Carbocationic Reaction Intermediates:
Factors that influence carbocation formation

Nature of the leaving group

Structural factors

Solvent effects

Salt effects

Isotope effects

Factors that influence carbocation formation

Nature of the leaving group

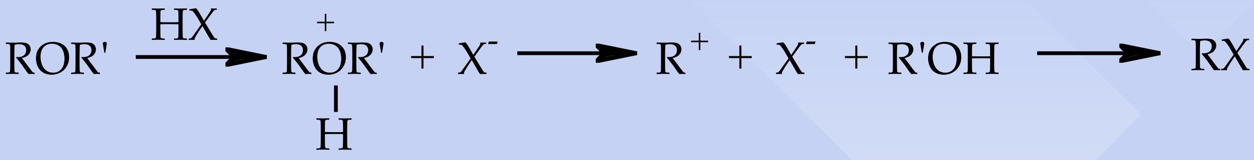
$$R-Z \xrightarrow[\text{cleavage}]{\text{heterolytic}} R^+ + Z$$

The leaving group may be a stable, neutral atom or molecule

i) $CH_3\text{-}T \xrightarrow[\text{gas phase}]{\beta\text{-decay}} (CH_3-{}^3He)^{+1} + 1e^{-1} \longrightarrow CH_3^+ + {}^3He^0$

ii) $C_6H_5-NH_2 \xrightarrow[HCl]{KNO_2} C_6H_5-N_2^+ + Cl^- \longrightarrow C_6H_5^+ + N_2 + Cl^- \longrightarrow C_6H_5-Cl$

iii)



$ROR' \xrightarrow{HX} R\underset{H}{\overset{+}{O}}R' + X^- \longrightarrow R^+ + X^- + R'OH \longrightarrow RX$

iv) $R-\overset{+}{N}R_3 \longrightarrow R^+ + NR_3$

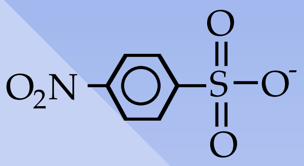
Factors that influence carbocation formation

Anionic leaving groups

$$R-Z \longrightarrow R^+ + Z^-$$

The greater the ability of the departing anionic species to stabilize negative charge, the better a leaving group it is.

Ease of displacement of common anionic leaving groups:



nosylate

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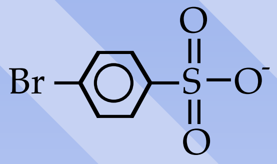

brosylate

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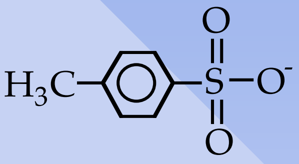
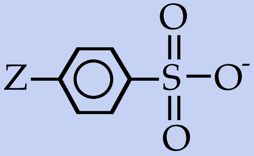
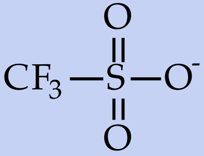


tosylate

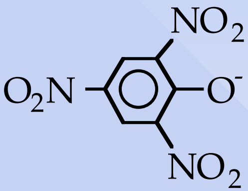


$> I^- > Br^- > Cl^- > F^- \cong CH_3COO^- > OH^- \cong OR^- > NR_2^-$

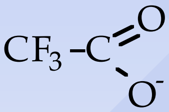
Other particularly good anionic leaving groups:



triflate



picrate



trifluoroacetate

Factors that influence carbocation formation

Structural factors

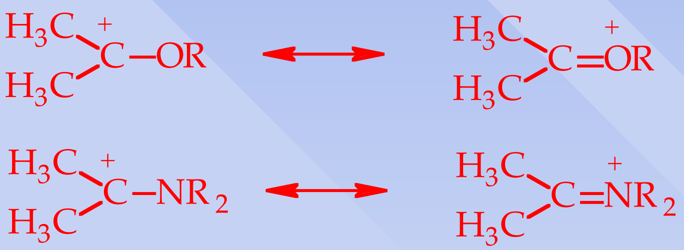
Alkyl substitution - The greater the degree of alkyl substitution at the cationic center, the greater will be the stability of the carbocation produced.

