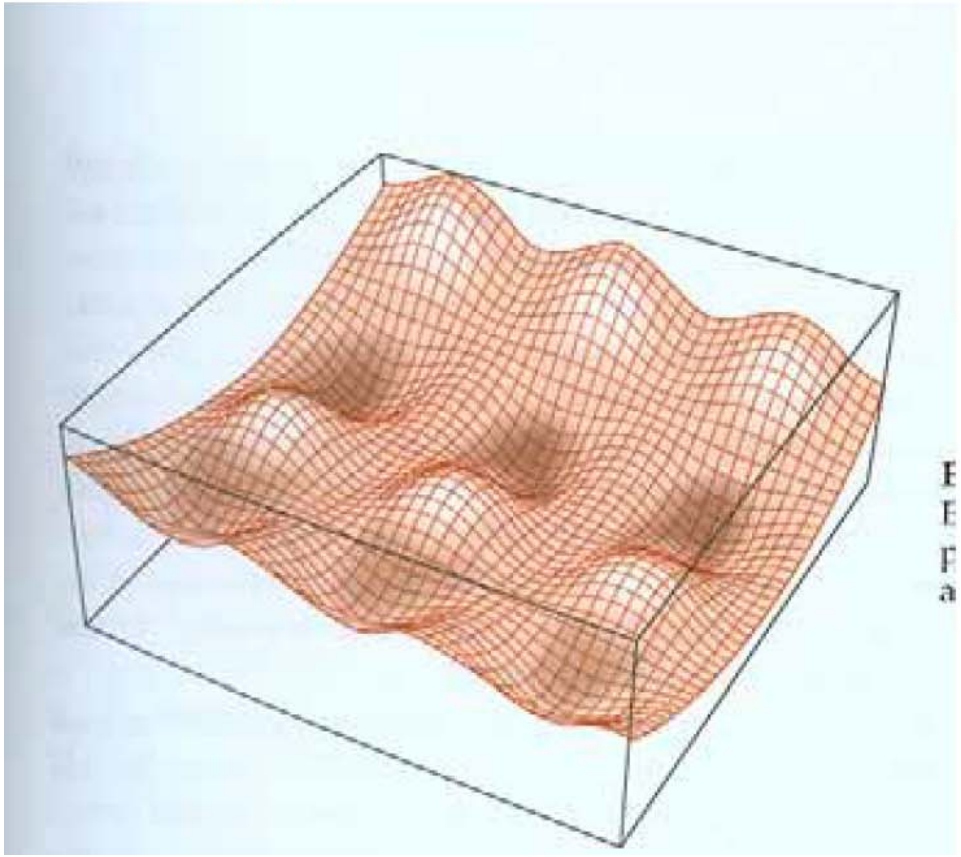
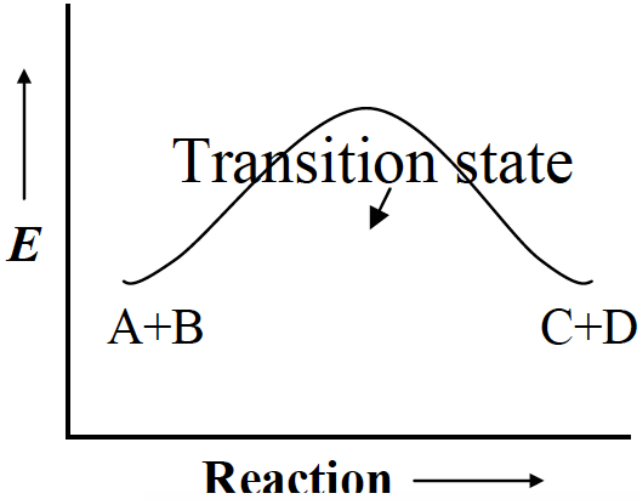
Reactive Intermediates

