Advanced Organic Chemistry

By LIMING JIANG & WEIPU ZHU (朱蔚璞)

Department of Polymer Science & Engineering
Zhejiang University
Email: zhuwp@zju.edu.cn
13735471052 (581052)

Chapter 4

Reactive Intermediates

OUTLINE

Definition: a reaction intermediate or an intermediate as a molecular entity (atom, ion, molecule...) with a lifetime appreciably longer than a molecular vibration that is formed (directly or indirectly) from the reactants and reacts further to give (either directly or indirectly) the products of a chemical reaction.

Main carbon reactive intermediates:

- Carbocations and their stabilized equivalents such as oxonium ions
- Carbanions and their stabilized equivalents such as enolates
- Free radicals
- Carbenes

Common features

♦ Low concentration

♦ Dot not obey the Lewis octet rule with the exception of carbanions, hence the high reactivity

♦ Often generated on chemical decomposition

♦ It is often possible to prove the existence of this species by spectroscopic means

♦ Cage effects have to be taken into account

♦ Often stabilisation by conjugation or resonance

♦ Often difficult to distinguish from a transition state

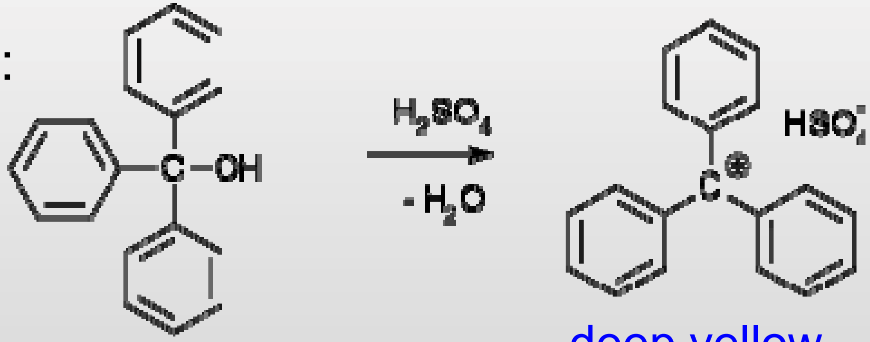
♦ Prove existence by means of chemical trapping

4.1 Carbocations

- A **carbocation** is an ion with a positively-charged carbon atom.

Carbocation
- *Carbenium ion* (trivalent positive species) CH_3^+, $C_2H_5^+$...
- *Carbonium ion* (pentavalent positive species, nonclassical carbocation)

Norris and Kehrman (1902):



deep yellow

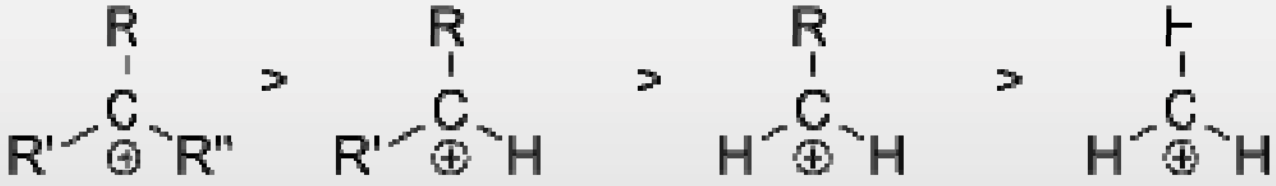
In 1962 Olah directly observed the *tert*-butyl carbocation by NMR as a stable species on dissolving tert-butyl fluoride in magic acid.

I. Structure and Stability

In solution, the carbocation may be free (this is more likely in polar solvents, in which it is solvated) or it may exist as an ion pair. Ion pairs are more likely in nonpolar solvents.

A. Simple alkyl carbocations

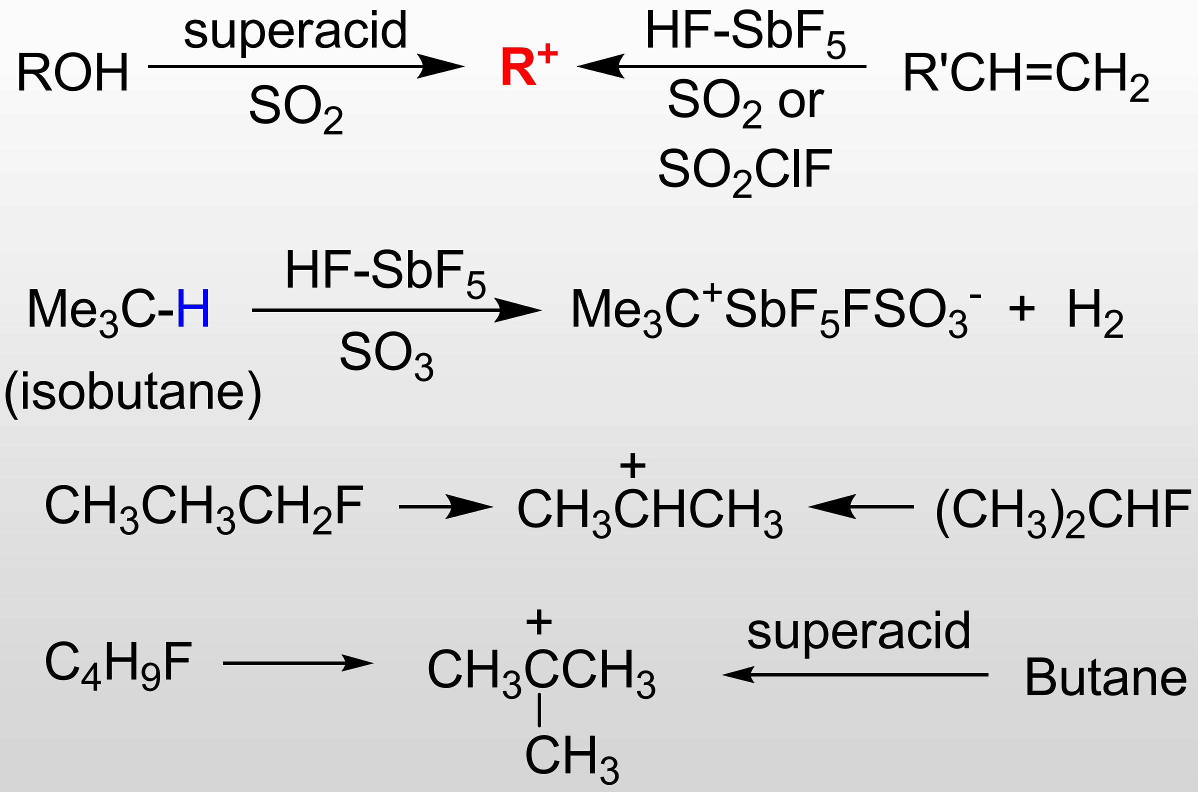
Stability: tertiary > secondary > primary



III II I

The most stable of all alkyl cations is the *tert*-butyl cation. Methane, ethane, and propane, treated with superacid, also yield *tert*-butyl cation as the main product (rearrangement).

No matter how they are generated, study of the simple alkyl cations has provided dramatic evidence for the stability. Both propyl fluorides gave the isopropyl cation; all four butyl fluorides gave the *tert*-butyl cation. Butane, in superacid, gave only the *tert*-butyl cation.



$$\mathrm{ROH} \xrightarrow[\mathrm{SO_2}]{\text{superacid}} \mathbf{R^+} \xleftarrow[\mathrm{SO_2\ or\ SO_2ClF}]{\mathrm{HF\text{-}SbF_5}} \mathrm{R'CH{=}CH_2}$$

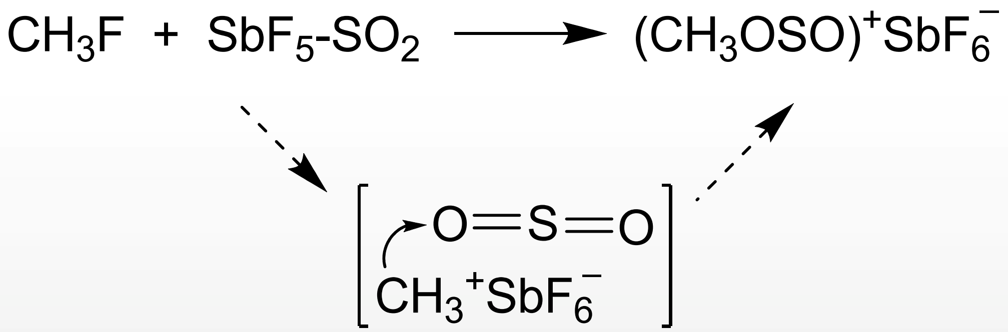
$$\underset{\text{(isobutane)}}{\mathrm{Me_3C\text{-}H}} \xrightarrow[\mathrm{SO_3}]{\mathrm{HF\text{-}SbF_5}} \mathrm{Me_3C^+SbF_5FSO_3^-} + \mathrm{H_2}$$

$$\mathrm{CH_3CH_3CH_2F} \longrightarrow \mathrm{CH_3\overset{+}{C}HCH_3} \longleftarrow \mathrm{(CH_3)_2CHF}$$

$$\mathrm{C_4H_9F} \longrightarrow \mathrm{CH_3\overset{+}{\underset{\displaystyle CH_3}{C}}CH_3} \xleftarrow{\text{superacid}} \text{Butane}$$

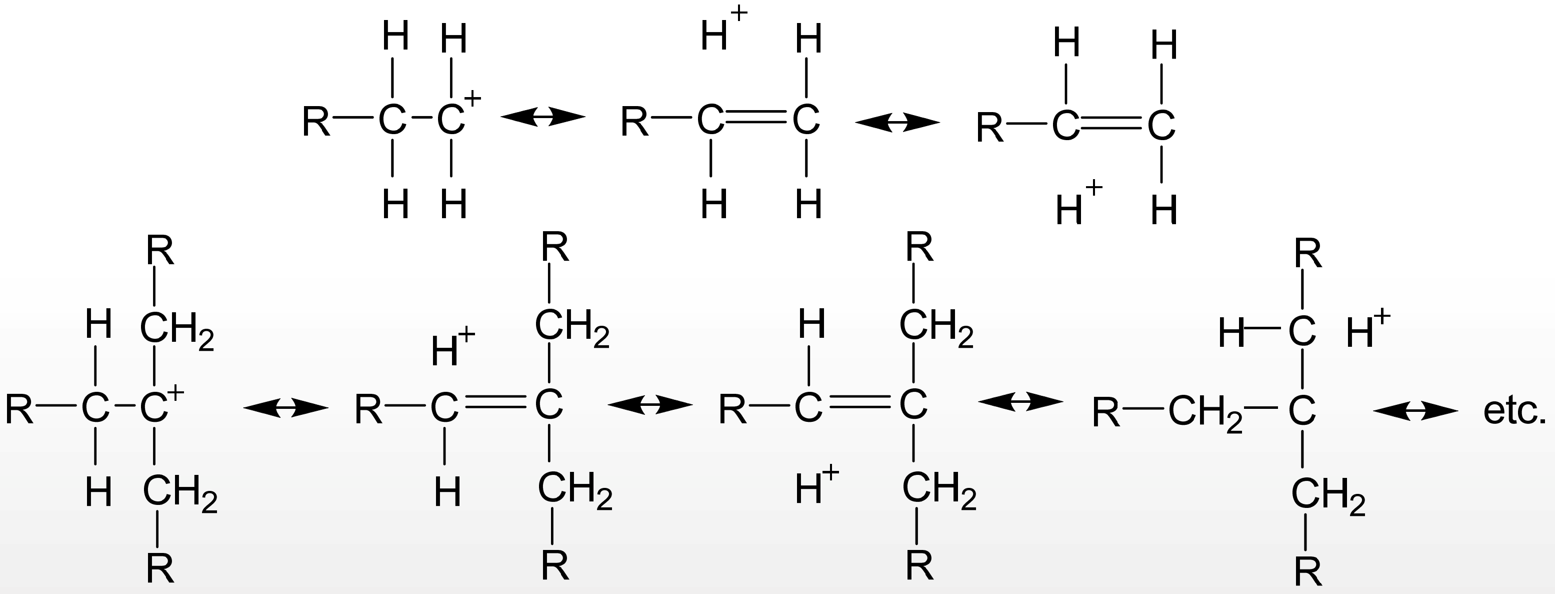
To date, no primary cation has survived long enough for detection.

CH_3^+ ?



$$CH_3F + SbF_5\text{-}SO_2 \longrightarrow (CH_3OSO)^+SbF_6^-$$

- **The field effect.** The electron-donating effect of alkyl groups increases the electron density at the charge-bearing carbon, reducing the net charge on the carbon, and in effect spreading the charge over the α carbons.
- **Hyperconjugation.** Tertiary carbocations are more stable (and form more readily) than secondary carbocations; primary carbocations are highly unstable because, while ionized higher-order carbons are stabilized by **hyperconjugation**, unsubstituted (primary) carbons are not.



$$\underset{(1)}{(CD_3)_3C^+} + (CH_3)_3CH \overset{K}{\rightleftharpoons} \underset{(2)}{(CH_3)_3C^+} + (CD_3)_3CH$$

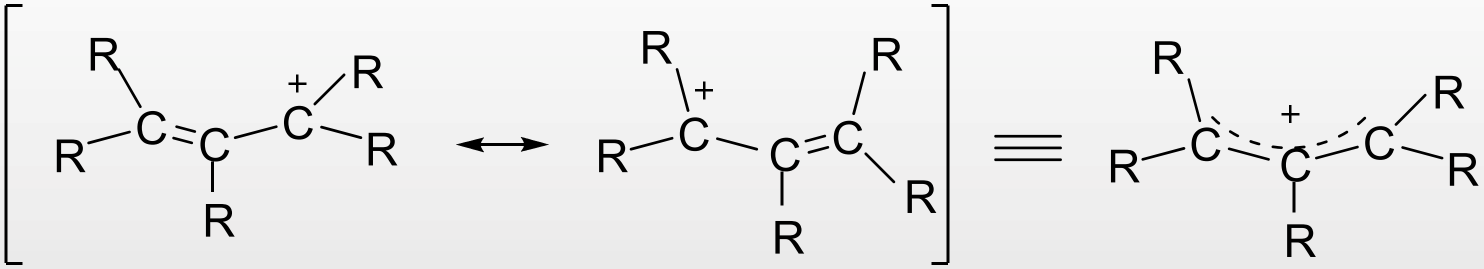
K_{298} =1.97±0.20

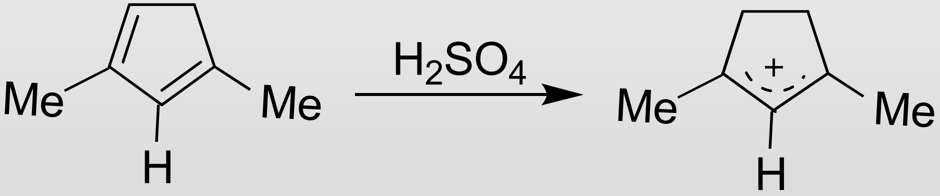
K is 1.97, showing that 2 is more stable than 1. This is a secondary isotopic effect; there is less hyperconjugation in 1 than 2.

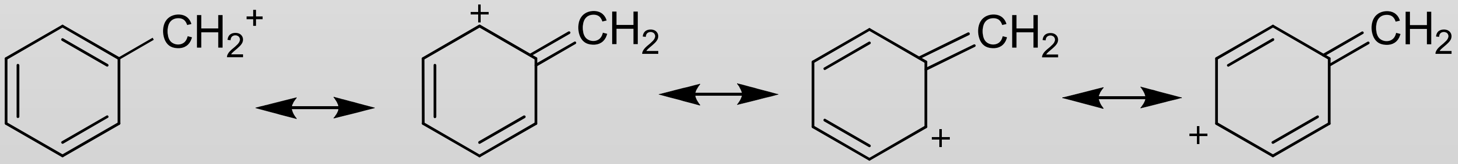
It is a general rule that the more concentrated any charge is, the less stable the species bearing it will be. 电荷越集中，物种越不稳定

B. Stable allylic-type cations

Allyl cation and benzyl cation are more stable than most other carbocations. Molecules which can form allyl or benzyl carbocations are especially reactive. Stable allylic cations have been obtained by the reaction between alkyl halides, alcohols, or alkenes (by hydride extraction) and SbF_5 in SO_2 or SO_2ClF.

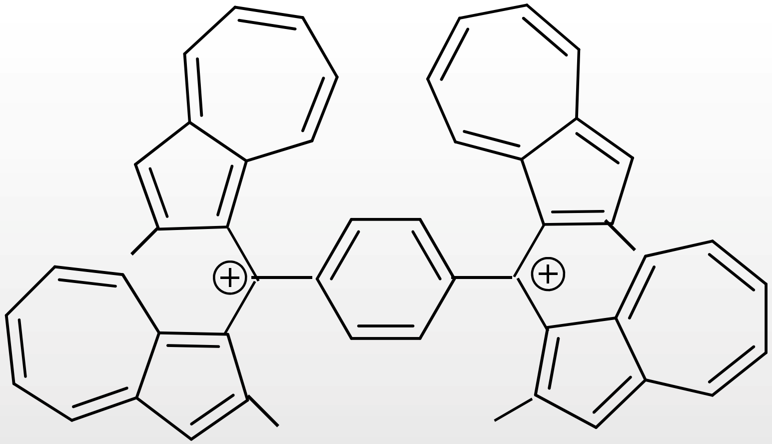




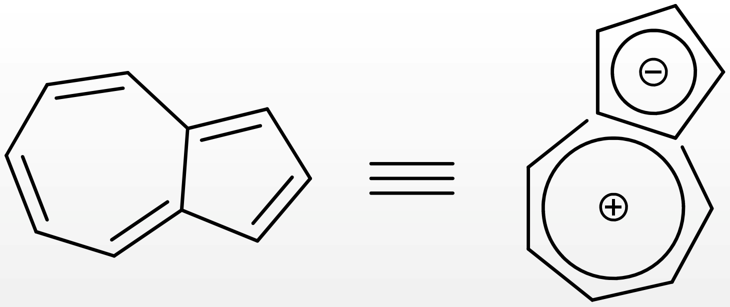


$$Ph_3CCl \overset{SO_2}{\rightleftharpoons} Ph_3C^+ + Cl^-$$

(I)



(II)



azulene

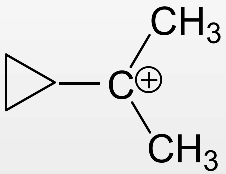
Both triphenylmethyl (I) and diphenylmethyl cations have been isolated as solid salts and, in fact, $Ph_3C^+BF_4$ and related salts are available commercially. Positively charged benzylic carbon (II) is stabilized by two azulene rings.