$$3^{o} > 2^{o} > 1^{o} > CH_3^{+}$$

Aryl substitution - The greater the degree of conjugation of the cationic center with delocalizing groups, the greater will be the stability of the carbocation produced.

$$(C_6H_5)_3C^{+} > (C_6H_5)_2CH^{+} > C_6H_5CH_2^{+}$$

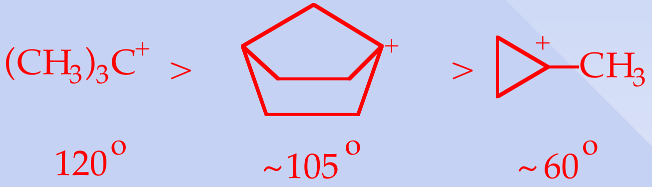
Conjugation with heteroatoms:



R = H or alkyl

R = H or alkyl

Steric factors - Carbocations prefer a planar geometry: Any structural feature that interferes or prevents the attainment of 120 ° interbond angles will hinder (retard) carbocation formation.



(all are 3°)

Factors that influence carbocation formation

Solvent effects: Any property of a solvent system that can lower the energy of activation for heterolytic bond cleavage will favor carbocation formation.

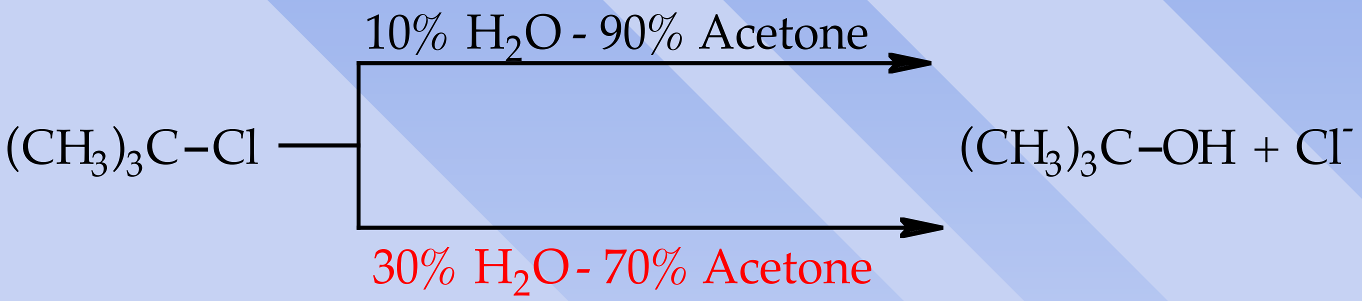
The role of solvent in carbocation formation

- **Dielectric constant -** a rough measure of the ability of the solvent to separate oppositely charged ions.
- **Hydrogen-bonding ability**
- **Acid-base properties**
- **Nucleophilicity:** As the nucleophilicity of a solvent decreases, the likelihood of discrete carbocation formation increases.

Salt Effects: Ionic Strength

As the ionic concentration of a solvent system increases, the overall polarity of the medium increases. Increased solvent polarity favors ionization of neutral molecules.

Consider the hydrolysis of tert-butyl chloride shown below:



$10\%\ H_2O - 90\%\ \text{Acetone}$

$(CH_3)_3C{-}Cl \longrightarrow (CH_3)_3C{-}OH + Cl^-$

$30\%\ H_2O - 70\%\ \text{Acetone}$

Observation: In both solvent systems, as the hydrolysis proceeds the reaction rate gradually increases. The increase is more pronounced for the less aqueous medium .

Rationale: As the hydrolysis reaction progresses, chloride ion concentration builds. The polarity of the medium increases favoring carbocation formation and subsequent attack by water to form product. The %-increase in polarity is more keenly felt in the less aqueous (less polar) medium.

