Reactive intermediates in organic reactions

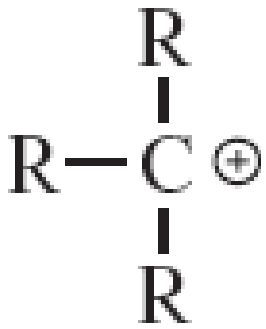
Common reactive intermediates :

- Carbocations
- Carbanions
- Free radicals

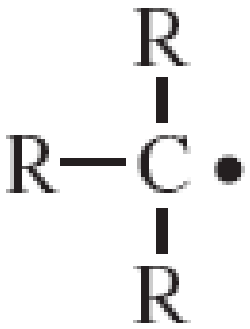
Thermodynamic parameters related to Reactive intermediates

- Carbocations: **Hydride Ion Affinity (HIA)**
- Carbanions: **pKa**
- Free radicals: **BDE**

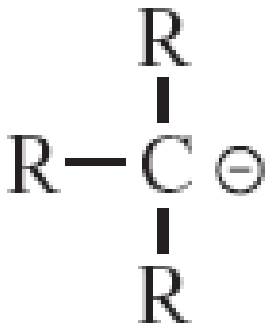
Common reactive intermediates



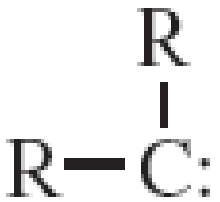
A



B



C



D

Only carbanions have a complete octet around the carbon

Common reactive intermediates

A: carbocations

B: free radicals

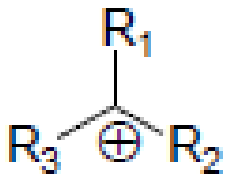
C: carbanions

D: carbenes

• There are many other organic ions and radicals with charges and unpaired electrons on atoms other than carbon

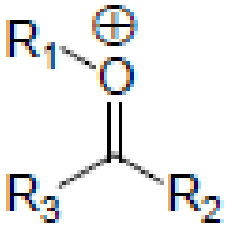
Carbocations

Carbon-substituted

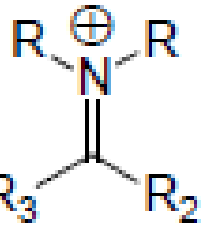


R–R_3 = alkyl or aryl

Heteroatom–stabilized



R–R_3 = alkyl or aryl



R–R_3 = alkyl or aryl

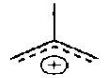
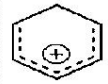
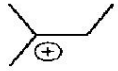
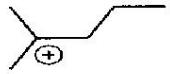
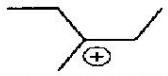
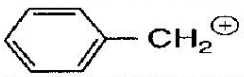
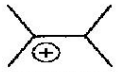
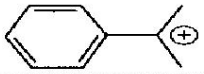
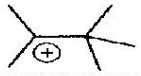
Thermochemistry of carbocations

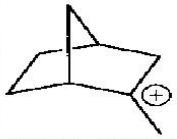
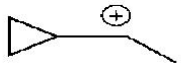
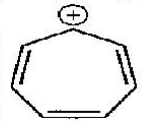
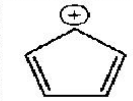
Stability in gas phase

--- Hydride Ion Affinity (HIA)

$$R\text{-}H \rightarrow R^{+} + H^{-} \qquad \Delta H^{o} = HIA$$

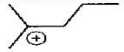
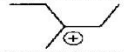
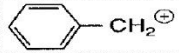
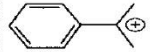
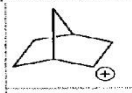
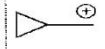
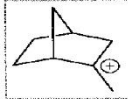
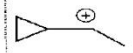
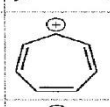
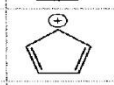
HIA for selected carbocations

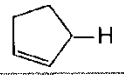
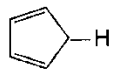
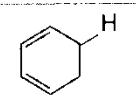
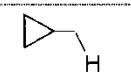
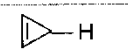
CH_3^+	312		256
$C_2H_5^+$	273		236
$CH_3CH_2CH_2^+$	266		225
$CH_3CH_2CH_2CH_2^+$	265		225
	265		248
	246		225
	247		212
	231	$HC\equiv C-CH_2^+$	270
	229	$H_2C=\overset{+}{C}H$	287
	228	$H_2C=\overset{+}{C}-CH_3$	258
	227		234
	226		220
	224		287