C. Cyclopropylmethyl cations

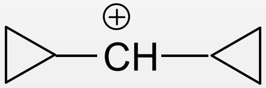
Cyclopropylmethyl cation are even more stable than the benzyl type. Compound (c) has been prepared by solution of the corresponding alcohol in H_2SO_4. Compounds *a*, *b*, and similar ions have been prepared by solution of the alcohols in FSO_3H-SO_2-SbF_5.

NMR spectrum of a dimethyl derivative (a), identical signals are found for the two methyl groups.

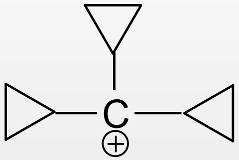
J. Am. Chem. Soc. 1970, 92, 3234–3235



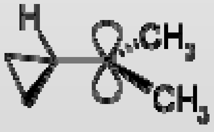
(a)



(b)

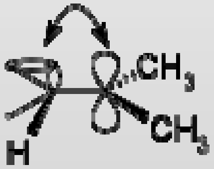


(c)



A

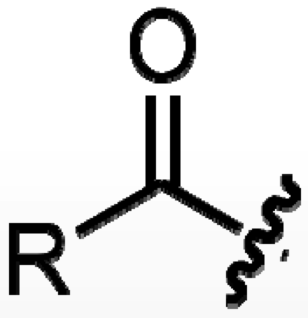
B

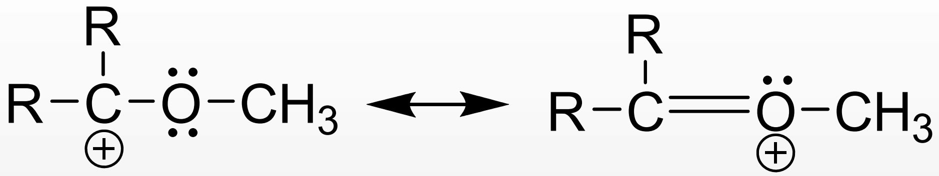


C

D. Other structural types

Another structural feature that increases carbocation stability is the presence, adjacent to the cationic center, of a heteroatom bearing an unshared pair.

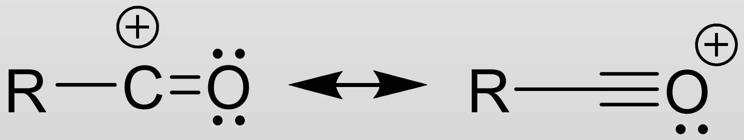




$$R-\underset{\oplus}{\overset{R}{\overset{|}{C}}}-\ddot{\underset{..}{O}}-CH_3 \longleftrightarrow R-\overset{R}{\overset{|}{C}}=\underset{\oplus}{\ddot{O}}-CH_3$$

(I) (II)

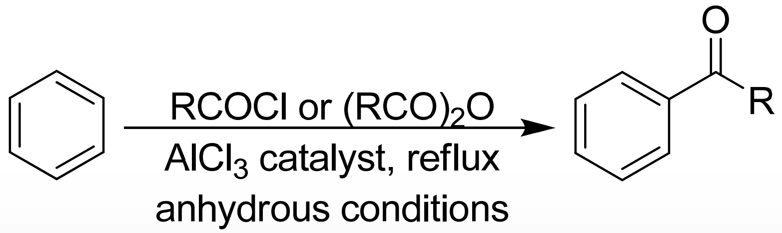
Simple acyl cations (RCO^+) have been prepared in solution and the gas state. The acetyl (CH_3CO^+) is about as stable as the *tert*-butyl cation. The 2,4,6-trimethylbenzoyl cations are especially stable (for steric reasons) and are easily formed in 96% H_2SO_4.



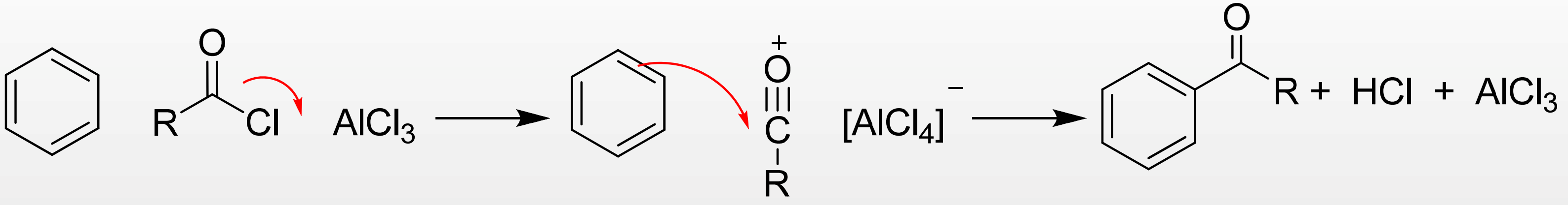
$$R-\overset{\oplus}{C}=\ddot{\underset{..}{O}} \longleftrightarrow R-C\equiv\overset{\oplus}{\underset{..}{O}}$$

(III) (IV)

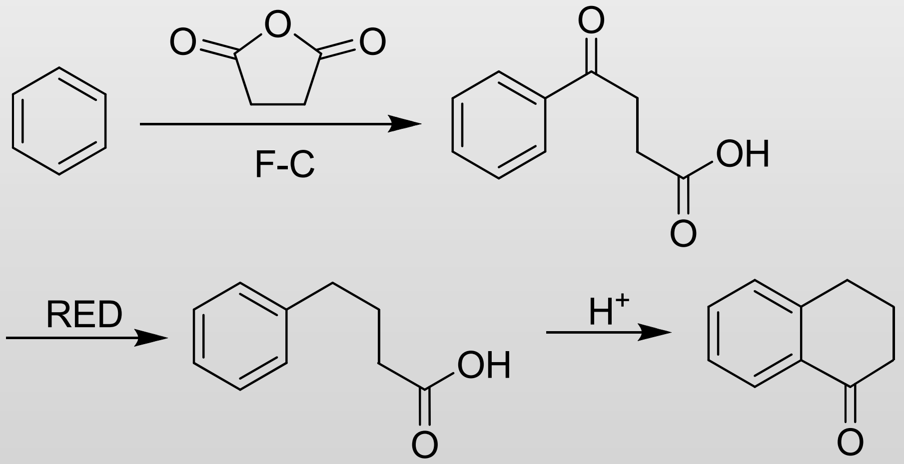
◆ Friedel-Crafts acylation



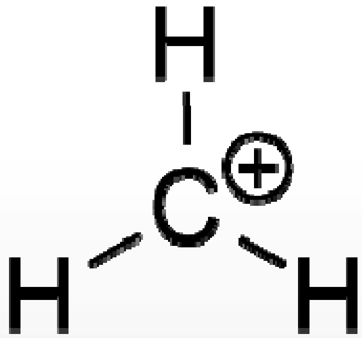
Mechanism:

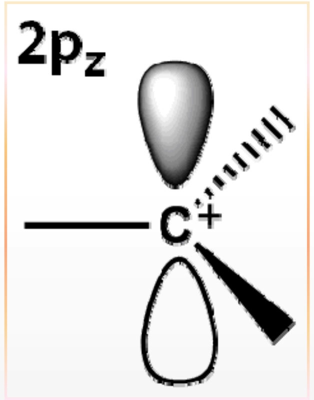


Haworth
reaction:

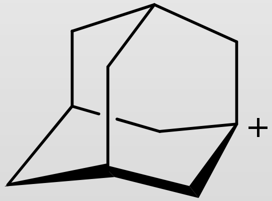


Carbocation structures: planar sp^2 hybrid



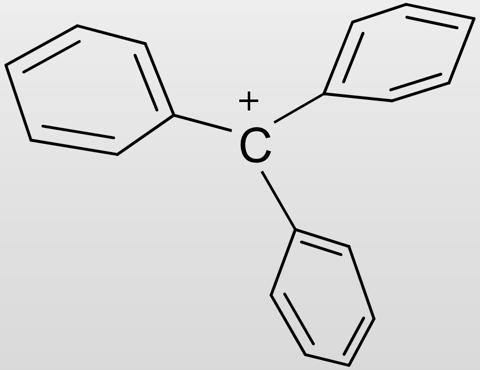


tert-butyl cation
demonstrating planar geometry



adamentyl

1-trishomobarrelyl



triphenylmethyl
propeller-shaped

◆ An important tool for the investigation of carbocation structure is measurement of the ^{13}C NMR chemical shift of the carbon atom bearing the positive charge. *This shift approximately correlates with electron density on the carbon*.

TABLE 1. The ^{13}C chemical shift values for the charged carbon atom of some carbocations in SO_2ClF-SbF_5, SO_2-FSO_3H-SbF_6, or SO_2-SbF_5.

Ion	Chemical shift (ppm)	Temp (°C)	Ion	Chemical shift (ppm)	Temp (°C)
Et_2MeC^+	-139.4	-20	$C(OH)_3^+$	+28.0	-50
Me_2EtC^+	-139.2	-60	$PhMe_2C^+$	-61.1	-60
Me_3C^+	-135.4	-20	$PhMeCH^+$	-40	
Me_2CH^+	-125.0	-20	Ph_2CH^+	-5.6	-60
Me_2COH^+	-55.7	-50	Ph_3C^+	-18.1	-60
$MeC(OH)_2^+$	-1.6	-30	$Me_2(cyclopropyl)C^+$	-86.8	-60
$HC(OH)_2^+$	+17.0	-30			

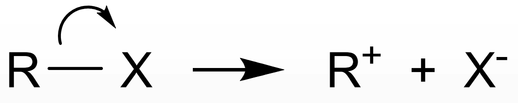
高场

低场

II. The Generation and Fate of Carbocations

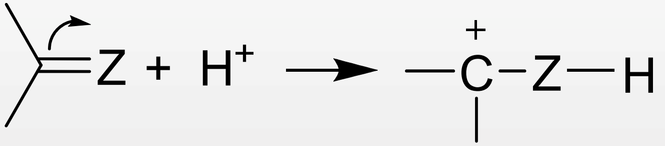
Two general ways to form carbocations:

i. A direct ionization:



$R-X \longrightarrow R^+ + X^-$ (may be reversible)

ii. Addition of a positive species toan unsaturateraed system:

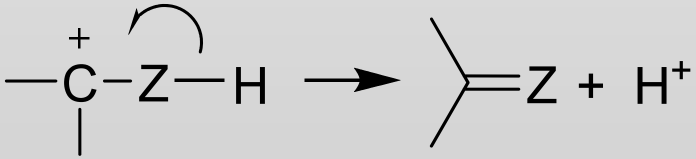


The reaction of carbocations:

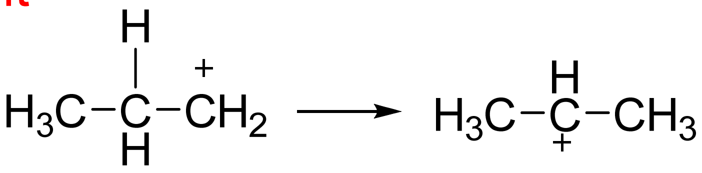
i. Combination with a species possessing an electron pair.

$$R^+ + X^- \longrightarrow R-X$$

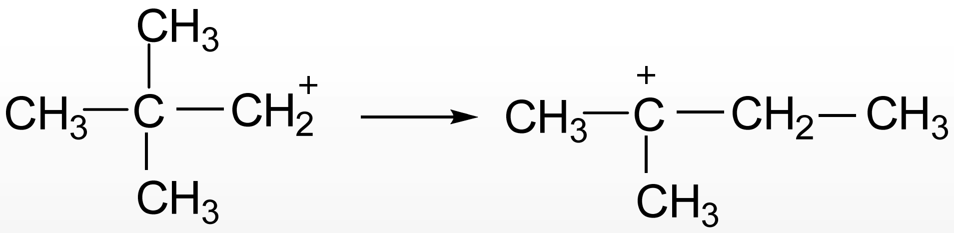
ii. The carbocation may lose a proton from the adjacent atom.



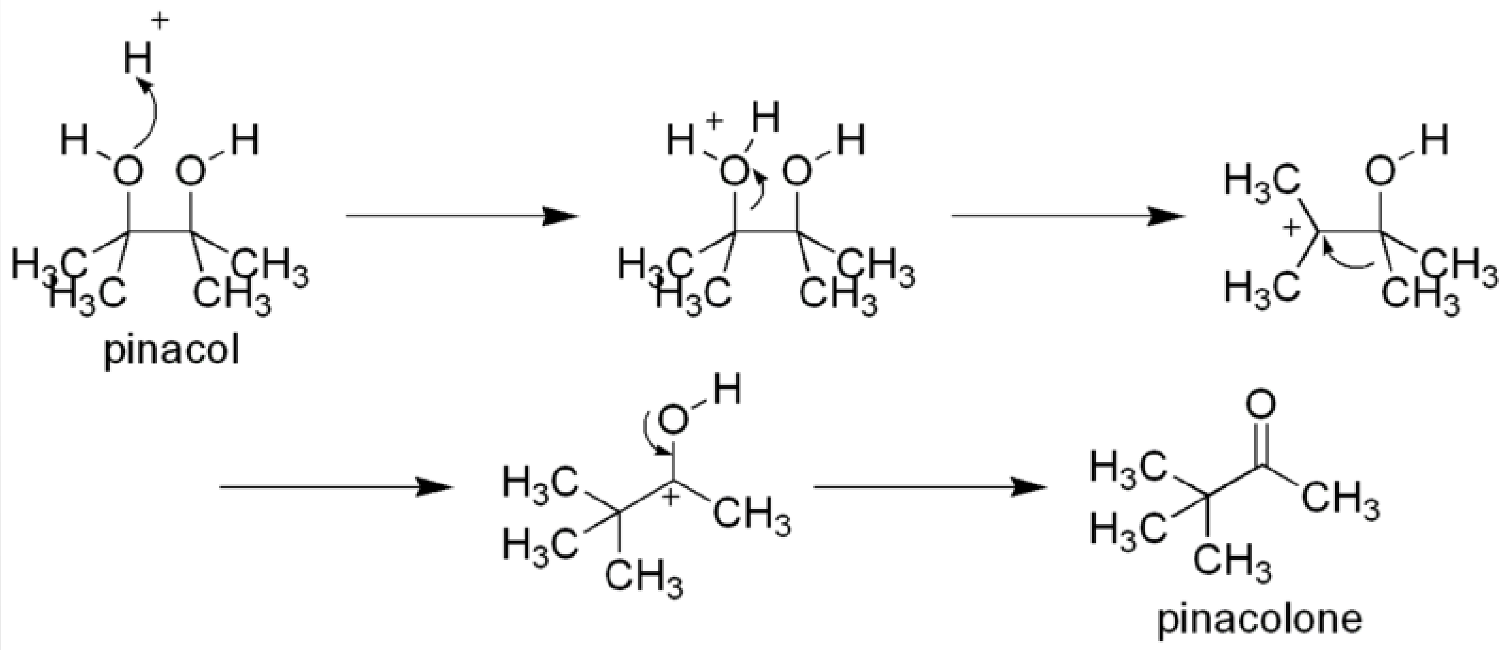
Rearrangement

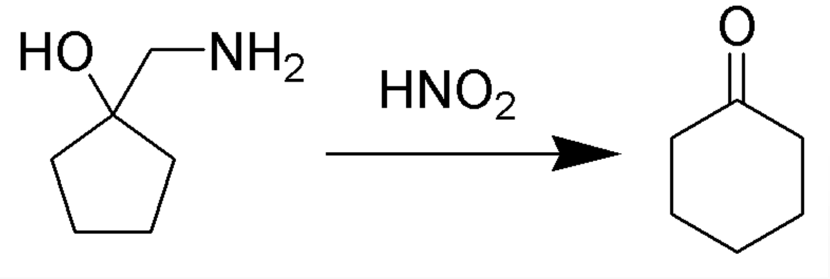


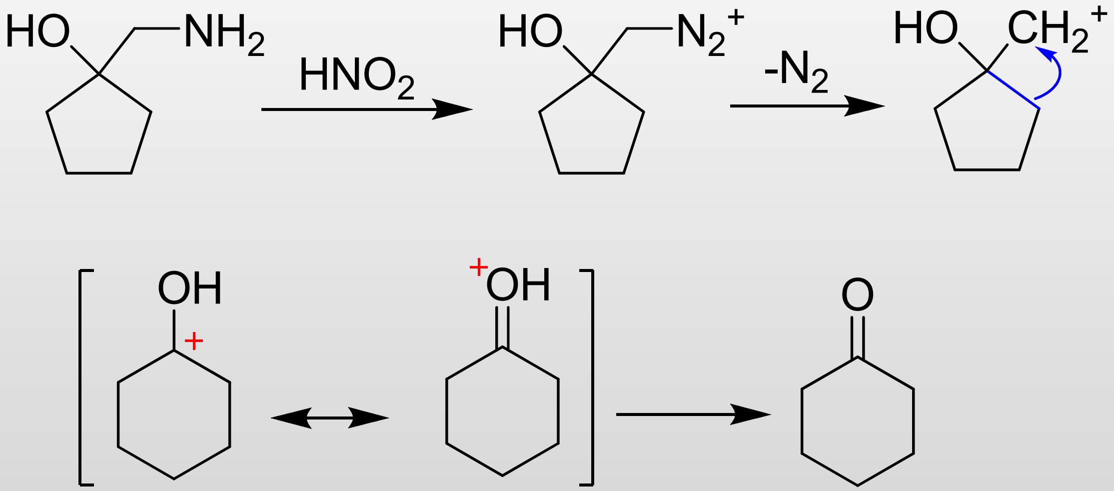
$$H_3C-\overset{H}{\underset{H}{C}}-\overset{+}{C}H_2 \longrightarrow H_3C-\overset{H}{\underset{+}{C}}-CH_3$$



$$CH_3-\overset{CH_3}{\underset{CH_3}{C}}-\overset{+}{C}H_2 \longrightarrow CH_3-\overset{+}{\underset{CH_3}{C}}-CH_2-CH_3$$