COMMON ION (MASS LAW) EFFECT

Consider the following observations:

$$(CH_3)_3C{-}Cl \xrightarrow[10\%\ H_2O]{90\%\ \text{Acetone}} (CH_3)_3C{-}OH + Cl^-$$

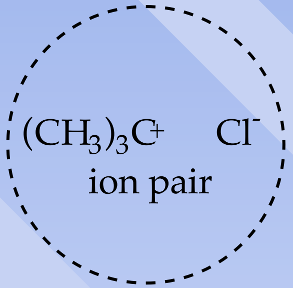
Added Cl^- enhances the rate of hydrolysis slightly

$$(C_6H_5)_2CH{-}Cl \xrightarrow[10\%\ H_2O]{90\%\ \text{Acetone}} (C_6H_5)_2CH{-}OH + Cl^-$$

Added Cl^- retards the rate of hydrolysis slightly

Rationale:

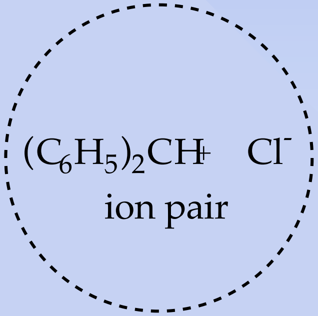
$(CH_3)_3C{-}Cl \longrightarrow$



solvent shell of H_2O - Acetone

As soon as $(CH_3)_3C^+$ is formed, it reacts rapidly with the H_2O molecules in the solvent shell. Increasing the [Cl^-] increases the polarity of the medium favoring $(CH_3)_3C^+$ formation.

$(C_6H_5)_2CH{-}Cl \longrightarrow$



$(C_6H_5)_2CH^+$ is a fairly stable (unreactive) carbocation. Although increasing the ionic strength of the medium favors its formation, $(C_6H_5)_2CH^+$ does not react immediately with H_2O from the solvent shell. During the lifetime of $(C_6H_5)_2CH^+$, the added Cl^- will favor return to reactant rather than conversion to product.

Special Salt Effect

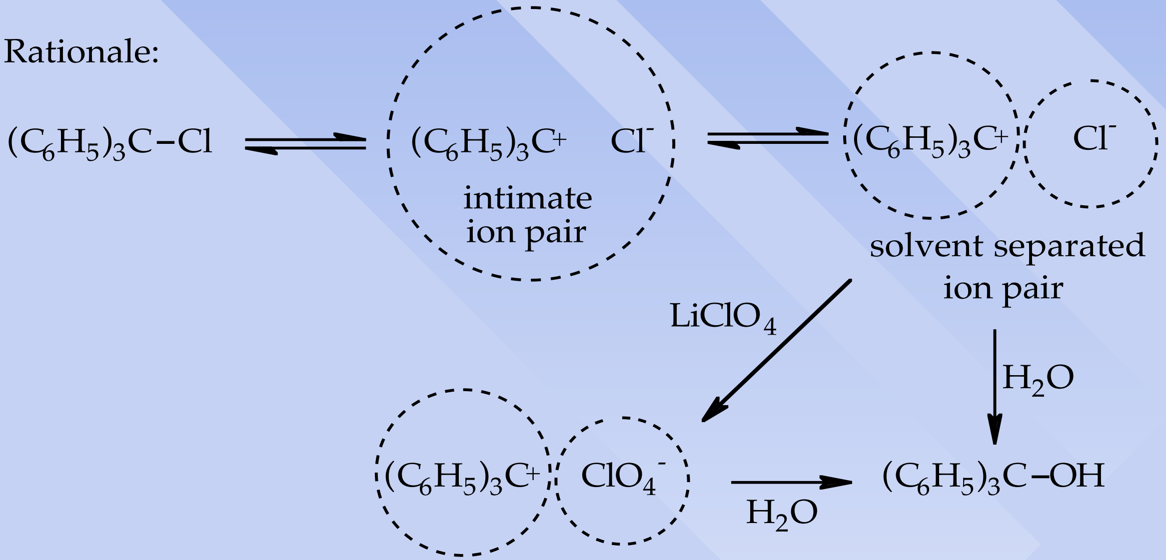
Consider the following reactions:

$$(C_6H_5)_3C{-}Cl \xrightarrow[\text{90\% ether}]{\text{10\% } H_2O} (C_6H_5)_3C{-}OH + Cl^-$$

$$(C_6H_5)_3C{-}Cl \xrightarrow[\substack{\text{90\% ether} \\ \text{Added } LiClO_4}]{\text{10\% } H_2O} (C_6H_5)_3C{-}OH + Cl^-$$

Observation: In the presence of $LiClO_4$, the rate of hydrolysis increases by a factor much larger than would be expected from an increase in ionic strength alone.

Rationale:



$(C_6H_5)_3C{-}Cl \rightleftharpoons$ $(C_6H_5)_3C^+ \; Cl^-$ intimate ion pair $\rightleftharpoons$ $(C_6H_5)_3C^+ \; Cl^-$ solvent separated ion pair

solvent separated ion pair $\xrightarrow{LiClO_4}$ $(C_6H_5)_3C^+ \; ClO_4^-$ $\xrightarrow[H_2O]{}$ $(C_6H_5)_3C{-}OH$

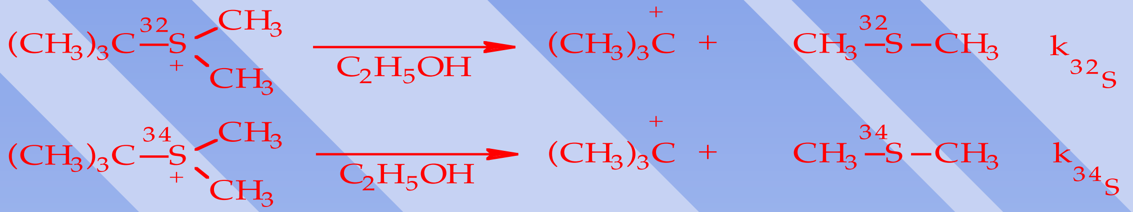
solvent separated ion pair $\xrightarrow{H_2O}$ $(C_6H_5)_3C{-}OH$

Perchlorate is essentially nonnucleophilic and is capable of displacing chloride from the solvent separated ion pair. By decreasing the likelihood of recombination of the intimate ion pair (regeneration of starting material), perchlorate permits more of the carbocation to form hydrolysis product per unit time.

Factors that influence carbocation formation

Isotope effects

a) Leaving group



$$(CH_3)_3C-\overset{+}{{}^{32}S}(CH_3)_2 \xrightarrow[C_2H_5OH]{} (CH_3)_3\overset{+}{C} + CH_3-{}^{32}S-CH_3 \qquad k_{^{32}S}$$

$$(CH_3)_3C-\overset{+}{{}^{34}S}(CH_3)_2 \xrightarrow[C_2H_5OH]{} (CH_3)_3\overset{+}{C} + CH_3-{}^{34}S-CH_3 \qquad k_{^{34}S}$$

Observation: $k_{^{32}S} / k_{^{34}S} = 1.01$

A primary kinetic isotope effect for ${}^{32}S / {}^{34}S$ consistent with a large degree of C-S bond breakage in the rate determining step

b) α-Isotope effect

$$CH_3O-CH_2Cl \xrightarrow[S_N1]{-Cl^-} CH_3O-\overset{+}{C}H_2 \longleftrightarrow CH_3\overset{+}{O}=CH_2 \xrightarrow[H_2O]{} CH_3OCH_2OH$$

$$CH_3O-CD_2Cl \xrightarrow[S_N1]{-Cl^-} CH_3O-\overset{+}{C}D_2 \longleftrightarrow CH_3\overset{+}{O}=CD_2 \xrightarrow[H_2O]{} CH_3OCD_2OH$$