	231		249
	225		230
$NH_2CH_2^+$	218		218
$HOCH_2^+$	243		201
FCH_2^+	290		258
$NCCH_2^+$	318		

From Bowers, M. T. (ed.) (1979), *Gas Phase Ion Chemistry*, Academic Press, New York

HIA *vs* BDE

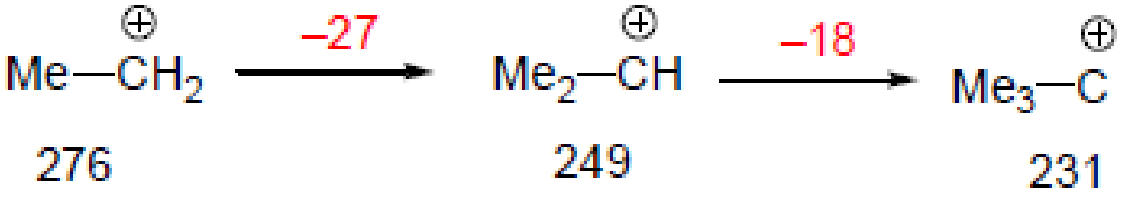
CH_3^+	312		256
$C_2H_5^+$	273		236
$CH_3CH_2CH_2^+$	266		225
$CH_3CH_2CH_2CH_2^+$	265		225
	265		248
	246		225
	247		212
	231	$HC\equiv C-CH_2^+$	270
	229	$H_2C=\overset{+}{C}H$	287
	228	$H_2C=\overset{+}{C}-CH_3$	258
	227		234
	226		220
	224		287
	231		249
	225		230
$NH_2CH_2^+$	218		218
$HOCH_2^+$	243		201
FCH_2^+	290		258
$NCCH_2^+$	318		

Bond	BDE	Bond	BDE	Bond	BDE
H–H	104.2 (104.2)	CH_2=CH–H	110 (110.7)	CH_3–CH_3	90.4 (90.1)
CH_3–H	105.1 (105.0)	C_6H_5–H	110.9 (112.9)	CH_3–F	109.9 (115)
CH_3CH_2–H	98.2 (101.1)	HC≡C–H	132 (131.9)	CH_3–Cl	84.6 (83.7)
$(CH_3)_2$CH–H	95.1 (98.6)	$C_6H_5CH_2$–H	88 (89.7)	CH_3–Br	70.9 (72.1)
$(CH_3)_3$C–H	93.2 (96.5)	CH_2=$CHCH_2$–H	86.3 (88.8)	CH_3–I	57.2 (57.6)
c$(CH_2)_3$–H	106.3	$CH_3C(O)$–H	86 (88.1)	CH_3–OH	92.3 (92.1)
c$(CH_2)_4$–H	96.5	HO–H	119 (118.8)	CH_3–NH_2	84.9 (85.2)
c$(CH_2)_5$–H	94.5	CH_3O–H	104.4 (104.6)	CH_3–SH	74
c$(CH_2)_6$–H	95.5	NH_2–H	107.4 (107.6)	CH_3–SiH_3	88.2
	82.3	CH_3S–H	90.7 (87.4)	CH_3–$SiMe_3$	89.4
		HO–OH	51	CH_3–$GeMe_3$	83
	71.1	CH_3O–OCH_3	37.6 (38)	CH_3–$SnMe_3$	71
		$HOCH_2$–H	94 (96.1)	CH_3–$PbMe_3$	57
	73	H_2C=CH_2	(174.1)	CH_3–OCH_3	(83.2)
	97.4	HC≡CH	(230.7)	CH_3–C_2H_5	(89.0)
	90.6	H_2C=O	(178.8)	CH_3–$CH(CH_3)_2$	(88.6)
CH_3–CH=CH_2	(101.4)	CH_3–C_6H_5	(103.5)	CH_3–$C(CH_3)_3$	(87.5)
C_6H_5–C_6H_5	(118)	CH_3–$CH_2C_6H_5$	(77.6)	CH_3–CH_2CH=CH_2	(76.5)