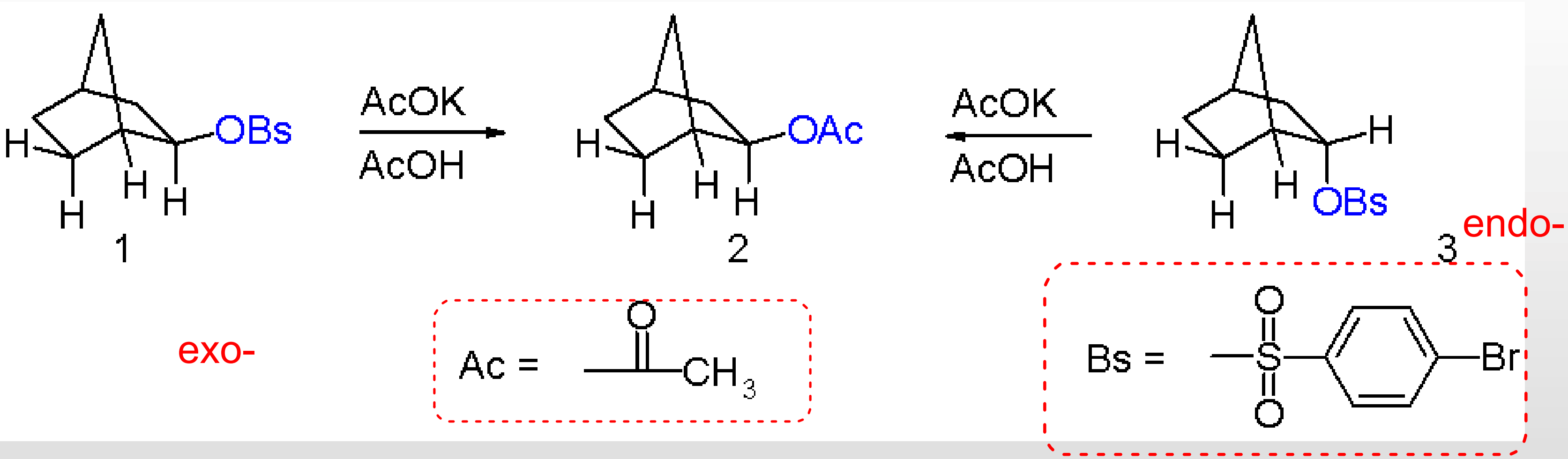

HO
NH_2
HNO_2
O


HO
NH_2
HNO_2
HO
N_2^+
$-N_2$
HO
CH_2^+
OH
+
^+OH
O

III. Non-classical Carbocations 非经典碳正离子

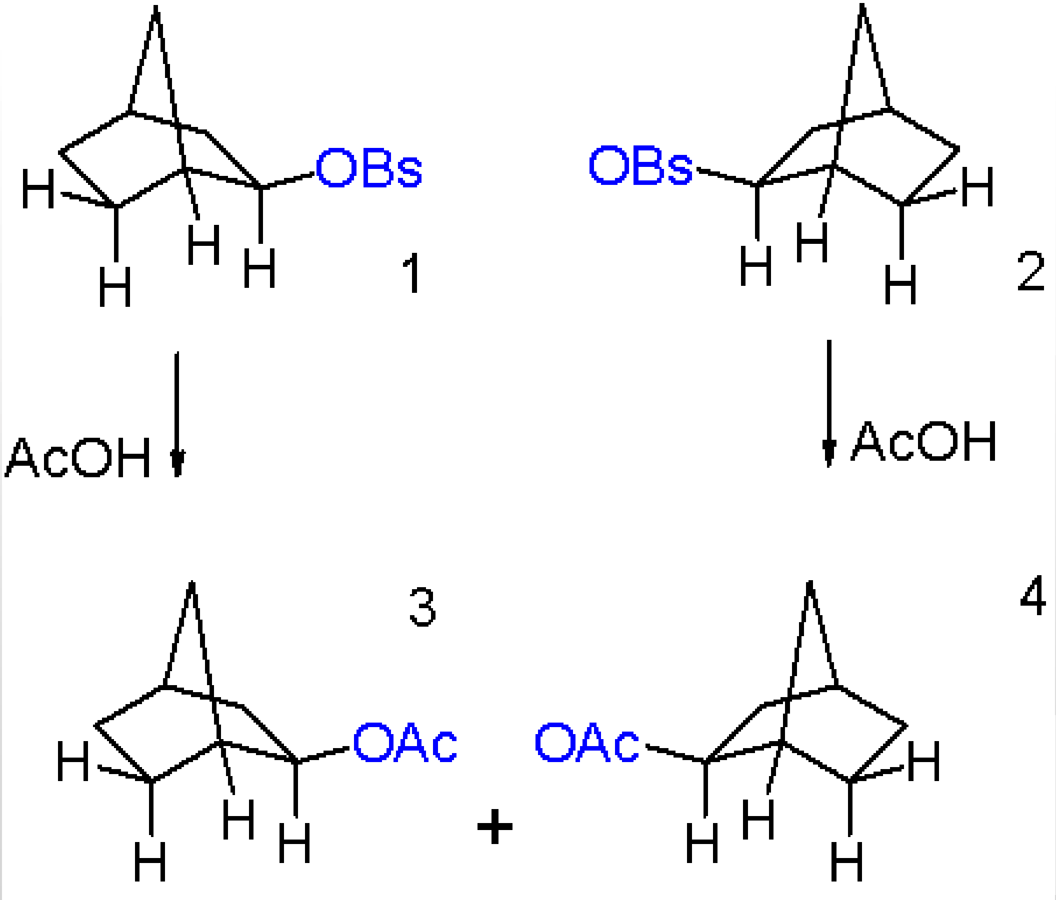
Non-classical ions are a special type of carbonium ions displaying delocalization of sigma bonds in 3-center-2-electron bonds of bridged systems.

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

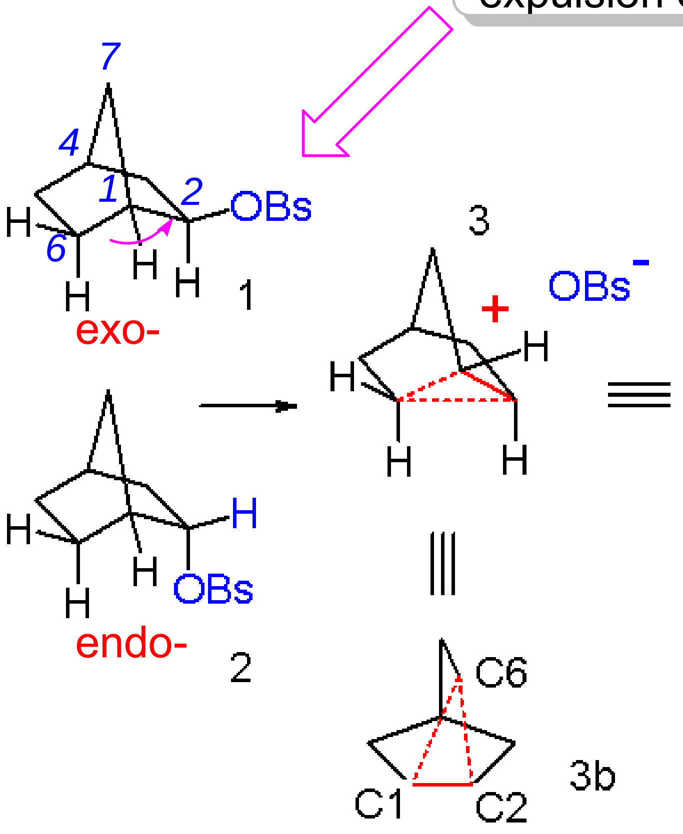


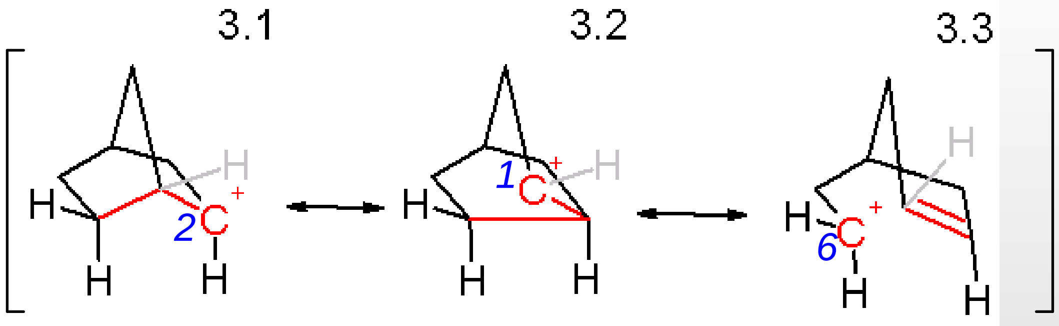
A key observation is that in this nucleophilic displacement both isomers give the same reaction product an exo-acetate 2. Also the reaction rate for the exo-reaction is 350 times the reaction rate for the endo reaction.

In a related experiment both enantiomers **1** and **2** of the exo-brosylate on solvolysis give the same racemic reaction product. The optical activity of the reaction disappears at the same reaction rate as that of the solvolysis.



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

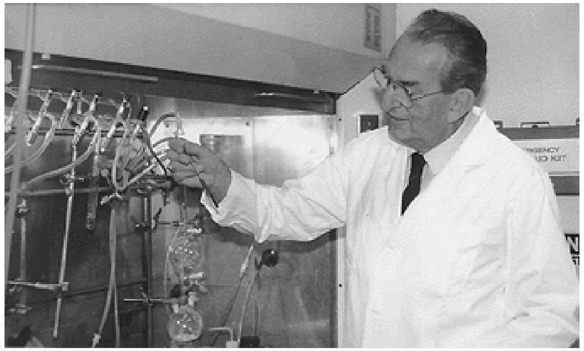


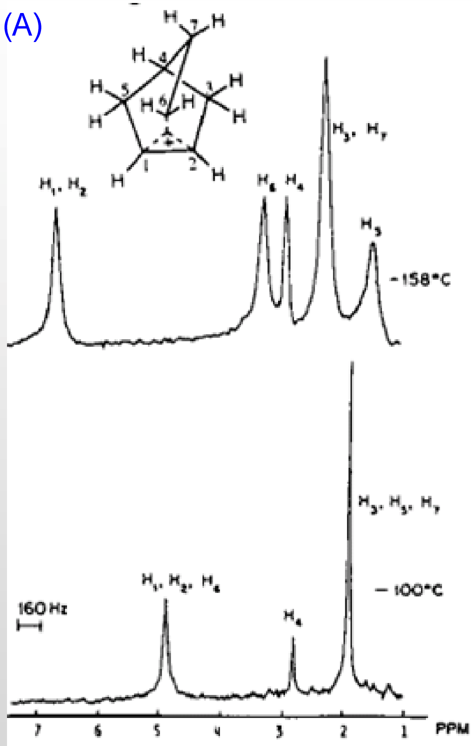


3. A non-classical ion: pentavalent, symmetrical

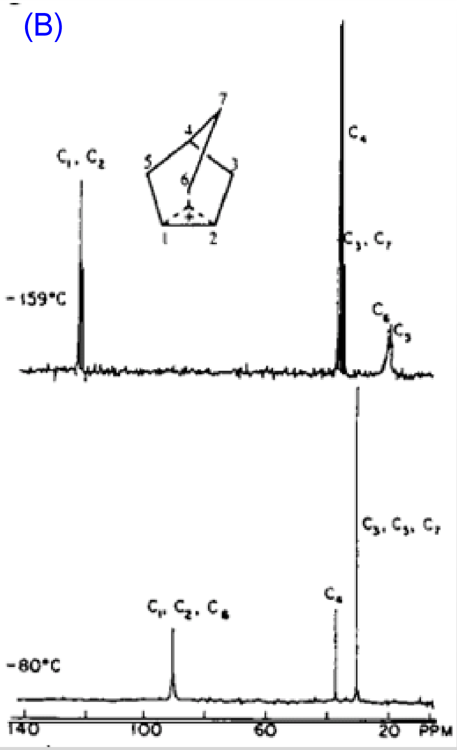
In a non-classical carbocations, the positive charge is delocalized by a double or triple bond that is not in the allylic position or by a single bond.

George A Olah (1964): direct evidence for the norbornyl cation by NMR analysis

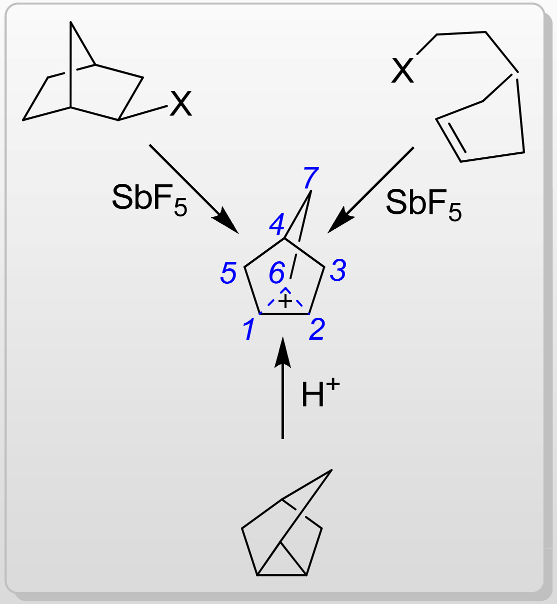




(A) 395 MHz 1HNMR of 2-norbornyl cation in $SbF_5/SO_2ClF/SO_2F_2$ solution.



(B) 50 MHz proton decoupled 13C NMR of 2-norbornyl cation in $SbF_5/SO_2ClF/SO_2F_2$.

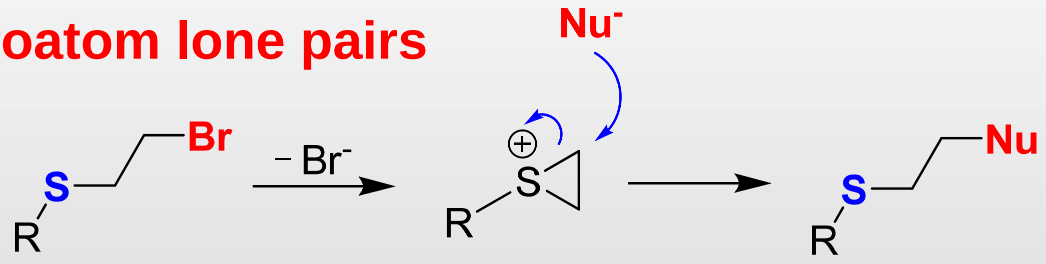


Olah, G.A., *J. Am.Chem.Soc.* **104**, 7105(1982)

IV. Neighbouring group participation (NGP)

Neighbouring group participation or NGP has been defined by IUPAC as the interaction of a reaction centre with a lone pair of electrons in an atom or the electrons present in a σ bond or π bond. When NGP is in operation it is normal for the reaction rate to be increased. It is also possible for the stereochemistry of the reaction to be abnormal (or unexpected) when compared with a *normal* reaction.

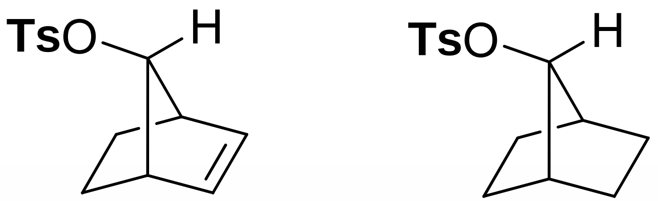
A. NGP by heteroatom lone pairs



R = $BrCH_2CH_2^-$,
sulfur mustard

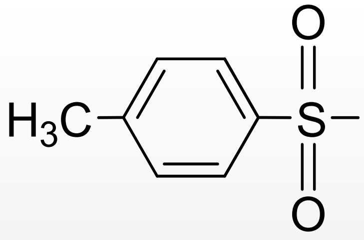
The rate of reaction is much higher for the sulfur mustard and a nucleophile than it would be for a primary alkyl chloride without a heteroatom.

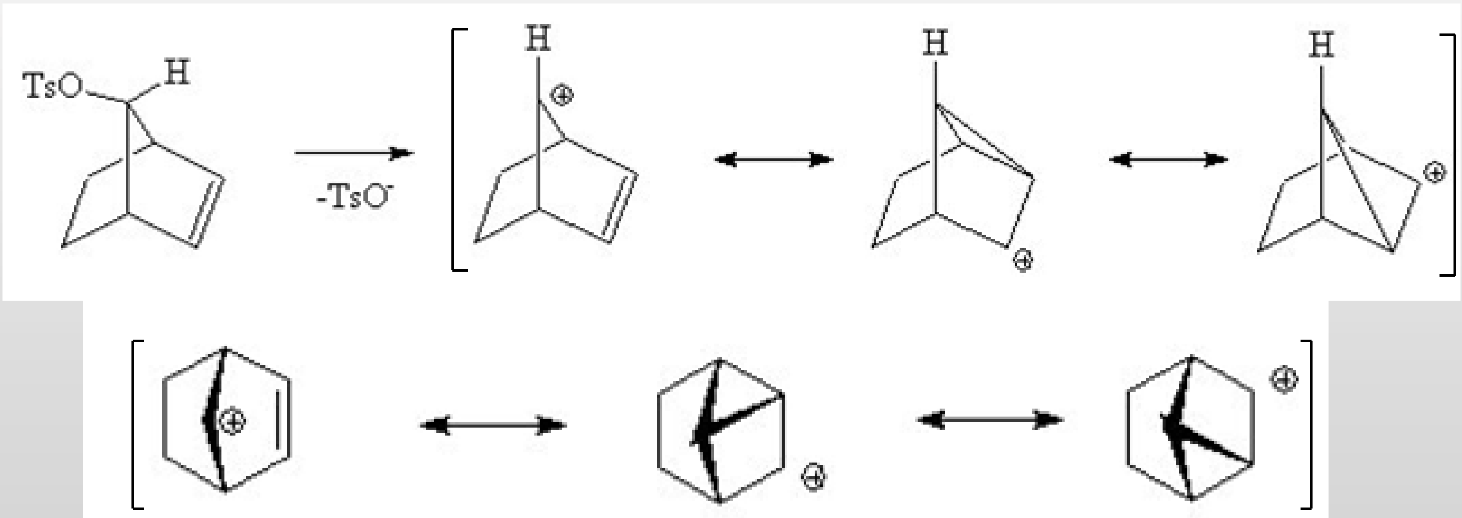
B. NGP by an alkene (C=C as a neighboring group)



The rate of acetolysis	100	1
Configuration	retention	retention

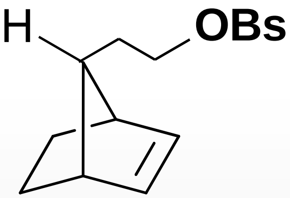
Ts =



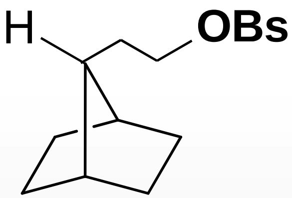


(a different view of the same intermediates)

Even if the double bond is more remote from the reacting center the alkene can still act in this way.



