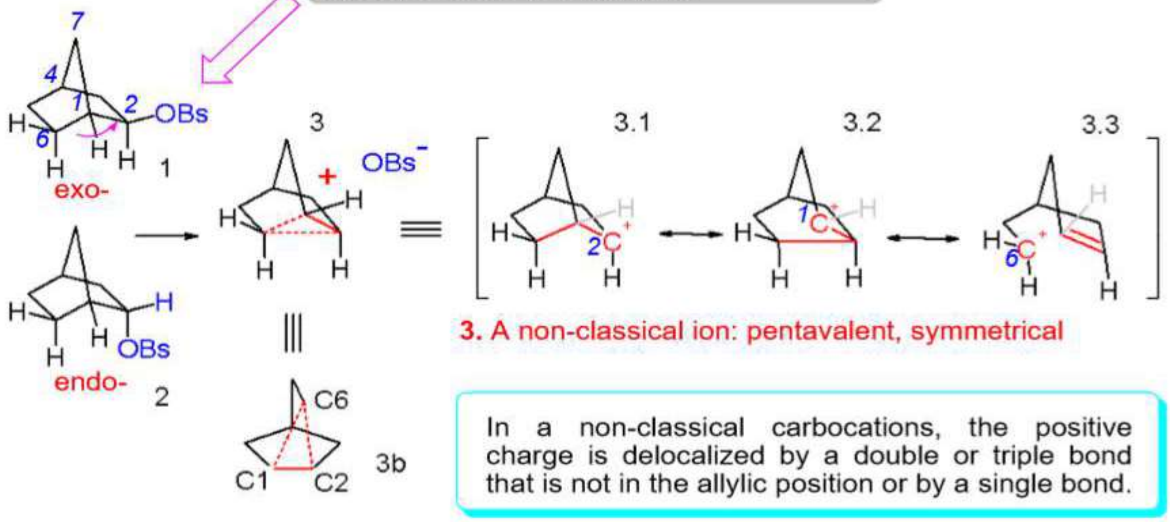
Non-classical ions are a special type of carbonium ions displaying delocalization of sigma bonds in 3-center-2-electron bonds of bridged systems.

S. Winstein (1949): Acylation (solvoysis) of norbornyl brosylate



A key observation is that in this nucleophilic displacement both isomers give the same reaction product an exo-acetate 2. Also the reaction rate for the exo-reaction is 350 times the reaction rate for the endo reaction.

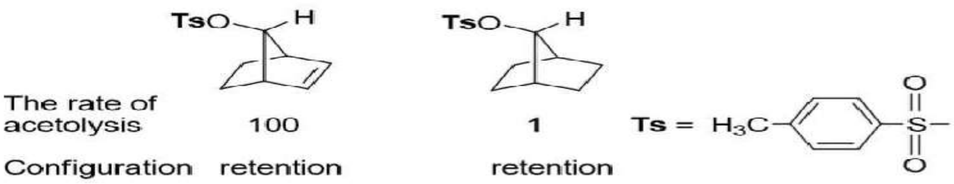
Sigma electrons in the C1-C6 bond assist by neighbouring group participation with the expulsion of the leaving group

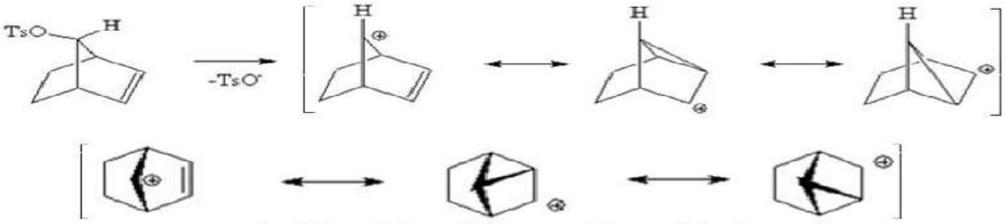


3. A non-classical ion: pentavalent, symmetrical

In a non-classical carbocations, the positive charge is delocalized by a double or triple bond that is not in the allylic position or by a single bond.

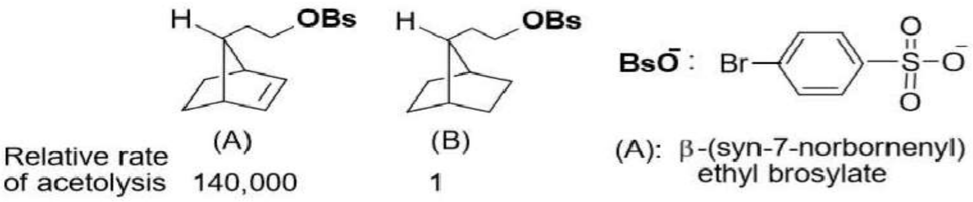
NGP BY AN ALKENE (C=C AS A NEIGHBORING GROUP)

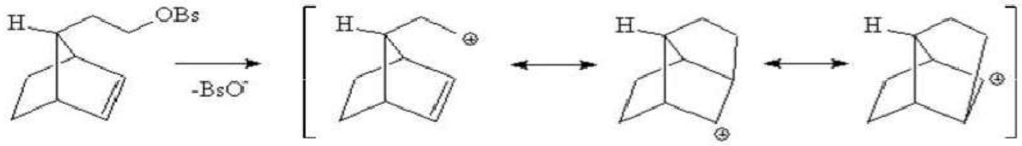




(a different view of the same intermediates)

EVEN IF THE DOUBLE BOND IS MORE REMOTE FROM THE REACTING CENTER THE ALKENE CAN STILL ACT IN THIS WAY.





a different view of the same carbocation:

The C-C single bond as a neighboring group

i. The 2-norbornyl system