Energy surface



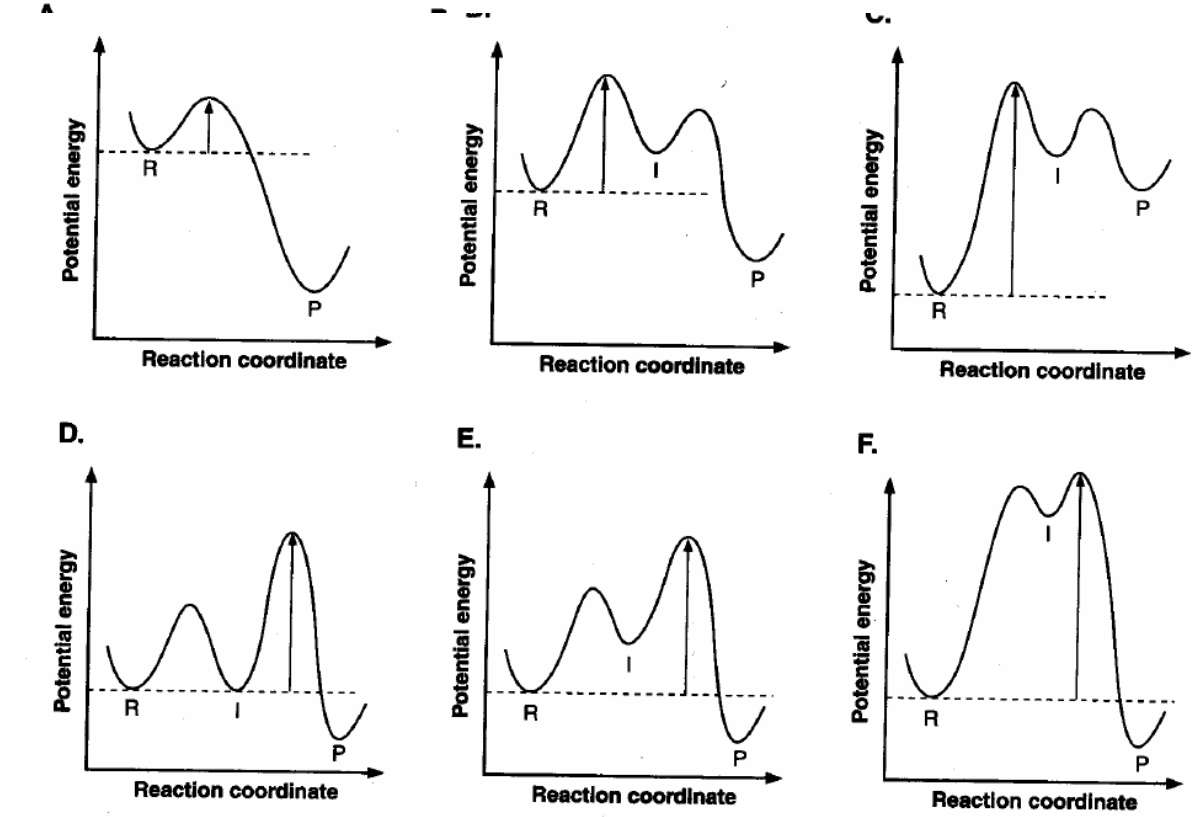
The plot of energy (potential and kinetic) as a function of 3N-6 coordinates of the chemical system (reactants, intermediates, products)

Reaction Coordinate diagram:

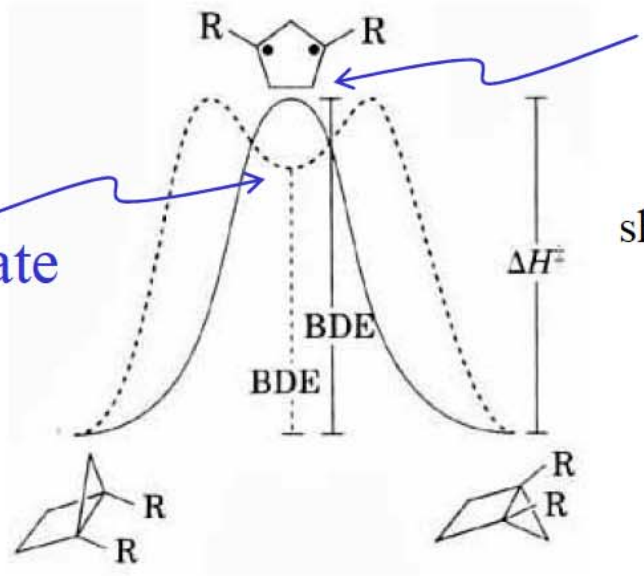


The reaction coordinate is a one-dimensional slice of a 3N-6+1dimensional potential surface.