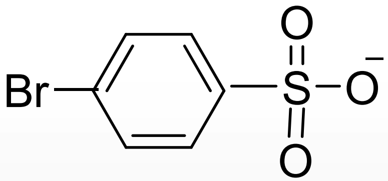
(A)



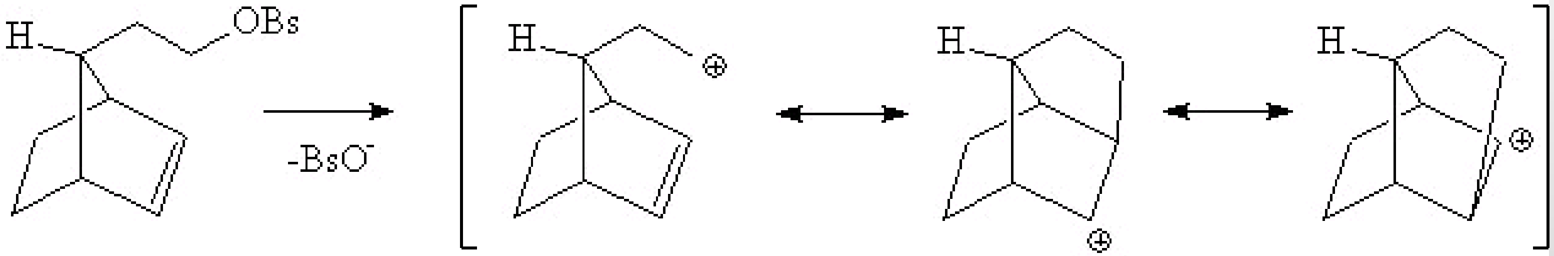
(B)

Relative rate of acetolysis 140,000 1

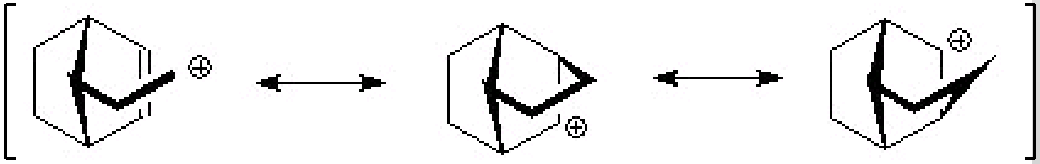
BsO$^-$:



(A): β-(syn-7-norbornenyl) ethyl brosylate



a different view of the same carbocation:

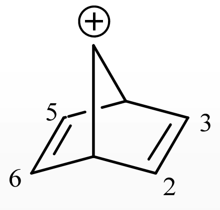


DISCUSSION

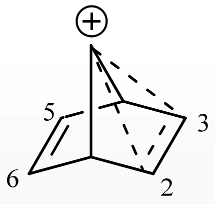
(i) Evidence for the non-classical cations.

(ii) A neighboring group lends anchimeric assistance only when there is sufficient demand for it.

(iii) The ability of C=C to serve as a neighboring group can depend on its electron density.

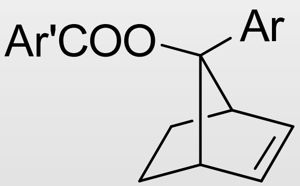


(A)

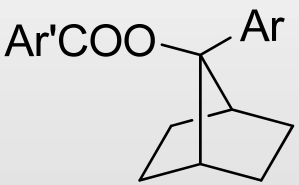


(B)

Norbornadienyl cation
^{1}H NMR:
2 and 3 protons are not equivalent to the 5 and 6 protons.



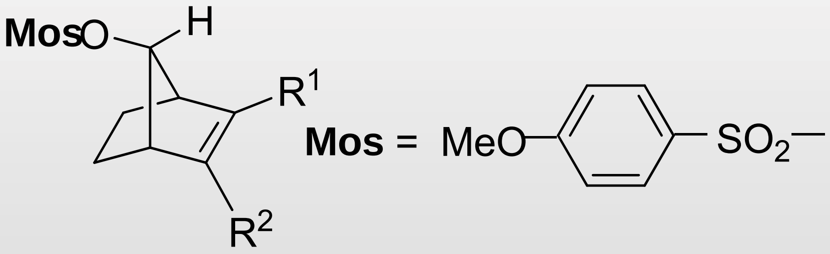
a



b

relative rates of solvolysis in acetone-water at 85°C	a	b
	2.5	**1**

Ar = p-MeOC$_6$H$_4$
Ar' = p-NO$_2$C$_6$H$_4$

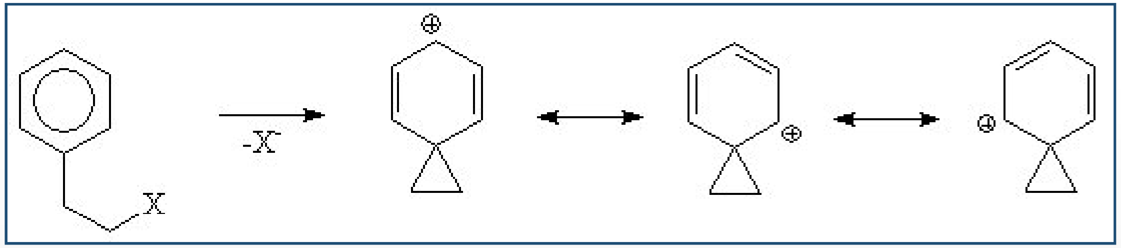


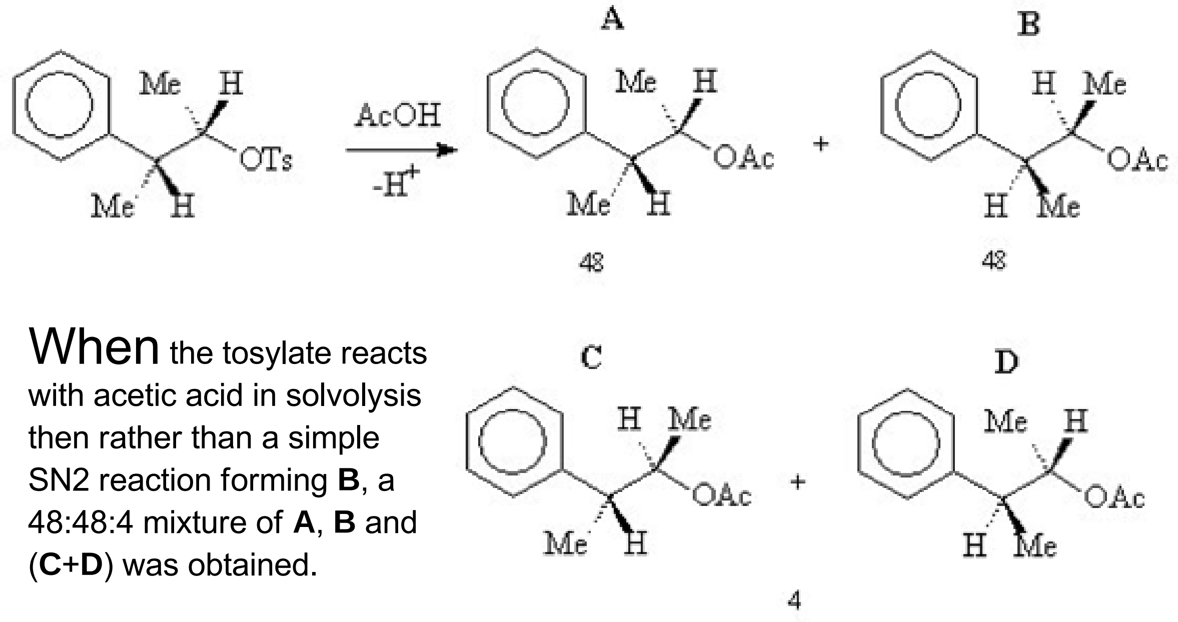
Relative rates of the solvolysis

$R_1 = R_2 = H$	1.4×10^{12}
$R_1 = H, R_2 = CF_3$	1.5×10^{6}
$R_1 = R_2 = CF_3$	1

C. NGP by an aromatic ring

An aromatic ring can assist in the formation of a carbocationic intermediate called a phenonium ion by delocalising the positive charge.

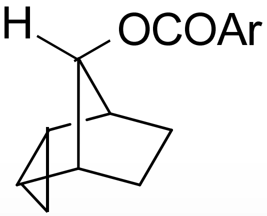




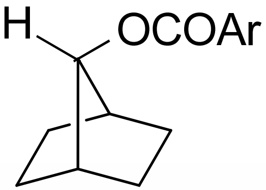
When the tosylate reacts with acetic acid in solvolysis then rather than a simple SN2 reaction forming **B**, a 48:48:4 mixture of **A**, **B** and (**C**+**D**) was obtained.

QUESION: please give a mechanism which forms A and B.

D. Cyclopropyl as a neighboring group

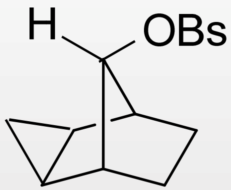


(A)

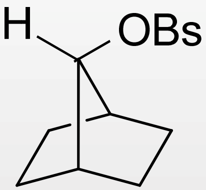


(B)

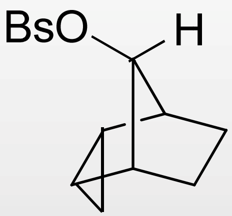
(Ar = p-$NO_2C_6H_4$)



(C)

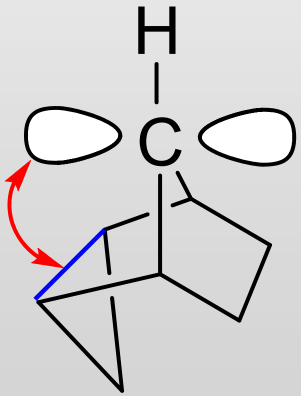


(D)



(E)

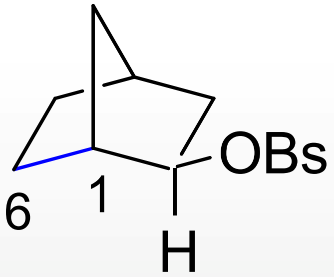
The relative rate of solvolysis		
(A)	(B)	
10^{14}	1	
(C)	(D)	(E)
1/3	1	5



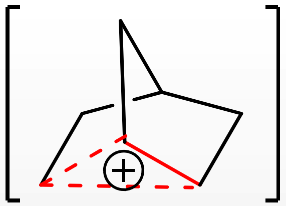
Where cyclopropyl lends considerable anchimeric assistance, the developing p orbita of the carbocation is orthogonal to the participating bond of the cyclopropane ring.

E. The C-C single bond as a neighboring group

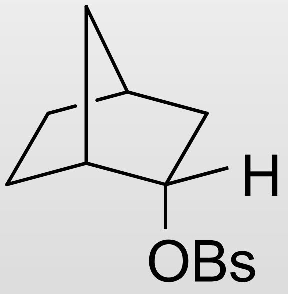
i. The 2-norbornyl system



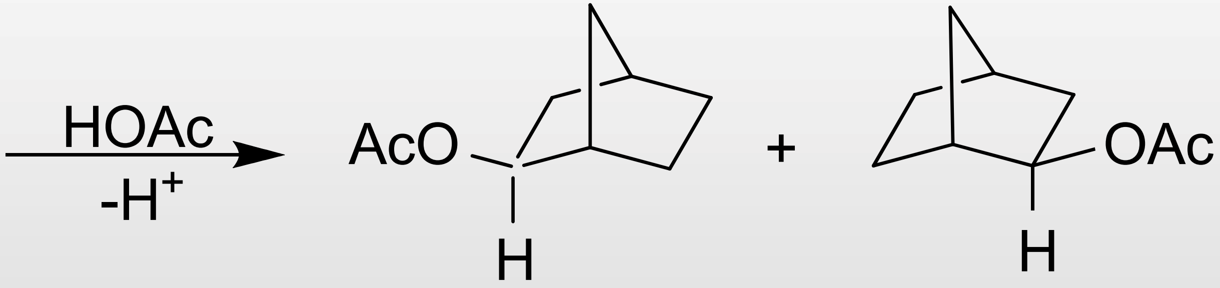
exo-2-norbornyl
brosylate



norbornenyl cation



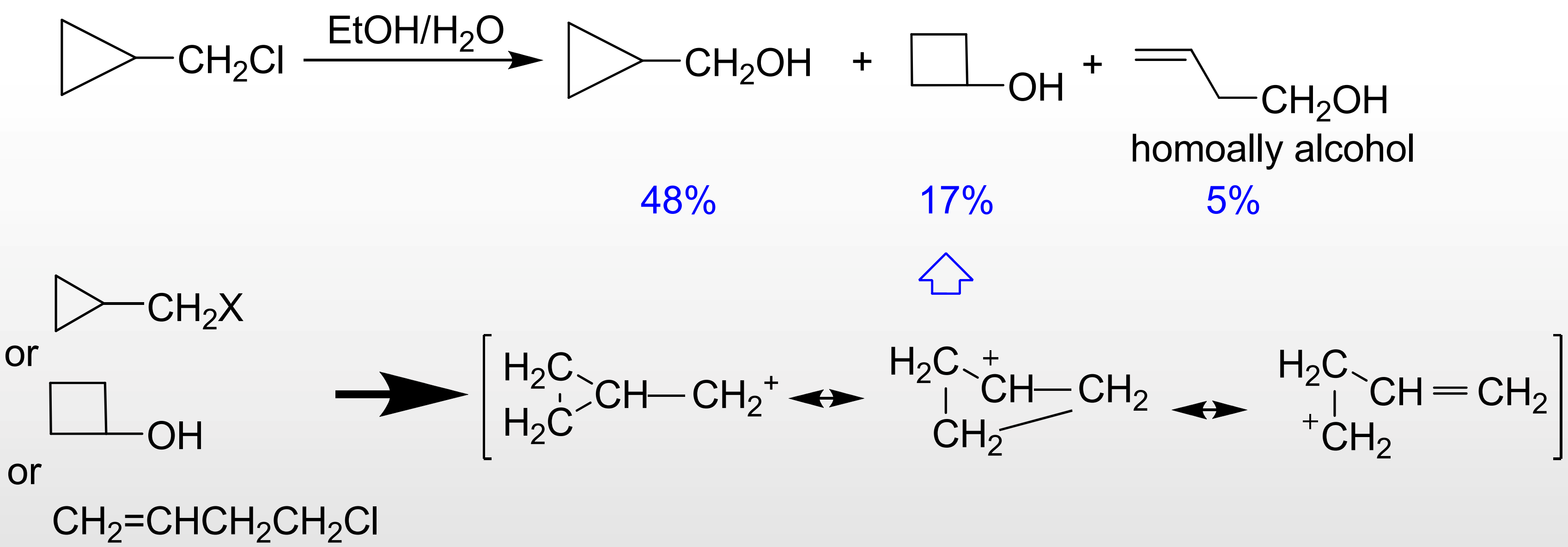
endo-2-norbornyl
brosylate



exo acetates
a racemic mixture

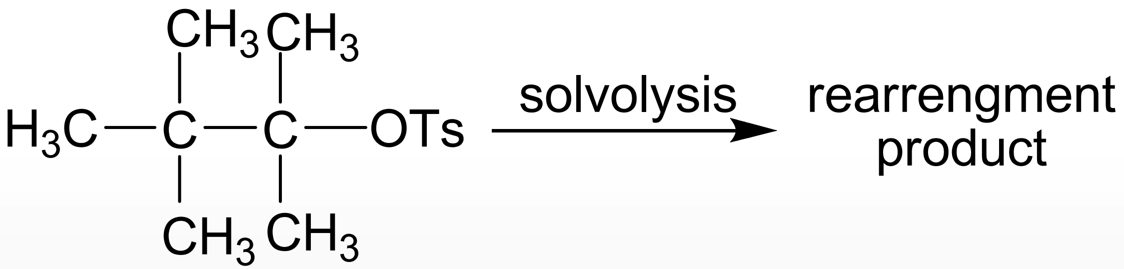
relative rate: exo/endo **350**

ii The Cyclopropylmethyl System

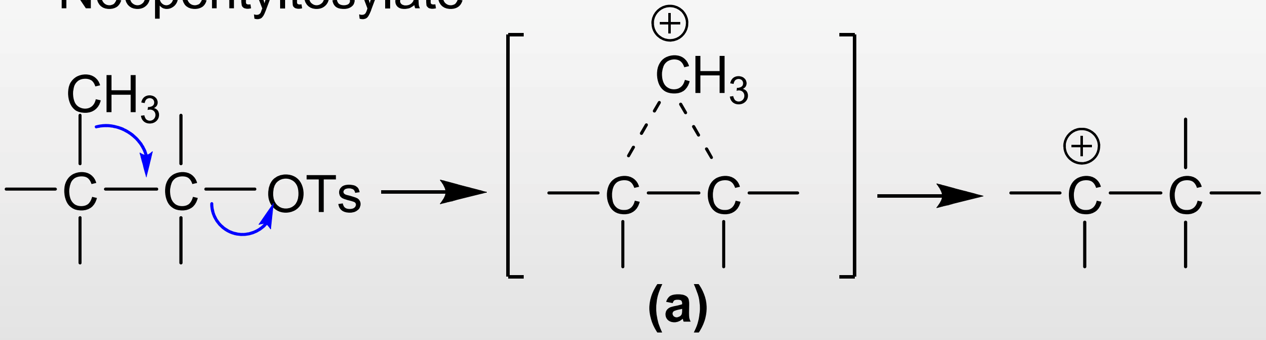


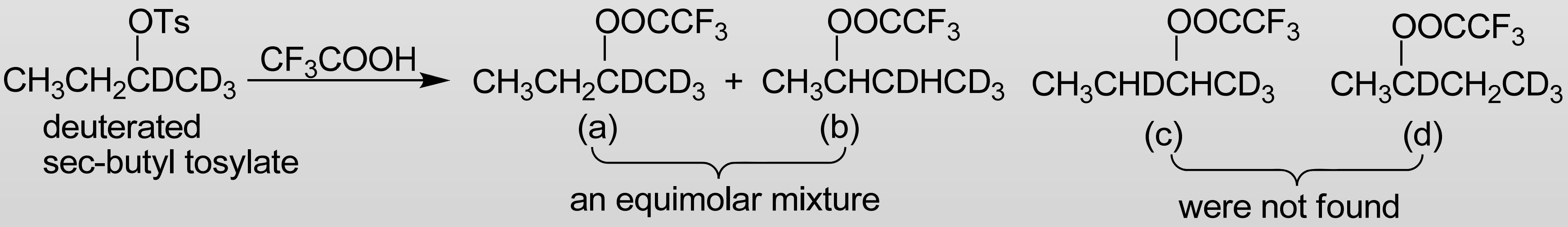
The carbocationic intermidate is delocalised onto many different carbons through a reversible ring opening.