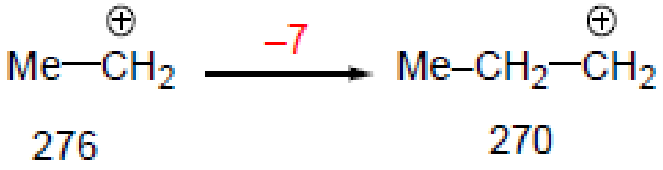
Stabilization of carbocations

- **Stabilization due to alkyl substitution — hyperconjugative interaction**

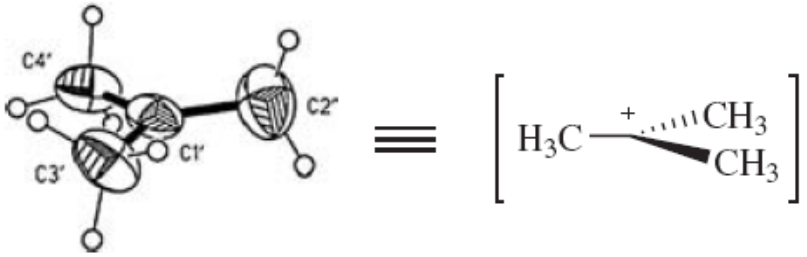
HIA of different carbocations



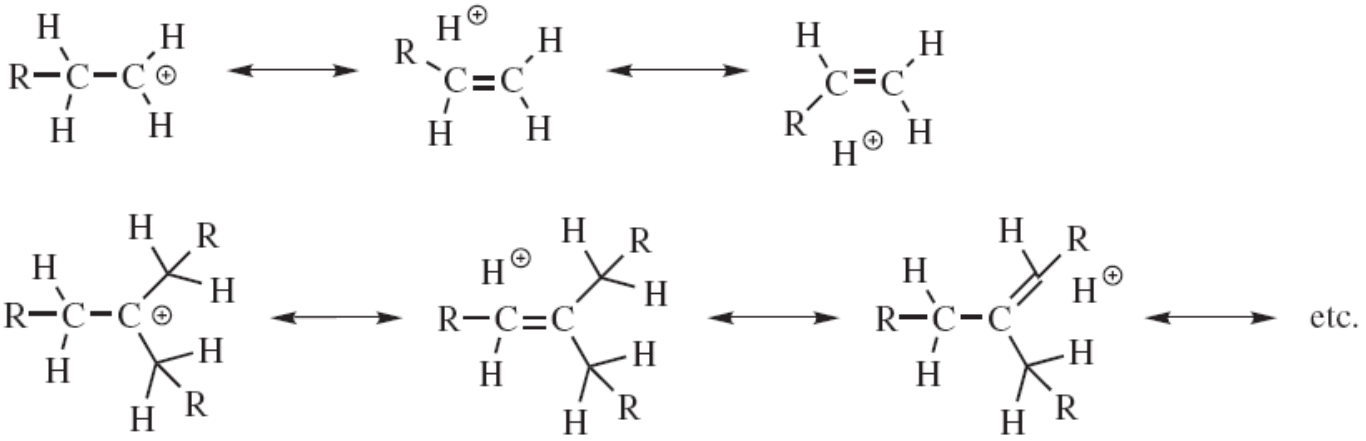
The effect of beta substituents: Rationalize



Carbocations stabilized by hyperconjugation



Stabilization due to alkyl substitution — hyperconjugative interaction



Carbocations stabilized by hyperconjugation

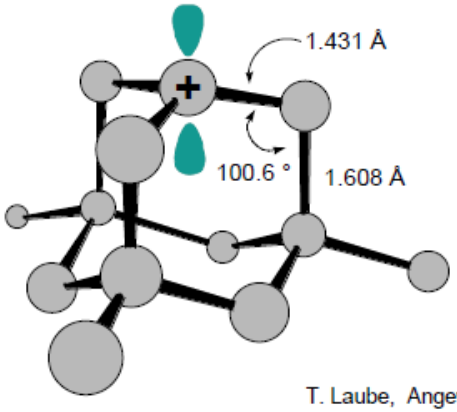
$(CD_3)_3C^{\oplus}$ less hyper-conjugation + $(CH_3)_3CH$ $\rightleftharpoons$ $(CH_3)_3C^{\oplus}$ + $(CD_3)_3CH$ $\quad K_{298} = 1.97 \pm 0.20$

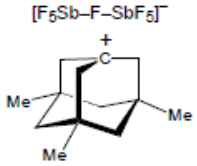
Meot-Ner, M. J. Am. Chem. Soc. **1987**, *109*, 7947

Physical Evidence for Hyperconjugation: The Adamantyl Cation

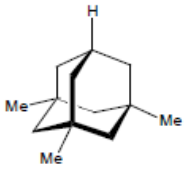
Bonds participating in the hyperconjugative interaction, e.g C–R, will be lengthened while the C(+)–C bond will be shortened.