Observation: $k_H / k_D = 1.12$

A secondary kinetic isotope effect caused by greater relief of strain in the unlabeled case relative to the labeled case when R^+ is formed

c) β-Isotope effect

$$(CH_3)_3C-Cl \xrightarrow[S_N1]{-Cl^-} \xrightarrow{H_2O} (CH_3)_3C-OH \qquad k_H$$

$$(CD_3)_3C-Cl \xrightarrow[S_N1]{-Cl^-} \xrightarrow{H_2O} (CD_3)_3C-OH \qquad k_D$$

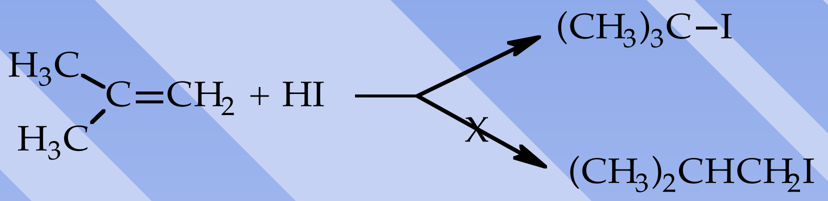
Observation: $k_H / k_D = 1.21$

A secondary kinetic isotope effect explained either by relief of steric strain or by hyperconjugative arguments

Nature of some carbocationic intermediates

Stability of the intermediate

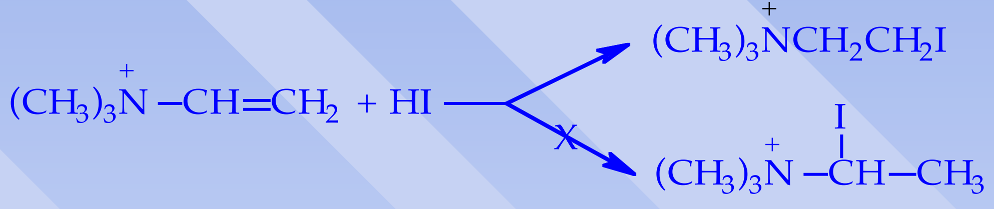
Example I:



$$\begin{tikzcd} (H_3C)_2C{=}CH_2 + HI \arrow[r] \arrow[dr, "X"'] & (CH_3)_3C{-}I \\ & (CH_3)_2CHCH_2I \end{tikzcd}$$

Rationale: $(CH_3)_3\overset{+}{C}$ is more stable than $(CH_3)_2CH\overset{+}{C}H_2$

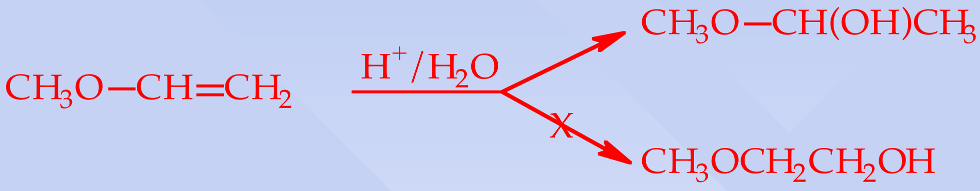
Example II:



$$\begin{tikzcd} (CH_3)_3\overset{+}{N}{-}CH{=}CH_2 + HI \arrow[r] \arrow[dr, "X"'] & (CH_3)_3\overset{+}{N}CH_2CH_2I \\ & (CH_3)_3\overset{+}{N}{-}\overset{\overset{I}{|}}{C}H{-}CH_3 \end{tikzcd}$$

Rationale: $(CH_3)_3\overset{+}{N}CH_2\overset{+}{C}H_2$ is more stable than $(CH_3)_3\overset{+}{N}\overset{+}{C}HCH_3$