iii. Methyl or Hydrogen as Neighboring Group



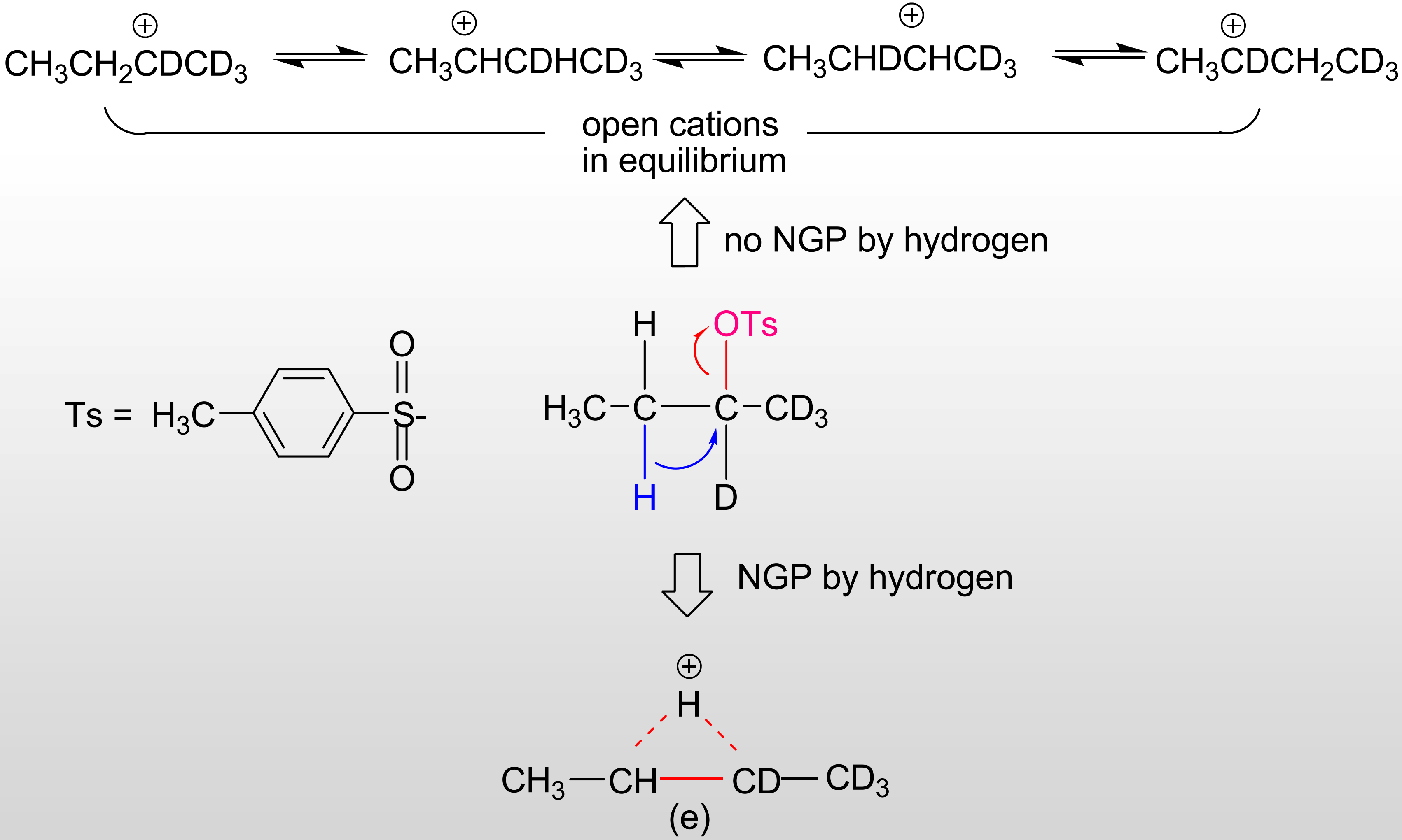
Neopentyltosylate





$$CH_3CH_2\overset{OTs}{C}DCD_3 \xrightarrow{CF_3COOH} \underbrace{\underset{(a)}{CH_3CH_2\overset{OOCCF_3}{C}DCD_3} + \underset{(b)}{CH_3\overset{OOCCF_3}{C}HCDHCD_3}}_{\text{an equimolar mixture}} \quad \underbrace{\underset{(c)}{CH_3CHD\overset{OOCCF_3}{C}HCD_3} \quad \underset{(d)}{CH_3\overset{OOCCF_3}{C}DCH_2CD_3}}_{\text{were not found}}$$

deuterated
sec-butyl tosylate



$CH_3CH_2\overset{\oplus}{C}DCD_3 \rightleftharpoons CH_3\overset{\oplus}{C}HCDHCD_3 \rightleftharpoons CH_3CHD\overset{\oplus}{C}HCD_3 \rightleftharpoons CH_3\overset{\oplus}{C}DCH_2CD_3$

open cations
in equilibrium

no NGP by hydrogen

NGP by hydrogen

4.2 Carbanions

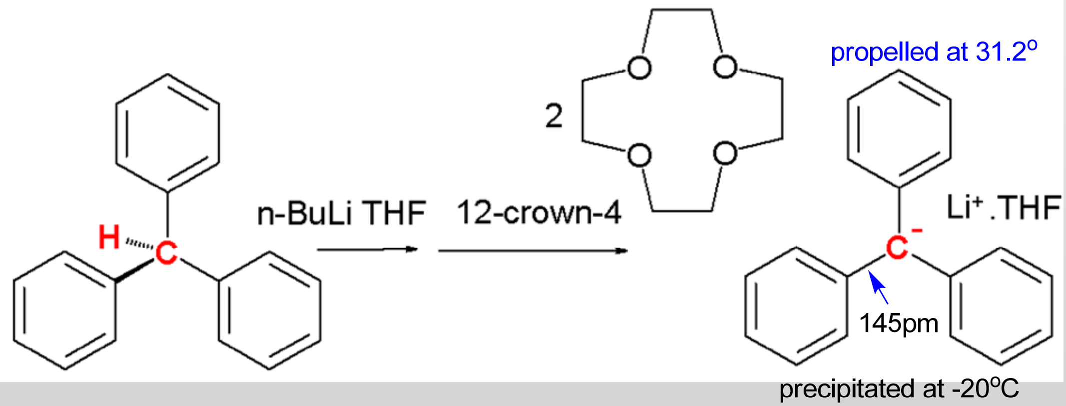
A **carbanion** is an anion in which carbon has an unshared pair of electrons and bears a negative charge usually with three substituents for a total of eight valence electrons.

Formally a carbanion is the conjugate base of a **carbon acid**.

$$R-\overset{|}{\underset{|}{C}}-H \rightleftharpoons R-\overset{|}{\underset{|}{C}}:^{-} + H^{+}$$

Stable carbanions do however exist although in most cases they are reactive.

Olmstead (1984):



I. Stability and Structure

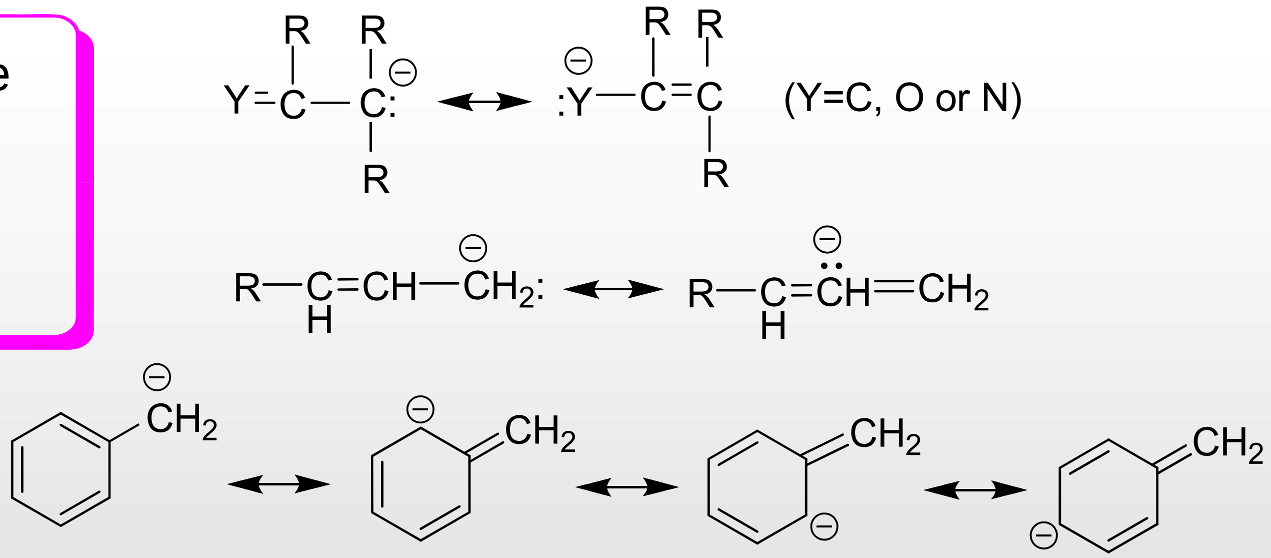
The stability of the carbanion is directly related to the strength of the conjugate acid. The weaker is the acid, the greater is the base strength and the lower is the stability of the carbanion.

Factors determining the stability and reactivity of a carbanion:

- The inductive effect. Electronegative atoms adjacent to the charge will stabilize the charge;
- Hybridization of the charge-bearing atom. The greater the *s*-character of the charge-bearing atom, the more stable the anion;
- The extent of conjugation of the anion. Resonance effects can stabilize the anion. This is especially true when the anion is stabilized as a result of aromaticity.

Relatively stable carbanions with certain structural features

Conjugation of the unshared pair of electrons with an unsaturated bond

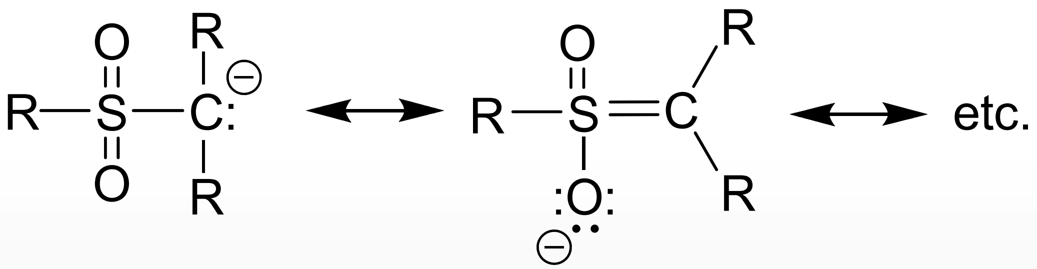


Carbanions increase in stability with an increase in the amount of *s* character at the carbanionic carbon.

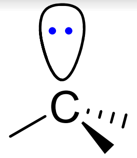
Stability:

$RC\equiv C^{-} > R_2{=}CH^{-} \approx Ar^{-} > RCH_2^{-}$

- Stabilization by sulfur or phosphorus.

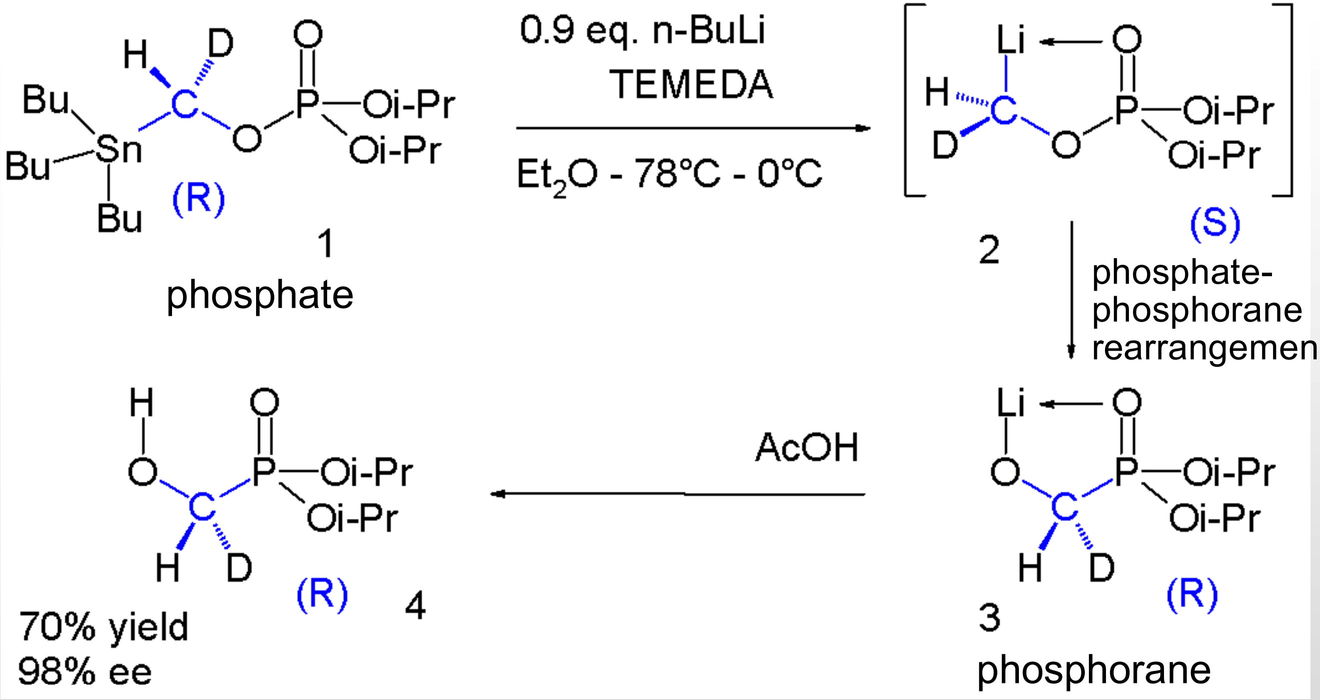


- **Field effect:**
  - Ylides are more stable than the corresponding simple carbanions.
  - Carbanions are stabilized by a field effect if there is any hetero atom (O, N or S) connected to the carbanionic carbon, provided that the hetero atom bears a positive charge in at least one important canonical form.



trigonal pyramid

Question:
Whether or not carbanions
can display chirality?



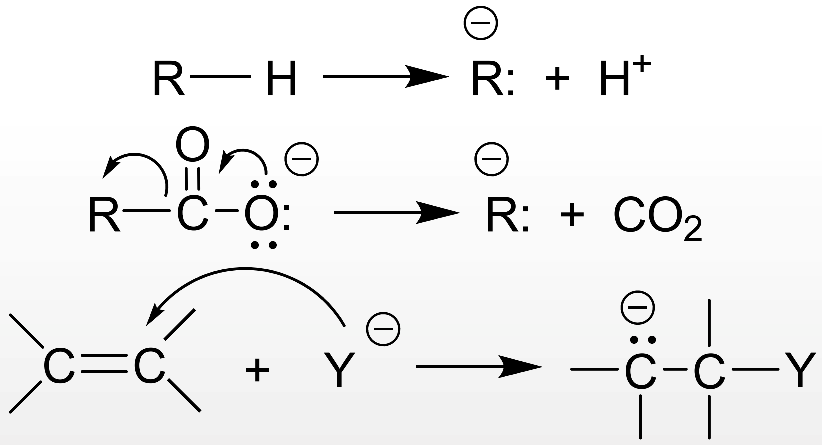
In the range of -78 to 0°C the chirality is preserved in this reaction sequence.