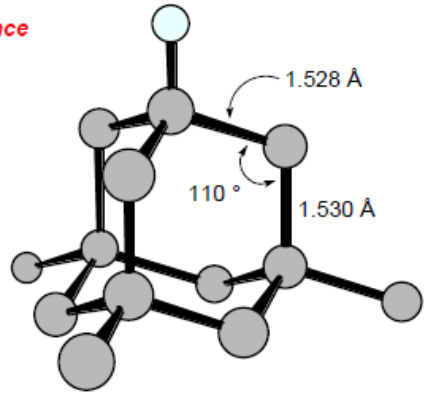
First X-ray Structure of an Aliphatic Carbocation





The Adamantane Reference (MM-2)



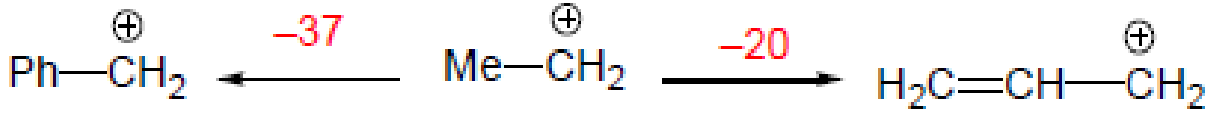


T. Laube, Angew. *Chem. Int. Ed.* 1986, *25*, 349

Stabilization of carbocations

- **Stabilization due to increasing delocalization**

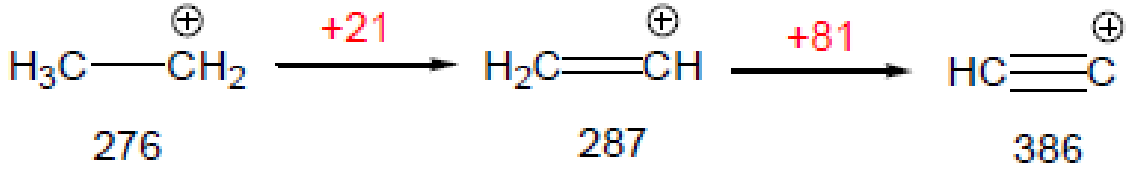
HIA of different carbocations



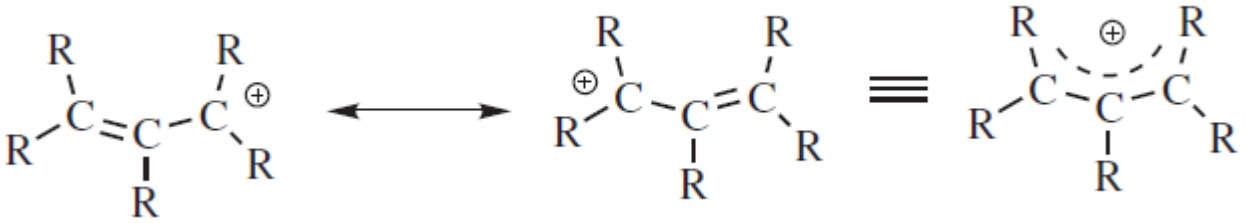
Benzylic cation

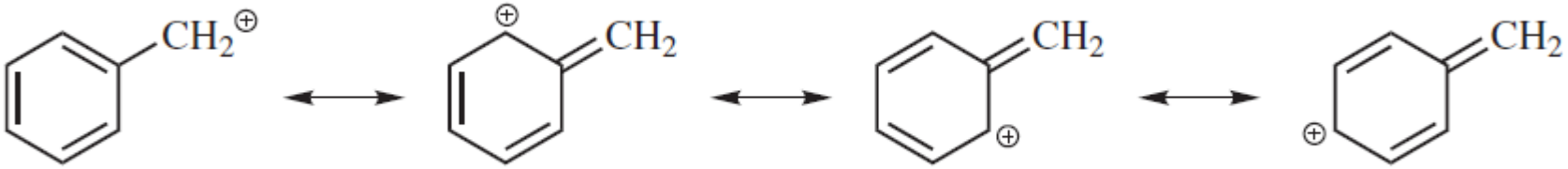
allylic cation

HIA of different carbocations



Carbocations stabilized by charge delocalization

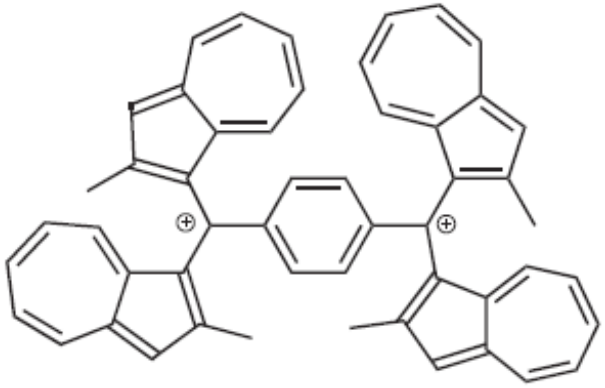




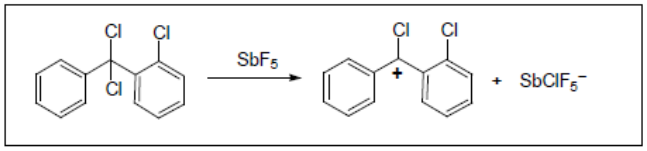
- In SO_2, this equilibrium has been known for many years