Example III:



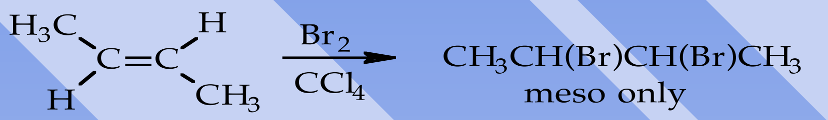
$$\begin{tikzcd} CH_3O{-}CH{=}CH_2 \arrow[r, "H^+/H_2O"] \arrow[dr, "X"'] & CH_3O{-}CH(OH)CH_3 \\ & CH_3OCH_2CH_2OH \end{tikzcd}$$

Rationale: $CH_3O{-}\overset{+}{C}HCH_3 \longleftrightarrow CH_3\overset{+}{O}{=}CHCH_3$ is more stable than

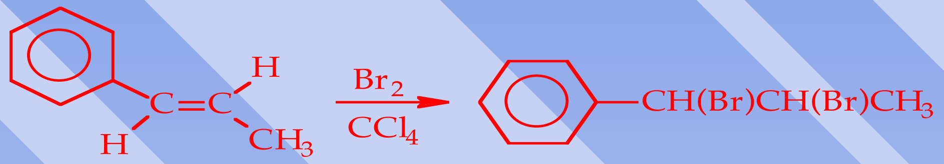
$CH_3O{-}CH_2\overset{+}{C}H_2$

Stereochemistry of Carbocations

Case I:

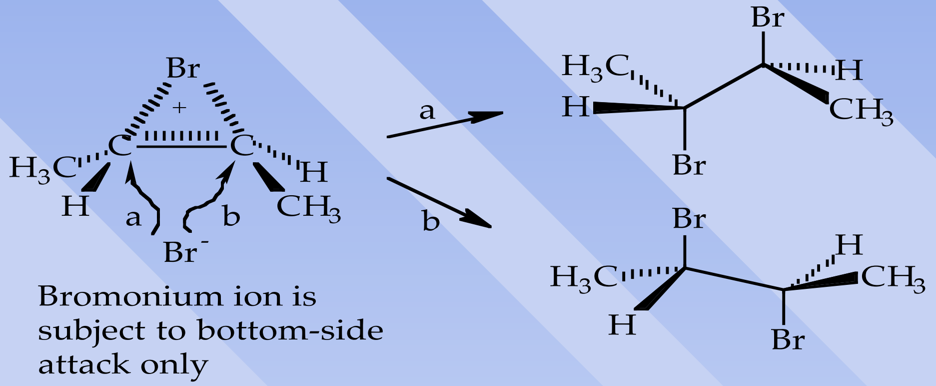


$CH_3CH(Br)CH(Br)CH_3$
meso only



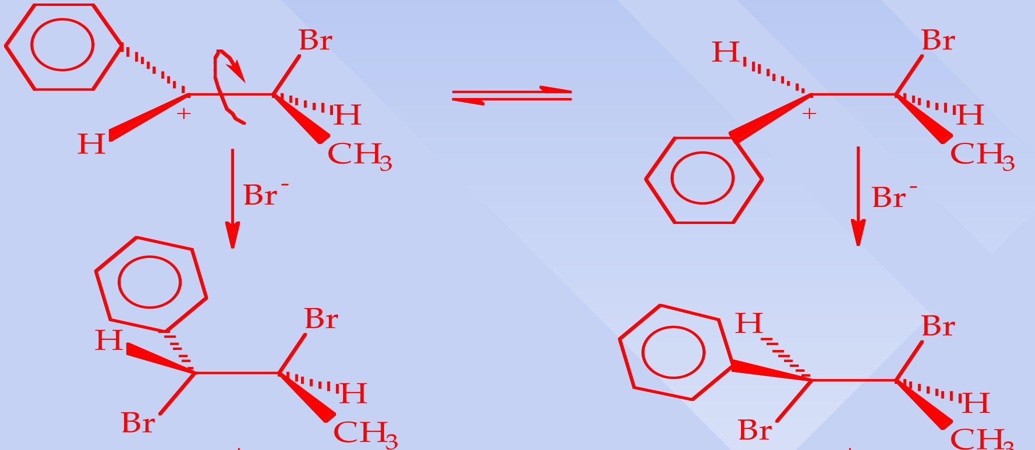
mixture of erythro and threo

Rationale:



Meso product

Bromonium ion is
subject to bottom-side
attack only



Stable benzyl
carbocation is
subject to rotation
and the formation
of two racemic
diastereomeric
products

Erythro

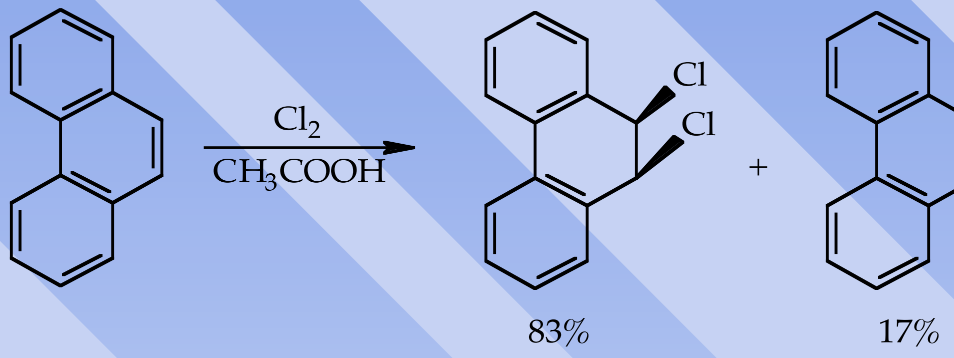
+
enantiomer

Threo

+
enantiomer

Stereochemistry of carbocations

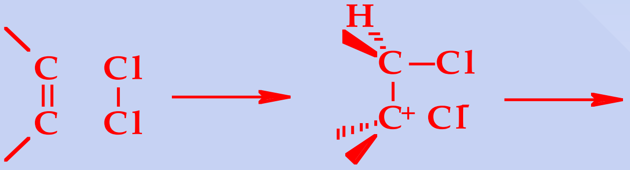
Case II



Rationale:

1. A chloronium ion is ruled out because it would lead exclusively to **trans** product.
2. A completely free carbocationic intermediate is ruled out because it would lead to an **ca. 1:1 mixture of cis and trans** products from top and bottom attack.
3. A combination of chloronium ion and completely free carbocationic intermediate is ruled out because an **excess of trans** product would be obtained.

Best possibility

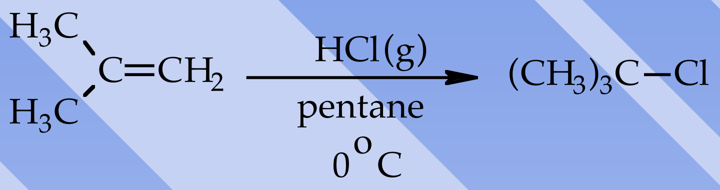


open ion pair

cis addition product predominates; trans product forms when chloride ion has an opportunity to diffuse to the other side of R^+

KINETICS OF CARBOCATION FORMATION

Observation:



$$\text{rate} = k\,[\text{alkene reactant}]^{1}\,[\text{HCl}]^{2.7\text{-}2.9}$$

Comments:

The rate law indicates that three molecules of HCl are involved in the addition process. In all likelihood, the extra two HCl molecules serve to increase the polarity of the medium (pentane is non-polar) in the immediate vicinity of the reaction site, thereby facilitating ionic cleavage of the attacking HCl molecule.

Possible Mechanism :