J. Am. Chem. Soc.; **2007**; 129(4), 914-923

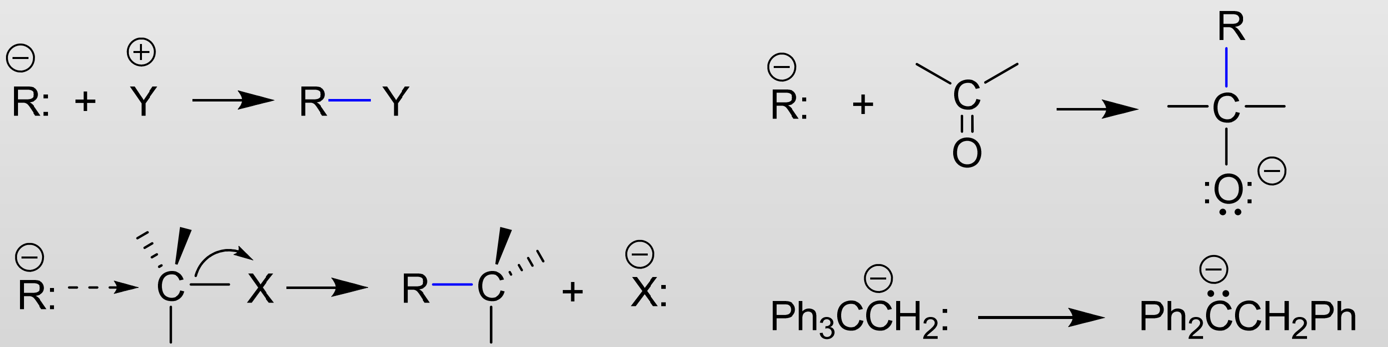
II. The Generation and Fate of Carbanions

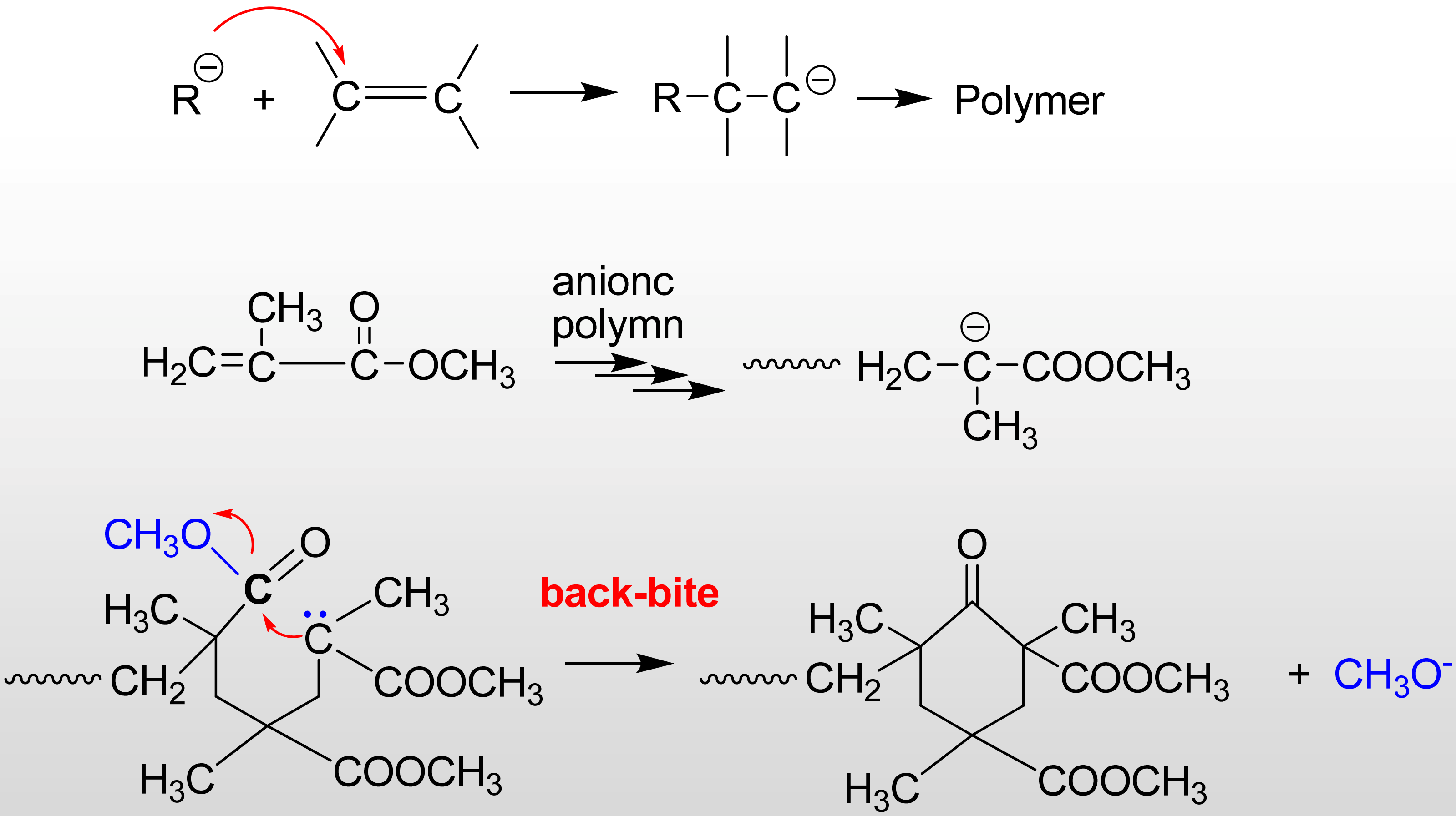
a) A group attached to a carbon leaves without its electron pair.

b) A negative ion adds to a carbon-carbon double or triple bond.



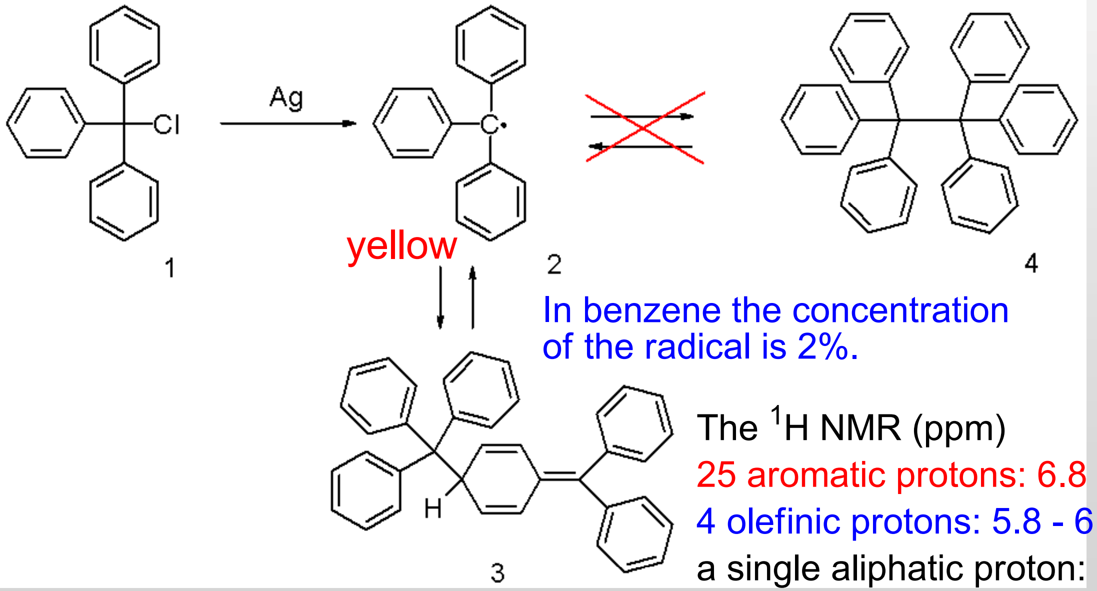
Reactions:




R⊖
+
C=C
R–C–C⊖
Polymer
anionc
polymn
$H_2C=C(CH_3)–C(=O)–OCH_3$
$H_2C–C^{\ominus}(CH_3)–COOCH_3$
CH_3O
back-bite
H_3C
CH_2
CH_3
$COOCH_3$
O
+ CH_3O^-

4.3 Free Radicals

- A free radical may be defined as a species that contains one or more unpaired electrons.
- Radicals play an important role in *combustion*, *atmospheric chemistry*, *polymerization*, *plasma chemistry*, *biochemistry*, and many other chemical processes, including human physiology.
- The first organic free radical identified was triphenylmethyl radical, by Moses Gomberg (the founder of radical chemistry) in 1900.



In benzene the concentration of the radical is 2%.

The ^{1}H NMR (ppm)
25 aromatic protons: 6.8 - 7.4
4 olefinic protons: 5.8 - 6.4
a single aliphatic proton: 5

Moses Gomberg
1866-1947

I. Stability and Structure

- Alkyl radical intermediates are stabilized by similar criteria as carbocations: *the more substituted the radical center is, the more stable it is.*

The stability order for radical: tertiary > secondary > primary

Hyperconjugation:

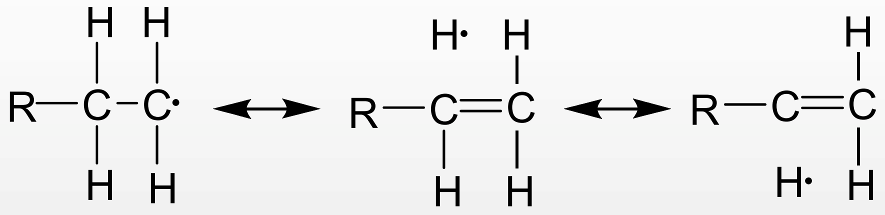
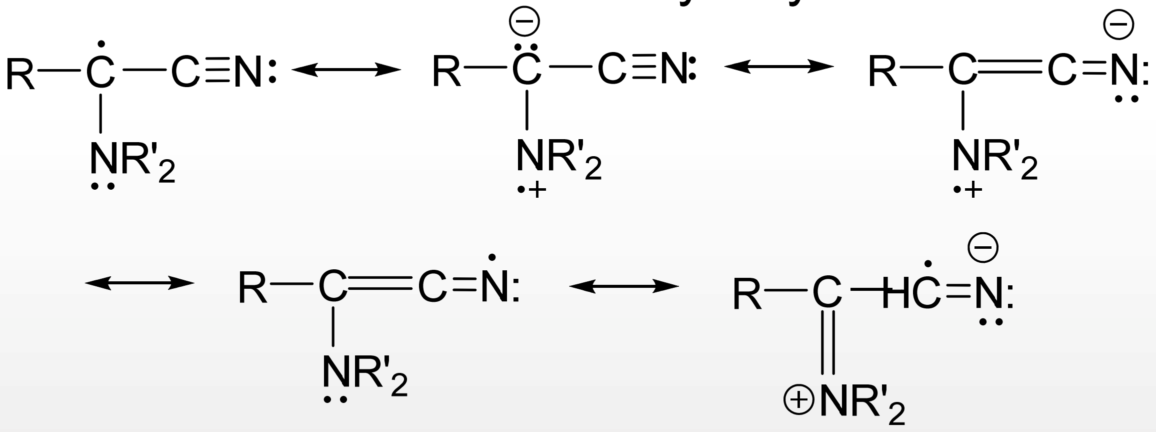


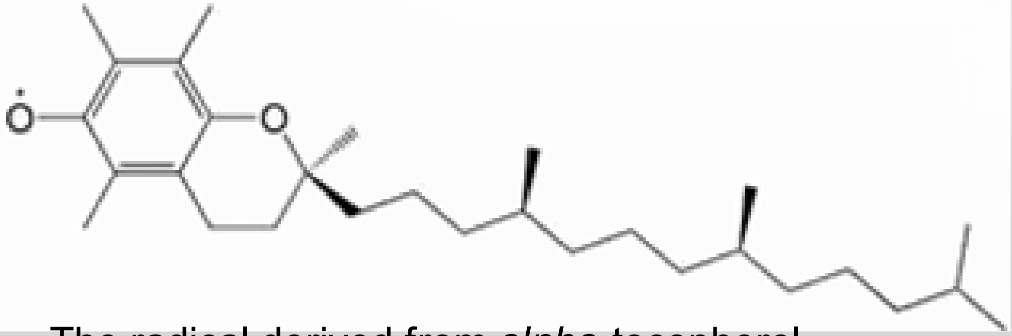
TABLE. The D_{298} values for R-H bonds					
R	***D*** (kJ/mol)	**R**	***D*** (kJ/mol)	**R**	***D*** (kJ/mol)
Ph	464	Et	419	Me_3C	401
CF_3	446	Me_3CCH_2	418	Cyclohexyl	400
$CH_2=CH$	444	Pr	417	$PhCH_2$	368
Cyclopropyl	444	Cl_3C	401	HCO	364
Me	438	Me_2CH	401	$CH_2=CH-CH_2$	361
Free radical stability is in reverse order.					

- Radicals next to functional groups, such as carbonyl, nitrile, and ether are even more stable than tertiary alkyl radicals.



Push-pull effect

- Organic radicals can be long lived if they occur in a conjugated π system.



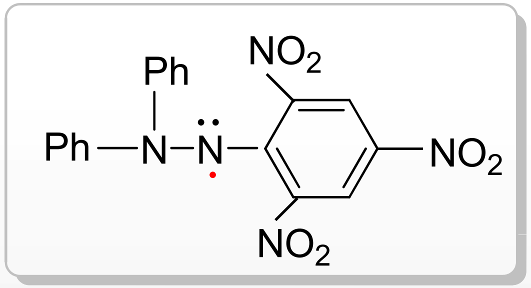
The radical derived from *alpha*-tocopherol

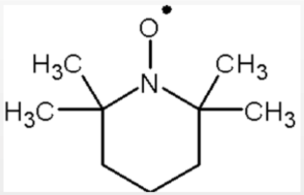
Persistent radical compounds are those whose longevity is due to steric crowding around the radical center and makes it physically difficult for the radical to react with another molecule.

Examples: Gomberg's triphenylmethyl radical

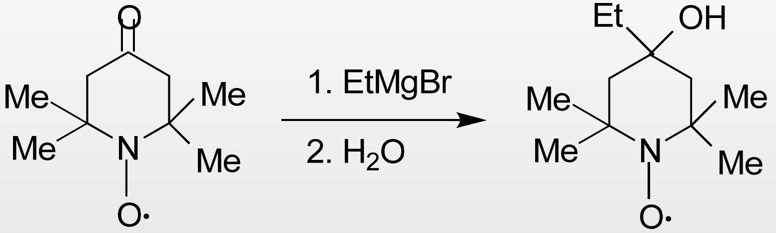
2,2-Diphenyl-1-picrylhydrazyl (DPPH)

2,2,6,6-Tetramethylpiperidine-1-oxyl (TEMPO)

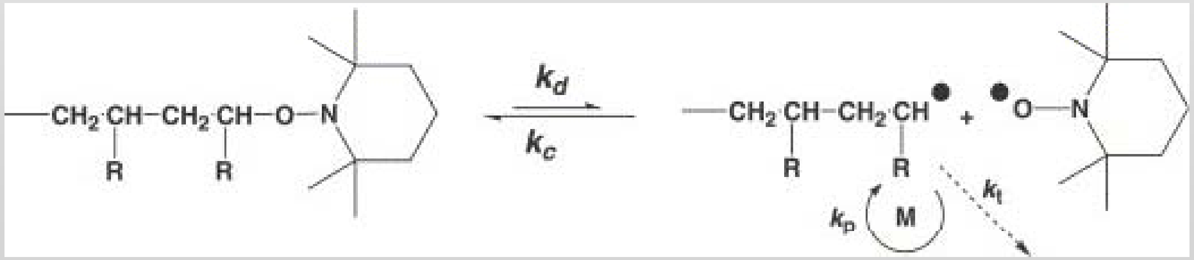




TEMPO

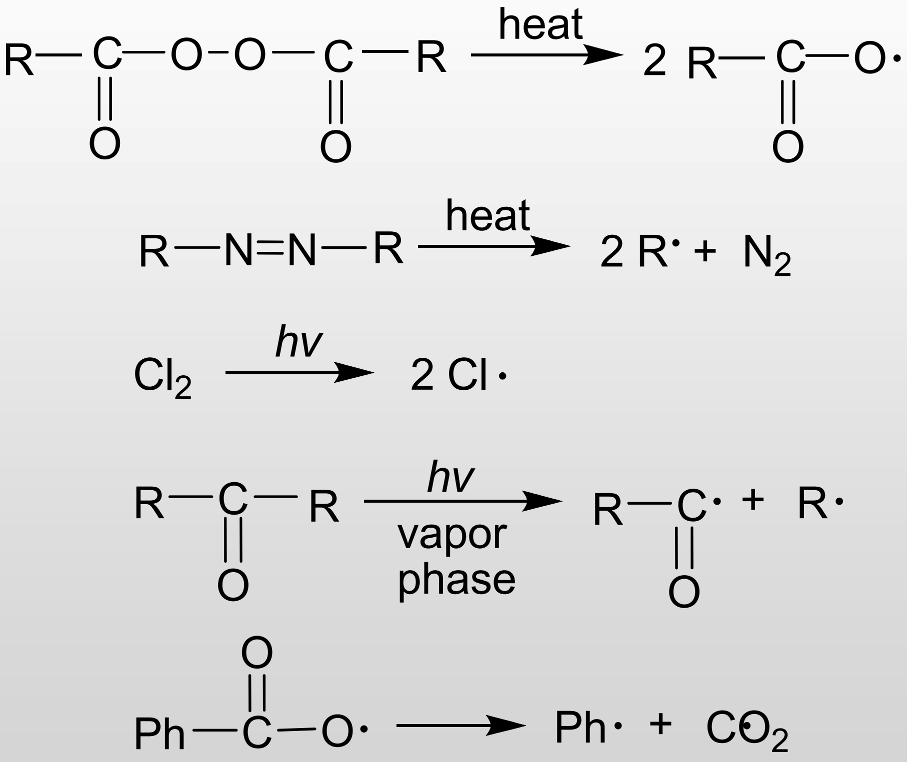


Application of TEMPO: as a radical trap, as a structural probe for biological systems in conjunction with electron spin resonance spectroscopy, as a reagent in organic synthesis, and as a mediator in controlled free radical polymerization.



II. The Generation and Fate of Free Radicals

- The formation of radicals may involve breaking of covalent bonds homolytically, a process that requires significant amounts of energy.
- Homolytic bond cleavage most often happens between two atoms of similar electronegativity.



$$R-C(=O)-O-O-C(=O)-R \xrightarrow{\text{heat}} 2\ R-C(=O)-O\cdot$$

$$R-N=N-R \xrightarrow{\text{heat}} 2\ R\cdot + N_2$$

$$Cl_2 \xrightarrow{hv} 2\ Cl\cdot$$

$$R-C(=O)-R \xrightarrow[\text{vapor phase}]{hv} R-\dot{C}(=O) + R\cdot$$

$$Ph-C(=O)-O\cdot \longrightarrow Ph\cdot + CO_2$$

- Free radicals take part in radical addition and radical substitution as reactive intermediates.
- Chain reactions involving free radicals can usually be divided into three distinct processes: *initiation*, *propagation*, and *termination*.