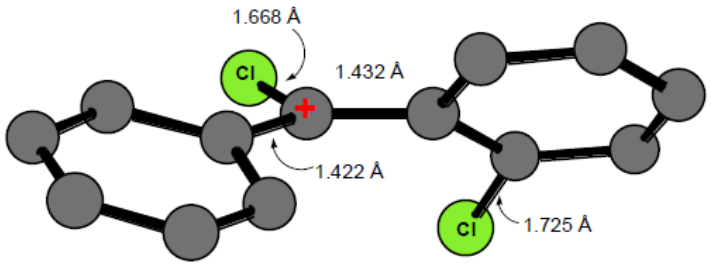
$$Ph_3CCl \rightleftharpoons Ph_3C^{\oplus} + Cl^{\ominus}$$

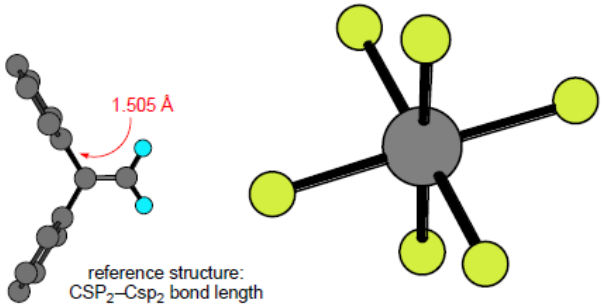
- $Ph_3C^+ BF_4^-$ and related salts are commercially available

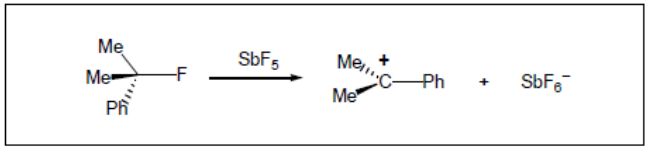


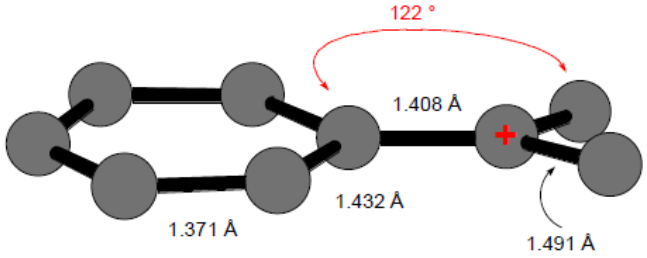
Confirmed structure of carbocations

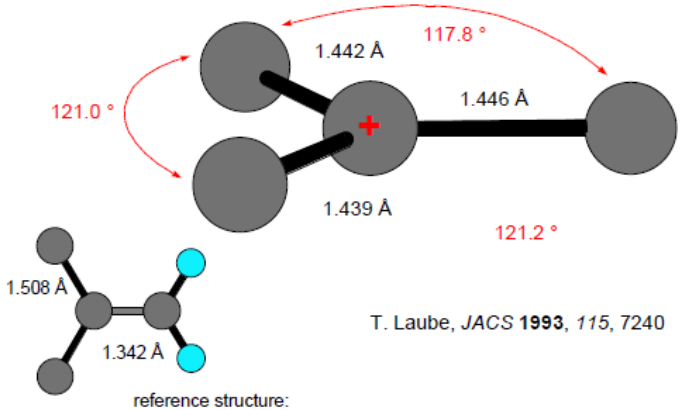






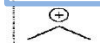
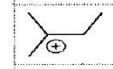
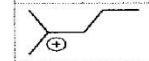
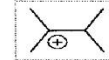
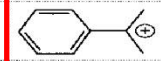
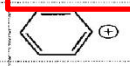


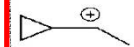
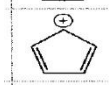