It goes through a maximum, but along a valley (potential minimum) with respect to motion perpendicular to the reaction coordinate



Intermediate & Transition State



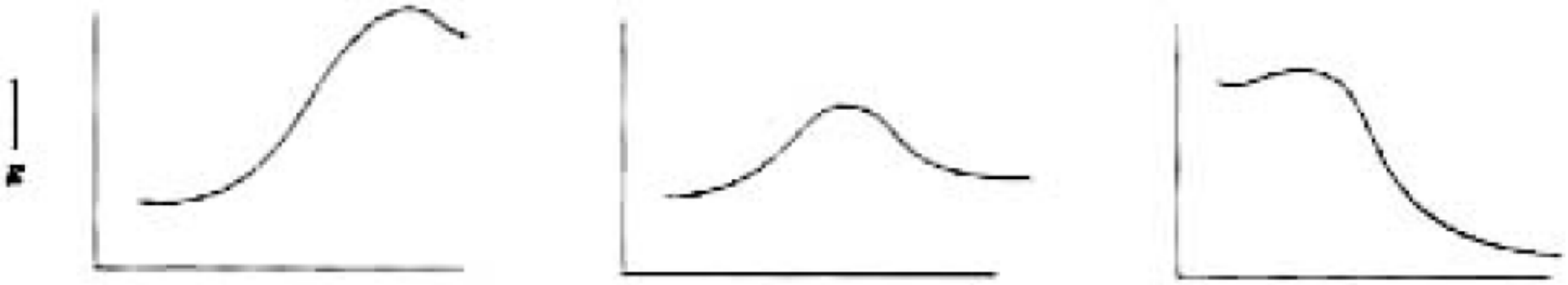
Experimental evidences

show the diradical as intermediate

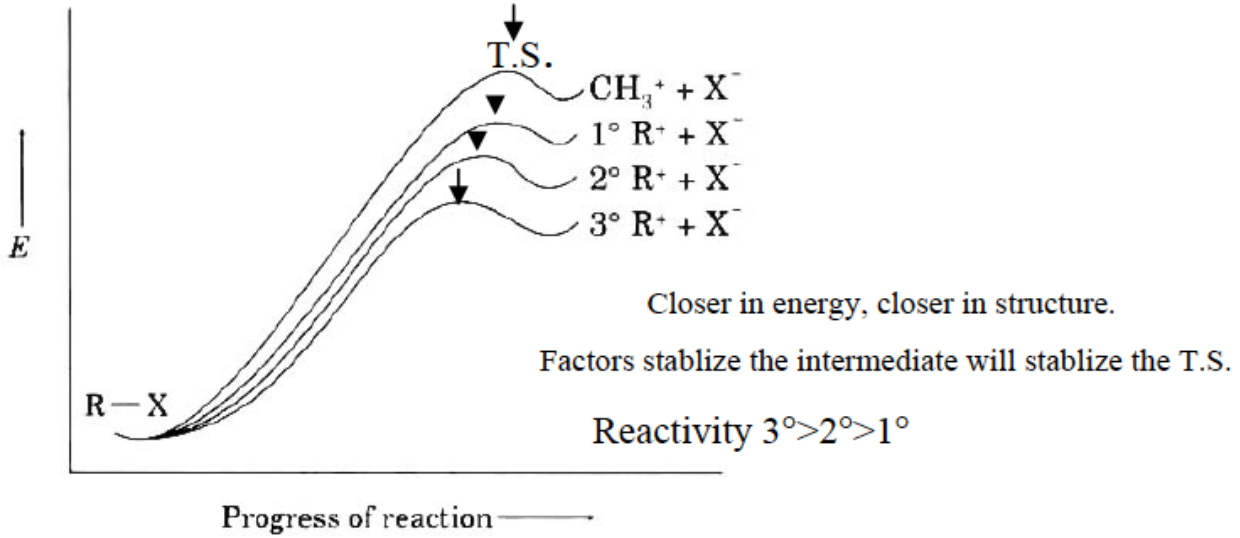
BDE = bond dissociation energy

Hammond Postulate

If two states, as for example, a transition state and an unstable intermediate, occur consecutively during a reaction process and have nearly the same energy content, their inter conversion will involve only a small reorganization of the molecular structure.
(→ close in energy, close in structure)