Termination reactions → stable products

(i) $R\cdot + R'\cdot \rightarrow R{-}R$

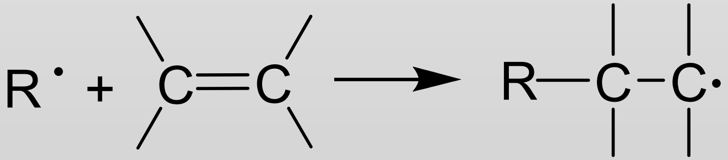
(ii) $2CH_3CH_2\cdot \rightarrow CH_3CH_3 + CH_2{=}CH_2$

Propagation reactions → other radicals (which usually react further)

(iii) abstraction of another atom or group, usually a hydrogen atom:

$R\cdot + R'{-}H \rightarrow R'\cdot + RH$

(iv) addition to a multiple bond:



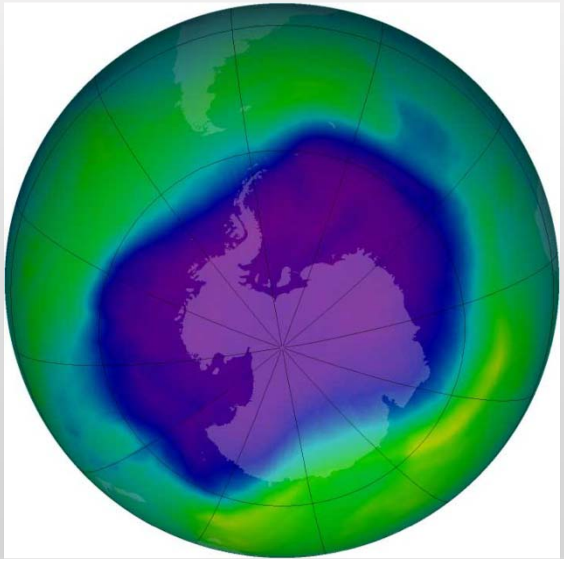
Atmospheric radicals — Ozone depletion

- Refrigerants: **Freon.** Freon-11 is trichlorofluoromrthane, while Freon-12 is dichlorodifluoromethane. Freon-113 (1,1,2-Trichloro-1,2,2-trifluoroethane).

- $CFCl_3 + h\nu \rightarrow CFCl_2 + Cl\bullet$

These free radicals then react with ozone in a catalytic chain reaction which destroys the ozone:

- $Cl\bullet + O_3 \rightarrow ClO\bullet + O_2$
- $ClO\bullet + O_3 \rightarrow Cl\bullet + 2\ O_2$



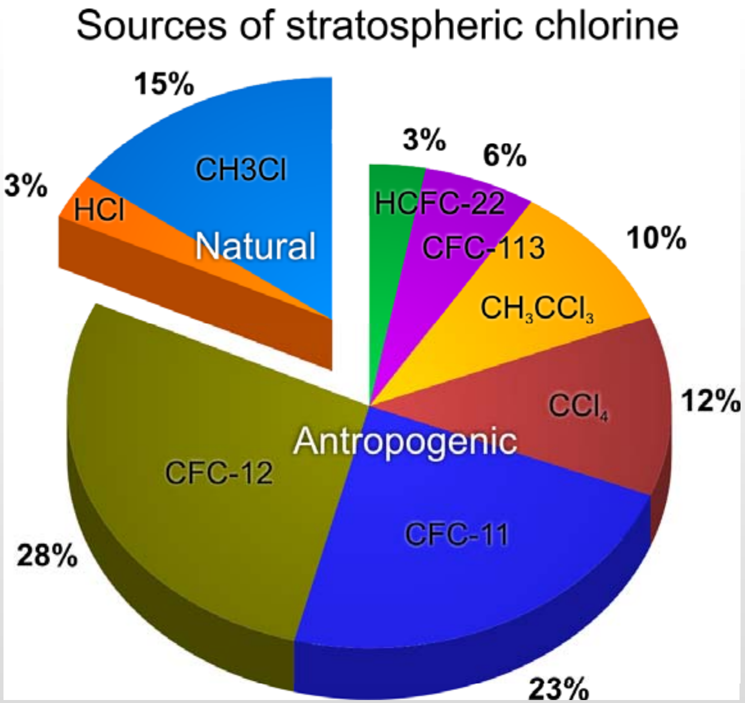
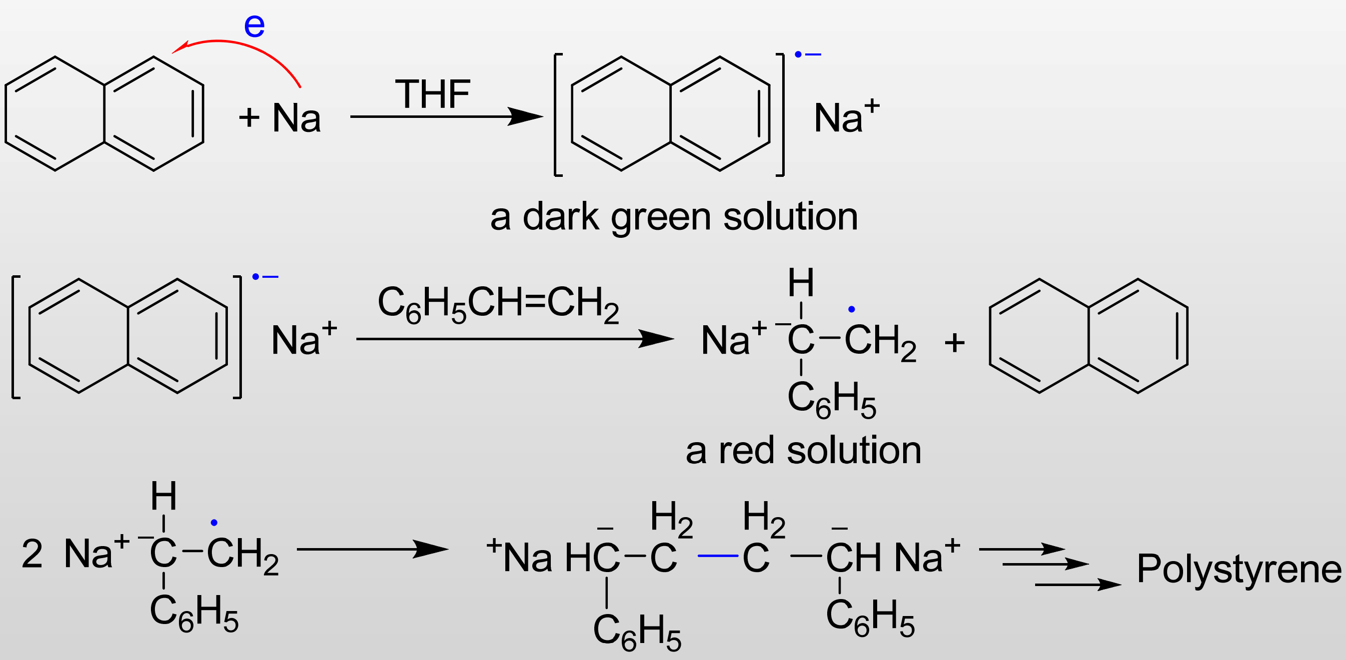


Image of the largest Antarctic ozone hole ever recorded (September 2006)

III. Radical ions

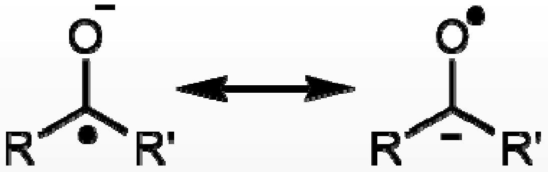
- A radical ion is a free radical species that carries a charge.
- Many aromatic compounds can undergo *one-electron reduction* by alkali metals.

Sodium naphthalenide: the reaction of naphthalene with sodium in an aprotic solvent.



Ketyl

- A **ketyl** group is an anion radical with the general structure C-O· in which an oxygen radical is bonded directly to carbon.



The intense blue coloration due to the benzophenone ketyl radical shows that the toluene is considered free of air and moisture.

Benzophenone radical anion

Sodium reduces benzophenone to the soluble ketyl radical, which reacts quickly with the water and oxygen dissolved in the solvent. The deep blue coloration qualitatively indicates dry, oxygen-free conditions.

$$Na + Ph_2CO \rightarrow Na^+ + Ph_2CO^{\cdot -}$$

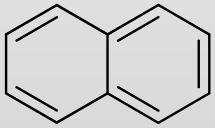
Radical cations

- Cationic radical species are much less stable. They appear prominently in mass spectroscopy (MS). When a gas-phase molecule is subjected to electron ionization, one electron is abstracted by an electron in the electron beam to create a radical cation **$M^{+\cdot}$**. *This species represents the molecular ion or parent ion and will tell the precise molecular weight*.

- Examples:

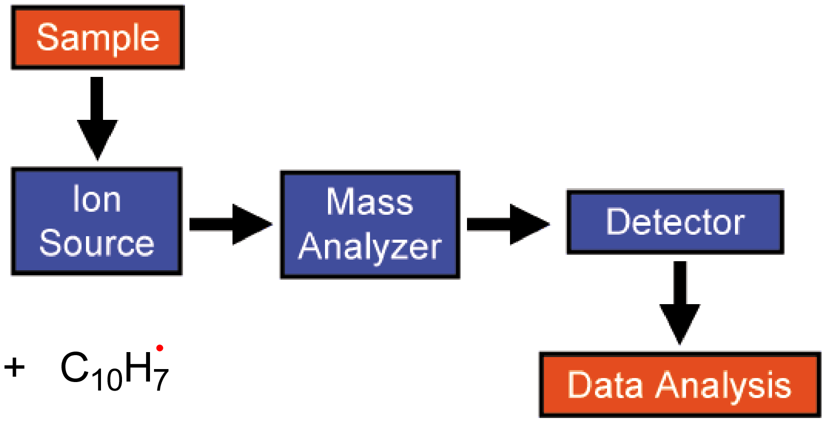
$CH_3OH \xrightarrow{-\,e} [CH_3OH]^{\bullet+} \longrightarrow CH_3^{+} + \dot{O}H$

parent ion
(M)



$\xrightarrow{-\,e} C_{10}H_8^{\bullet+} \longrightarrow C_{10}H_9^{+} + C_{10}H_7^{\bullet}$

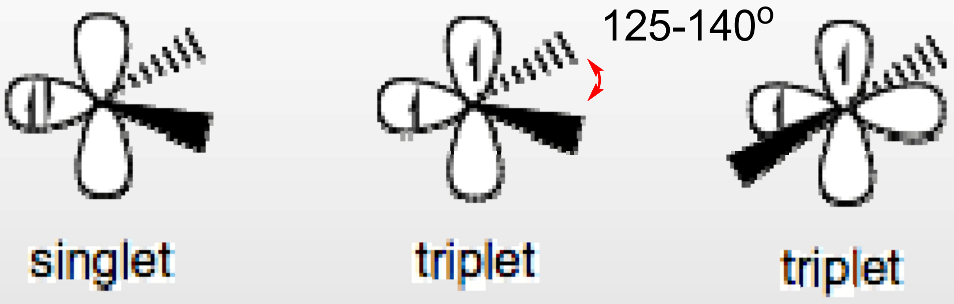
(M) (M+1) (M-1)



4.4 Carbenes

- A carbene is a highly reactive species containing a carbon atom with six valence electrons and having the general formula RR’C:, practically all having lifetimes considerably under 1 sec.

i. Structure and bonding



the total spin=0
bond angle = 102°
for single methylene

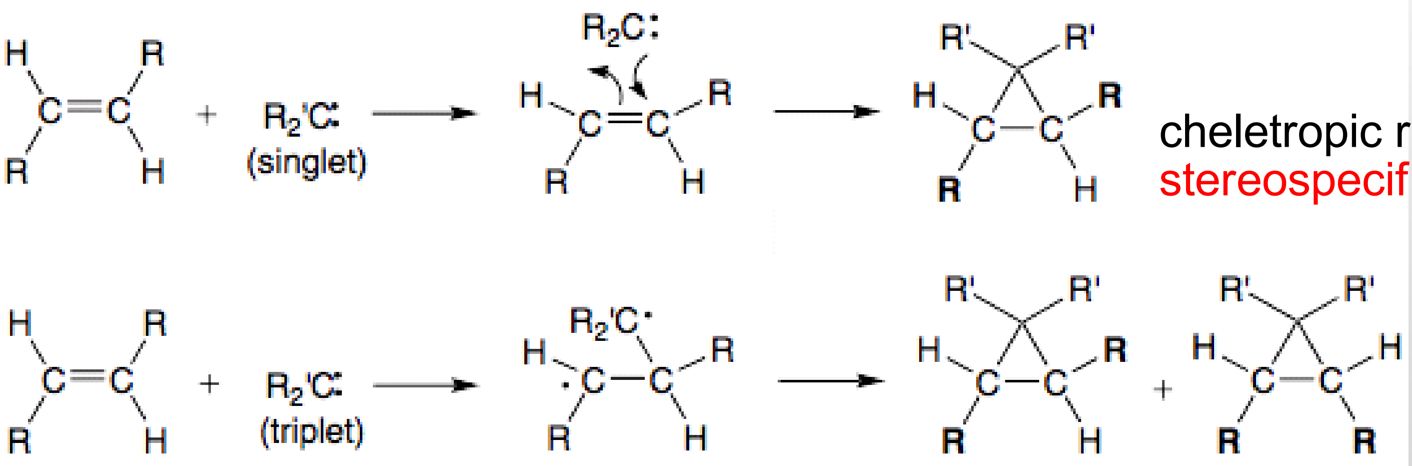
the total spin=1;
paramagnetic, may be
observed by
electron spin resonance
spectroscopy

Triplet carbenes are generally stable in the gaseous state, while singlet carbenes occur more often in aqueous media.

ii. Reactivity

- Singlet and triplet carbenes exhibit divergent reactivity. Singlet carbenes generally participate in cheletropic reactions. Singlet carbenes with unfilled *p*-orbital should be electrophilic. Triplet carbenes can be considered to be diradicals, and participate in stepwise radical additions.

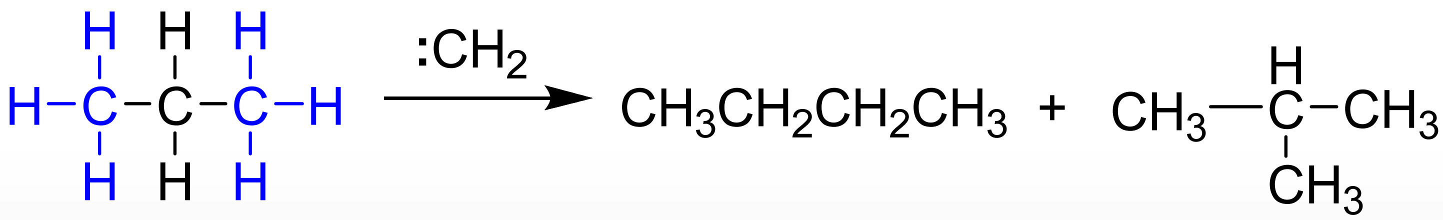
Addition to C=C:



cheletropic reaction
stereospecific

stepwise radical addition, may be stereoselective

Insertion reaction

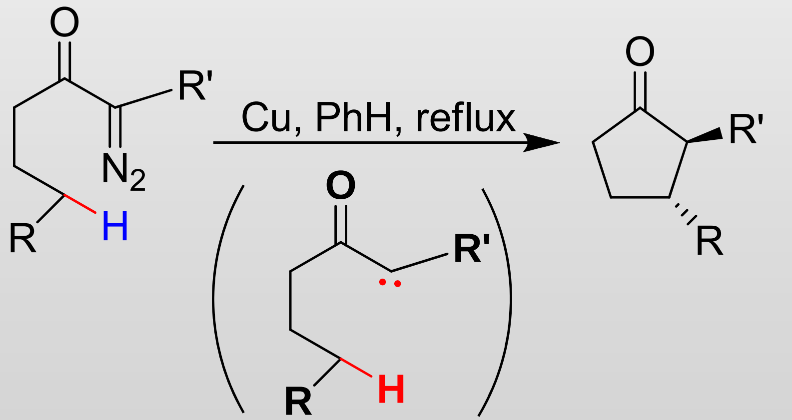


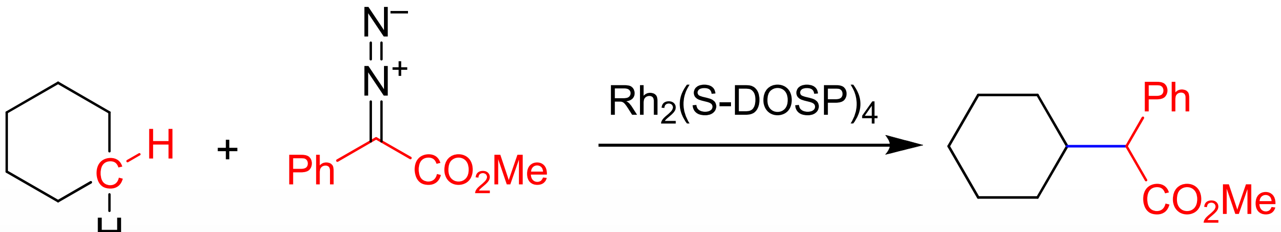
$$H_3C\text{–}CH_2\text{–}CH_3 \xrightarrow{:CH_2} CH_3CH_2CH_2CH_3 + CH_3\text{–}\overset{H}{\underset{CH_3}{C}}\text{–}CH_3$$

(one step insertion) **3 : 1**

- The order of preference: X–H (where X is not carbon) > C–H > C–C Insertions may or may not occur in single step.