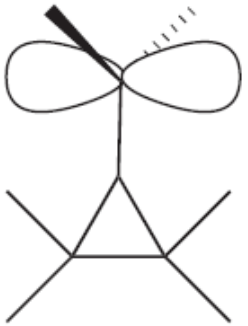


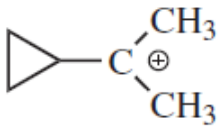
T. Laube, *JACS* **1993**, *115*, 7240

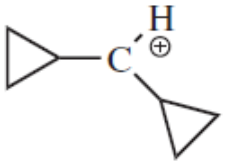
Cyclopropylmethyl cations

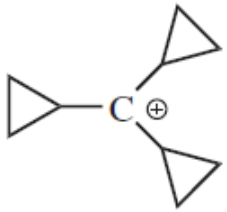
CH_3^+	312		256
$C_2H_5^+$	273		236
$CH_3CH_2CH_2^+$	266		225
$CH_3CH_2CH_2CH_2^+$	265		225
	265		248
	246		225
	247		212
	231	$HC\equiv C-CH_2^+$	270
	229	$H_2C=\overset{+}{C}H$	287
	228	$H_2C=\overset{+}{C}-CH_3$	258
	227		234
	226		220
	224		287

	249
	230
	218
	201
	258







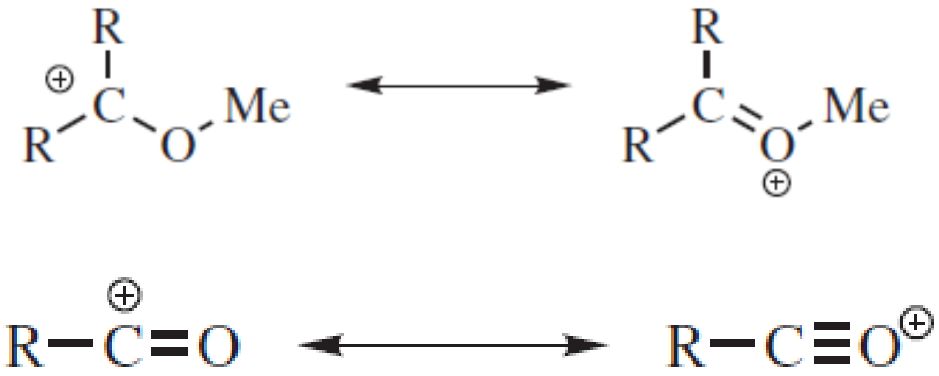


Deno, N.C., et. al, J. Am. Chem. Soc. 1962, *84*, 2016.

Stabilization of carbocations

- **Stabilization due to alkyl substitution — hyperconjugative interaction**
- **Stabilization due to increasing delocalization**
- **Heteroatom effects--- related to π donating ability and σ withdrawing ability of the heteroatom**

Carbocations stabilized by heteroatom



- Simple acyl cations RCO^+ have been prepared in solution and the solid state
- acetyl cation CH_3CO^+ is about as stable as t-butyl cation

Carbocations in solution

- **Stable ion media for carbocations** --- an enviroment devoid of nucleophiles and bases to make carbocations persistent

- SbF_5 developed by Olah et. al. as stable ion media

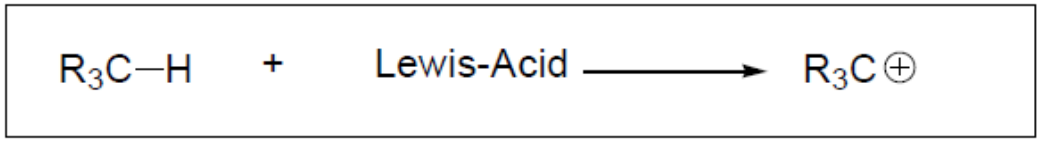
$$RX + SbF_5 \rightarrow R^+ + Sb_2F_{10}X^-$$

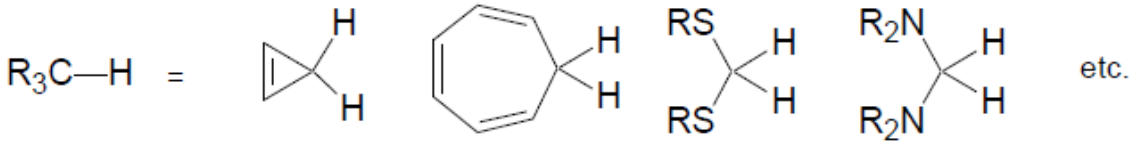
$Sb_2F_{10}X^-$ --- very poor nucleophile and very weak base