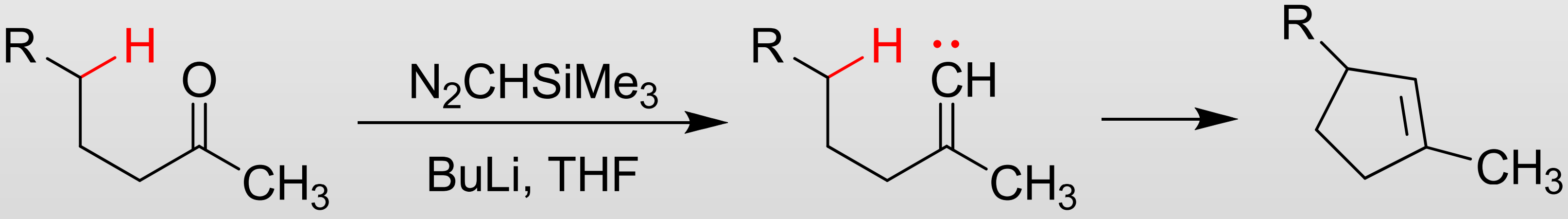
- When an intramolecular insertion is possible, no intermolecular insertions are seen. *In flexible structures, five-membered ring formation is preferred to six-membered ring formation.*





(intermolecular insertion of carbene)

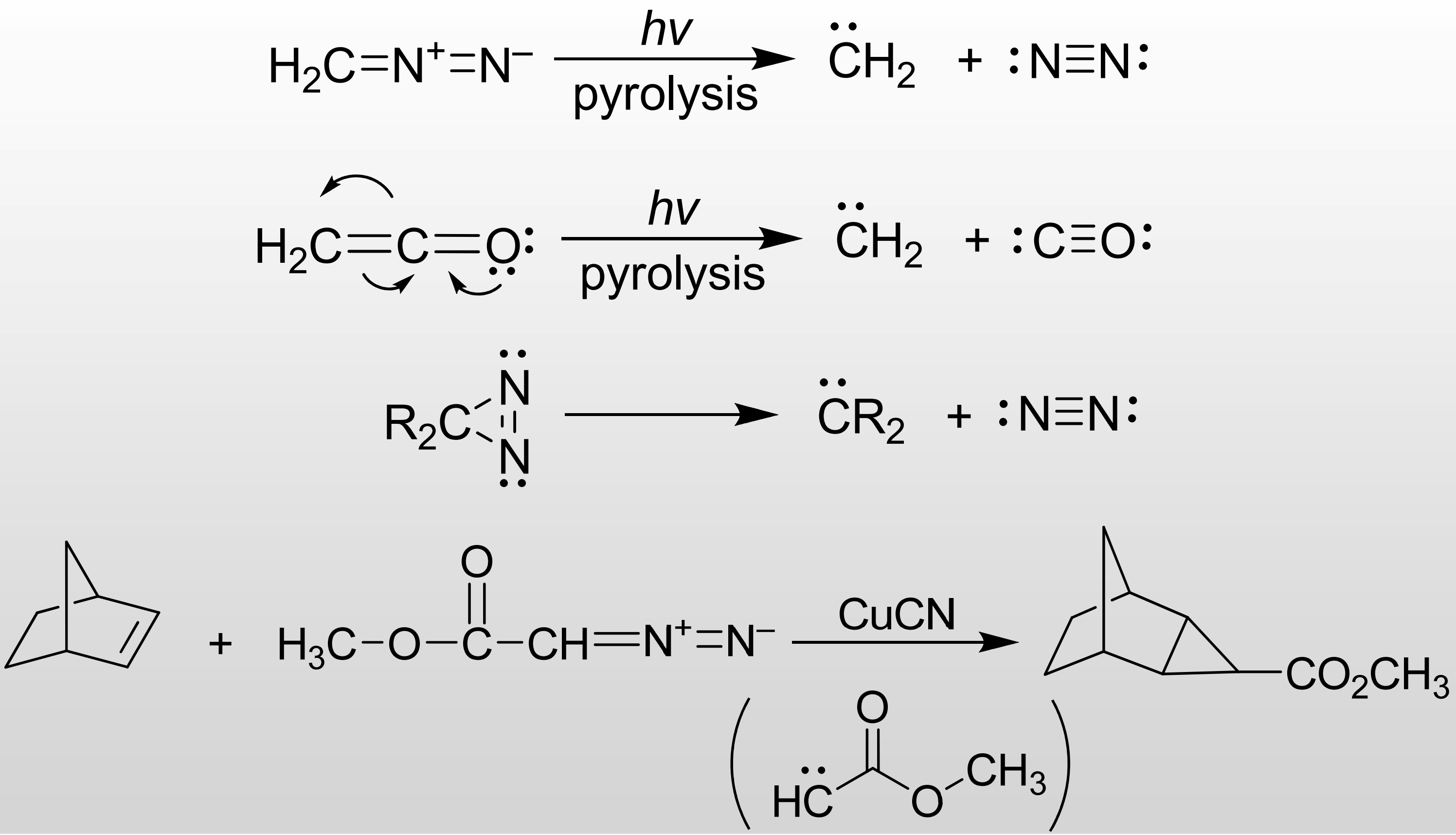
- Alkylidene carbenes are alluring in that they offer formation of cyclopentene moieties. To generate an alkylidene carbene a ketone can be exposed to trimethylsilyl diazomethane.



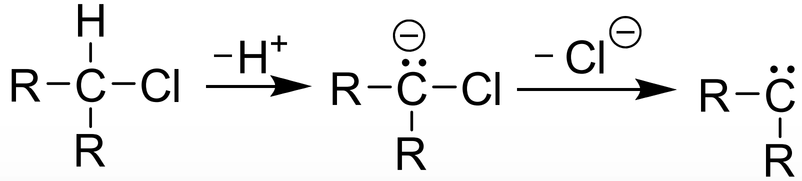
An alkylidene carbene

iii. Generation of carbenes

- Disintegration of diazoalkanes and their analogs, via photolytic, thermal, or transition metal (Rh, Cu)-catalyzed routes.

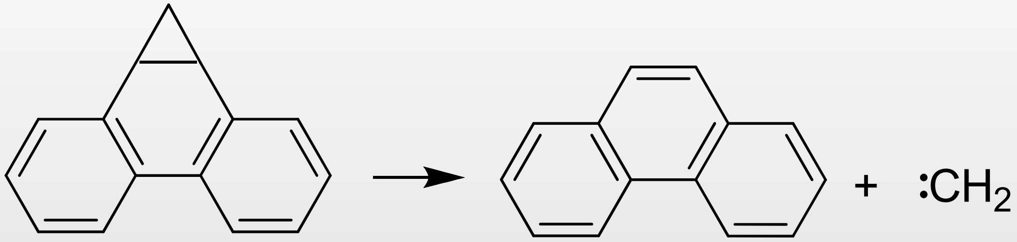


- Base-induced α-elimination

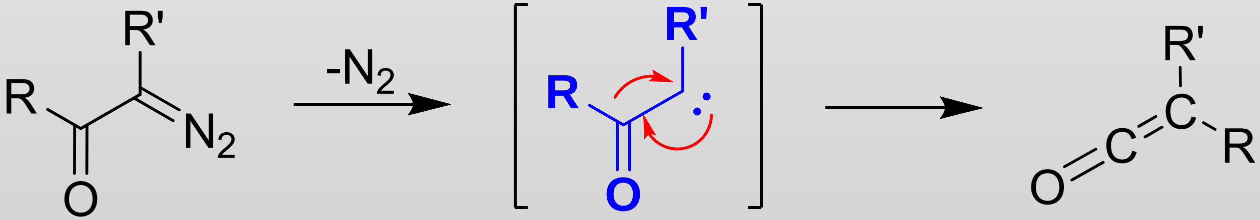


$$R-\underset{R}{\overset{H}{C}}-Cl \xrightarrow{-H^+} R-\underset{R}{\overset{\ominus}{\ddot{C}}}-Cl \xrightarrow{-Cl^{\ominus}} R-\underset{R}{\ddot{C}}$$

$$Cl_3C-COO^- \longrightarrow :CCl_2 + CO_2 + Cl^-$$



- Carbenes are intermediates in the *Wolff rearrangement*.



iv. Applications of carbenes

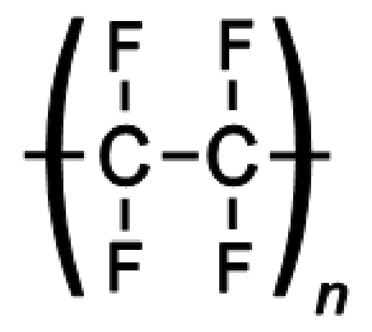
- A large scale application of carbenes is the industrial production of tetrafluoroethylene. Tetrafluoroethylene is generated via the intermediacy of difluorocarbene:

$$CHCl_3 + 2\,HF \rightarrow CHClF_2 + 2\,HCl$$

$$CHClF_2 \rightarrow :CF_2 + HCl$$

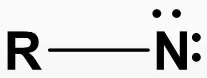
$$2\,:CF_2 \rightarrow F_2C{=}CF_2$$

- Polytetrafluoroethylene (PTFE, mp 327°C the DuPont brand name **Teflon**) is a synthetic fluoropolymer of tetrafluoroethylene which finds numerous applications: used as a non-stick coating for pans and other cookware.



4.5 Nitrenes

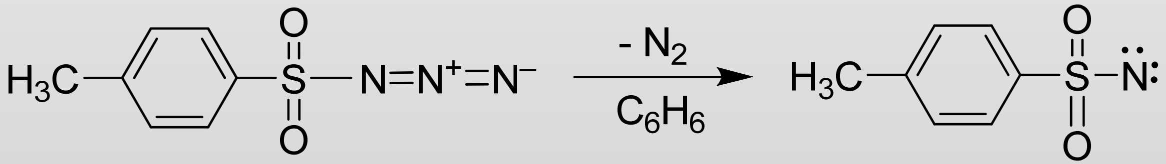
- A **nitrene** (R-N:) is the nitrogen analogue of a carbene. The nitrogen atom has only 6 electrons available and is therefore considered an electrophile. A nitrene is a reactive intermediate and is involved in many chemical reactions.



$R-\ddot{N}:$

The structure of a typical nitrene group

- **Formation of nitrenes**
- from thermolysis or photolysis of azides.
- from isocyanates, with expulsion of CO.

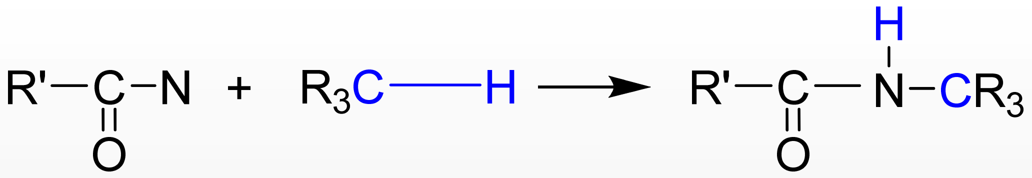


tosyl azide

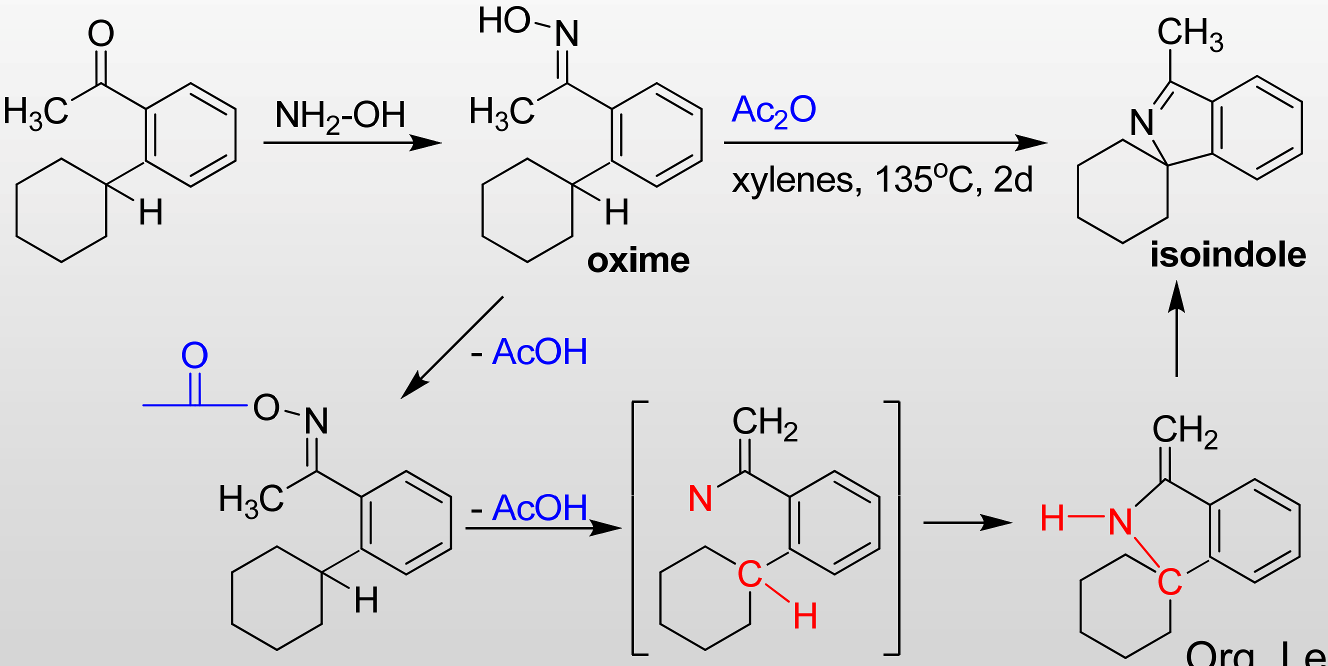
$$R-N=C=O \xrightarrow{-\ CO} R-\ddot{N}:$$

Reactions of Nitrene

- Nitrene C-H insertion. A nitrene can easily insert into a C-H bond yielding an amine or amide.

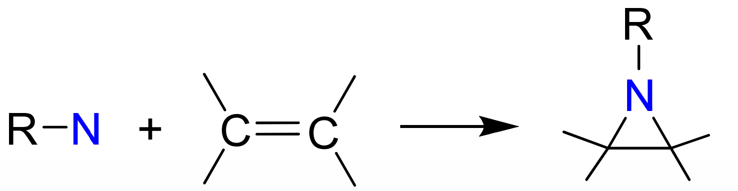


$$R'-\underset{\underset{O}{\|}}{C}-N + R_3C-H \longrightarrow R'-\underset{\underset{O}{\|}}{C}-\overset{\overset{H}{|}}{N}-CR_3$$



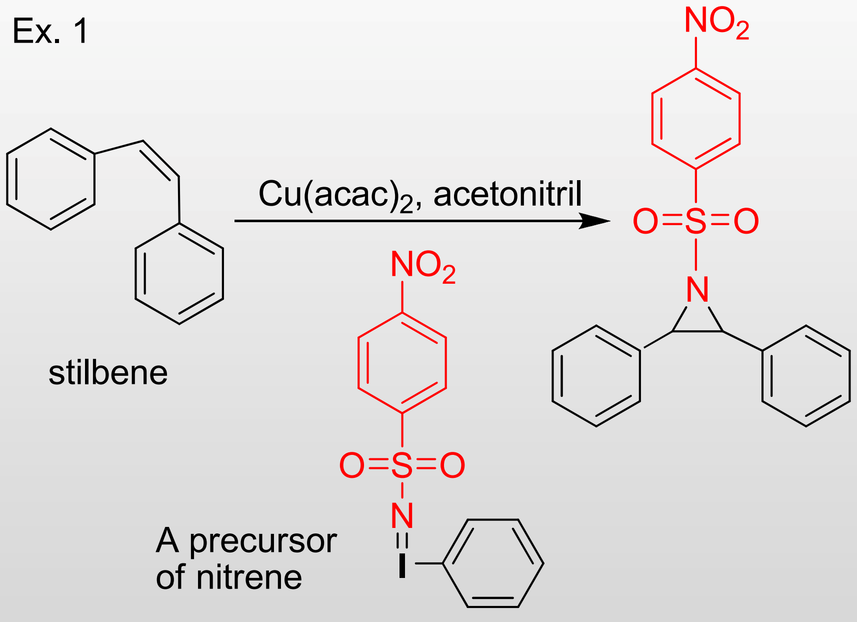
Org. Lett. **9**, 981(2007)

- Nitrene cycloaddition. With alkenes, nitrenes react to aziridines.



aziridines

Ex. 1

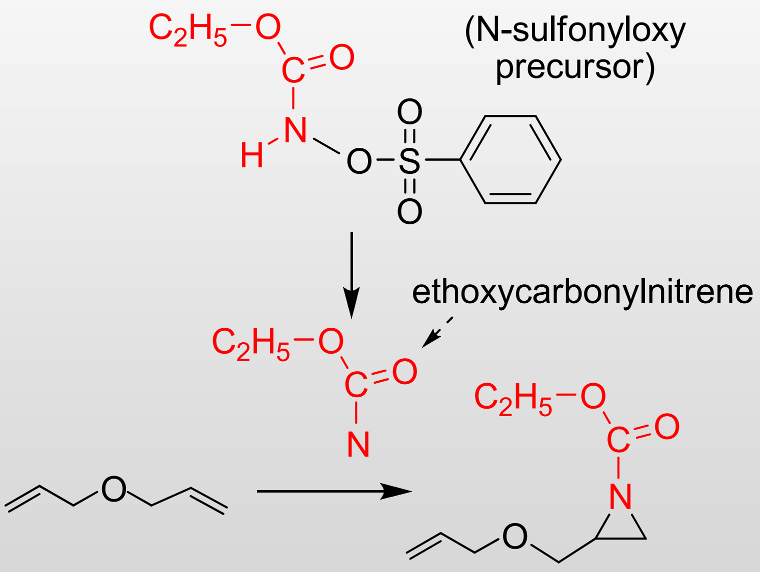


stilbene

Cu(acac)$_2$, acetonitril

A precursor of nitrene

Ex. 2



(N-sulfonyloxy precursor)

ethoxycarbonylnitrene

J. Org. Chem. **71**, 5876(2006)

Tetrahedron Letters, **25**, 4271(1984)

Overview of Chapter 4

- 碳正离子、碳负离子、碳自由基的杂化结构、形成方式、稳定因素、反应；
- 活性中间体与各种聚合机理之间的关系；
- 碳正离子：重排、非经典、邻基协助、取代反应产物
- 简单了解卡宾（**ROMP**）、氮烯