Other stable ion media: HF- SbF_5 ; FSO_3H-SbF_5 …

Generation of Carbocations

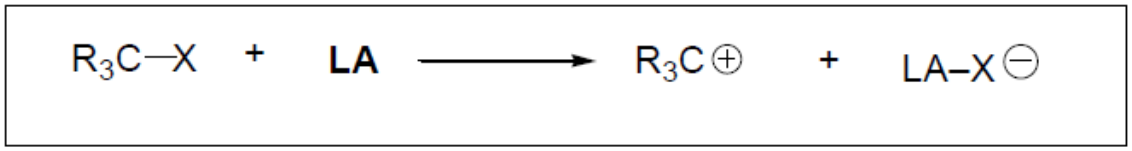
Hydride abstraction from neutral precursors





Lewis-Acid: $Ph_3C^{\oplus}\ BF_4^{\ominus}$, BF_3, PCl_5

Removal of an energy-poor anion from a neutral precursor via Lewis Acids



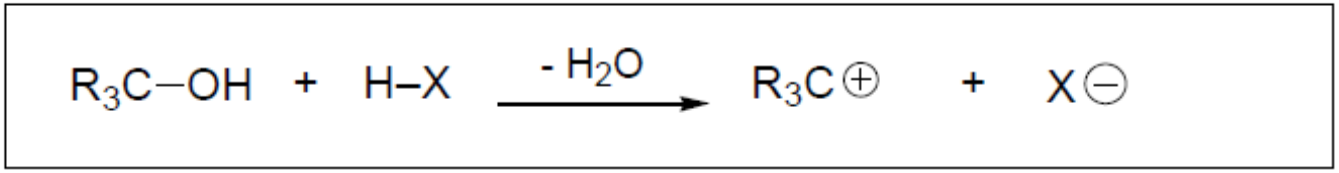
LA: Ag , $AlCl_3$, $SnCl_4$, $SbCl_5$, **SbF_5**, BF_3, $FeCl_3$, $ZnCl_2$, PCl_3, PCl_5, $POCl_3$

...

X: F, Cl, Br, I, OR

Generation of Carbocations

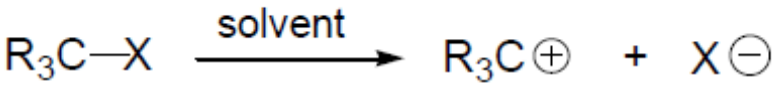
Acidic dehydratization of *secondary* and *tertiary* alcohols



R: Aryl + other charge stabilizing substituents

X: SO_4^{2-}, ClO_4^-, FSO_3^-, $CF_3SO_3^-$

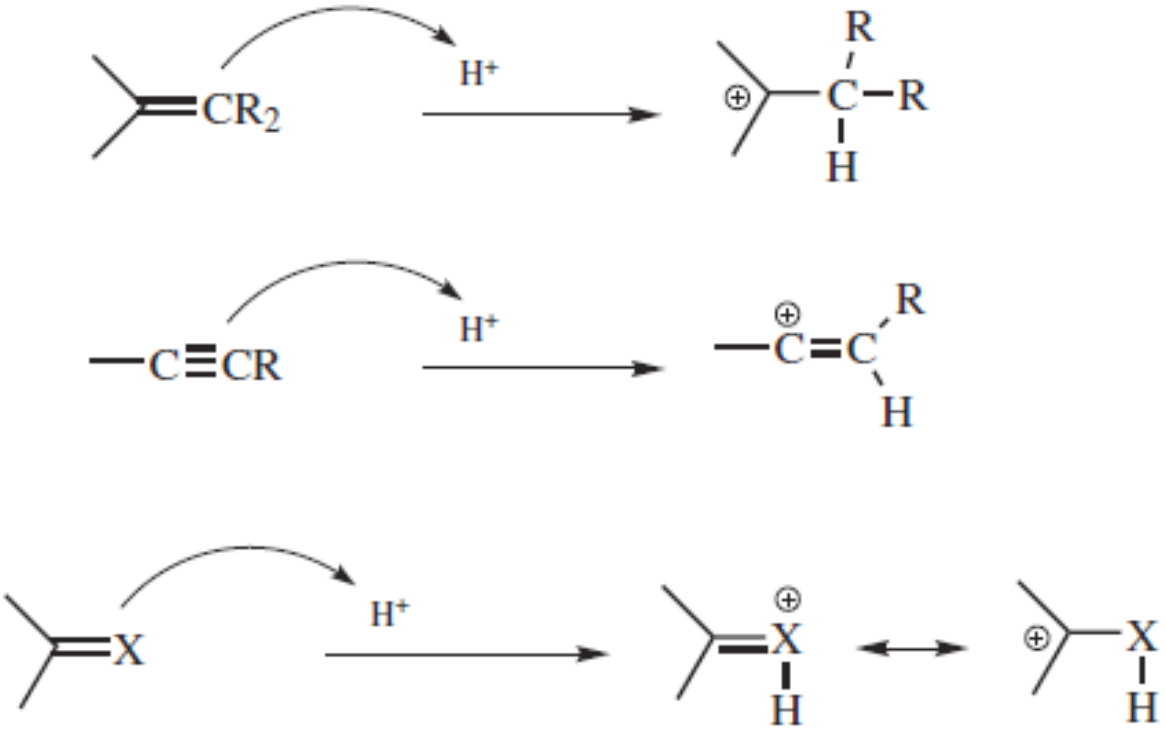
From neutral precursors via heterolytic dissociation (solvolysis) - First step in S_N1 or E1 reactions



Ability of X to function as a leaving group:

$-N_2^+ > -OSO_2R' > -OPO(OR')_2 > -I \geq -Br > Cl > OH_2^+$ ...

Generation of Carbocations



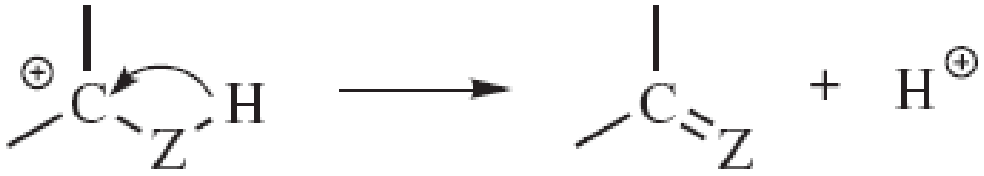
Fate of Carbocations

1. *The Carbocation May Combine with a Species Possessing an Electron Pair*

Fate of Carbocations

1. *The Carbocation May Combine with a Species Possessing an Electron Pair*

2. *The Carbocation May Lose a Proton* (or much less often, another positive ion)

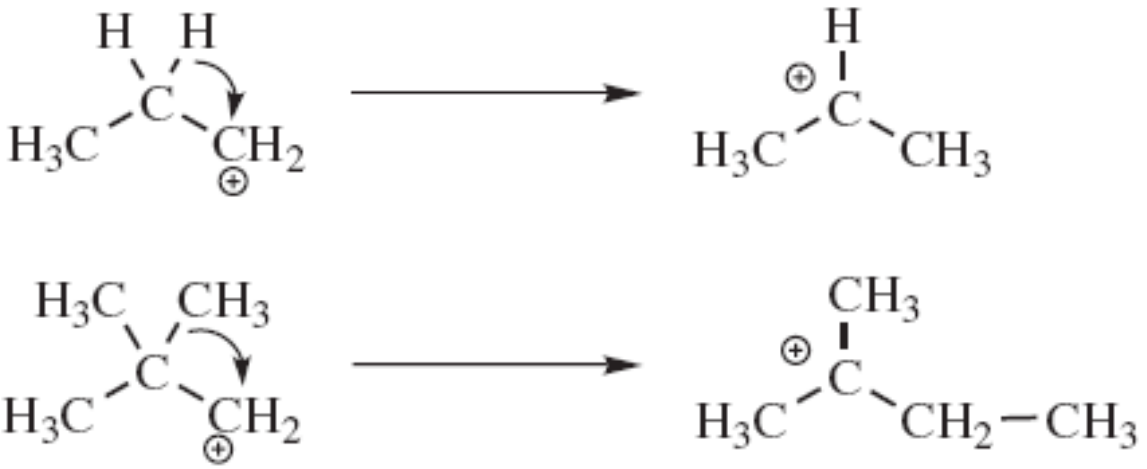


Fate of Carbocations

1. *The Carbocation May Combine with a Species Possessing an Electron Pair*

2. *The Carbocation May Lose a Proton* (or much less often, another positive ion)

3. *Rearrangement.*



Fate of Carbocations

1. *The Carbocation May Combine with a Species Possessing an Electron Pair*

2. *The Carbocation May Lose a Proton* (or much less often, another positive ion)

3. *Rearrangement.*

4. *Addition.*