endothermic rxn　　thermoneutral rxn　　exothermic rxn

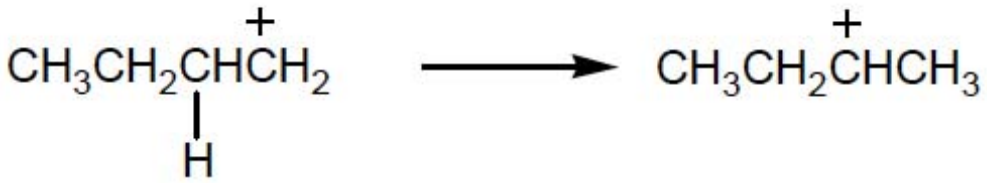


Closer in energy, closer in structure.

Factors stablize the intermediate will stablize the T.S.

Reactivity 3°>2°>1°

Rearrangement of carbocation



1° 2°

NMR shows singlet for ^{1}H at -70° in super acid

^{13}C one peak that couple to 9 H →

9 H become equivalent by fast rearrangement.

ESCA shows 4 uncharged carbon and one positively charged carbon

The contradiction is due to different time scale of NMR and ESCA

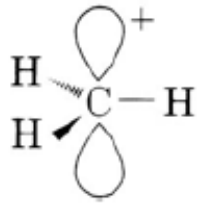
§ Carbocations

intermediates with formal charge of +1 on a carbon atom, or

a collection of carbon atoms

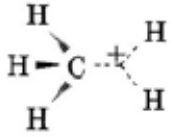
Carbocations

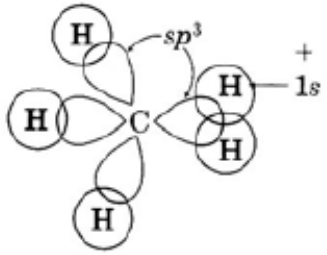
Trivalent-tricoordinate carbenium ions "Classical" ions CH_3^+



planar

Hypercoordinate carbonium ions "Nonclassical" ions CH_5^+ **(and those with three center-two electron bonding)**





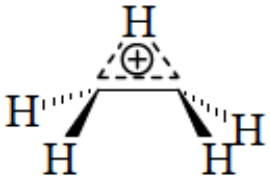


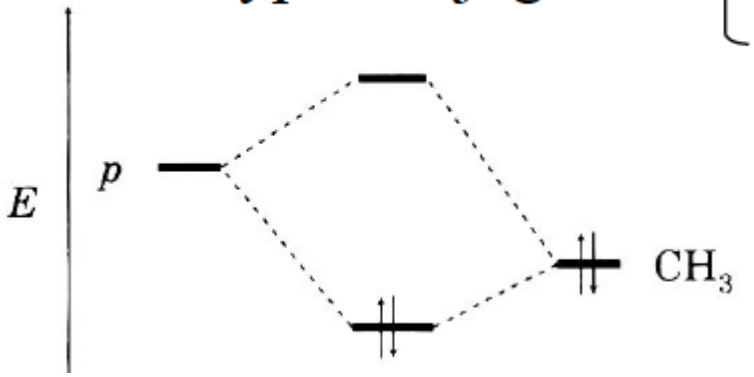
Table 5.2 Thermodynamic data for selected alkyl cations. (Reproduced from the compilation in reference 146.)

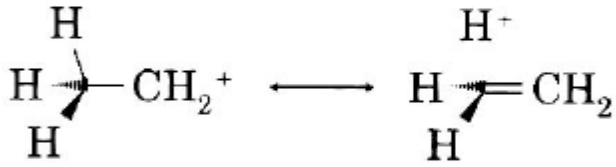
Cation	$\Delta H_f^0(R^+)$ (kcal/mol)	HIA (R^+) (kcal/mol)
Methyl	261	312
Ethyl	219	273
Isopropyl	192	247.4
t-Butyl	164	229.6
Allyl	226	256
Vinyl	266	287
Benzyl	213	234

formation of carbenium $3^\circ > 2^\circ > 1^\circ$

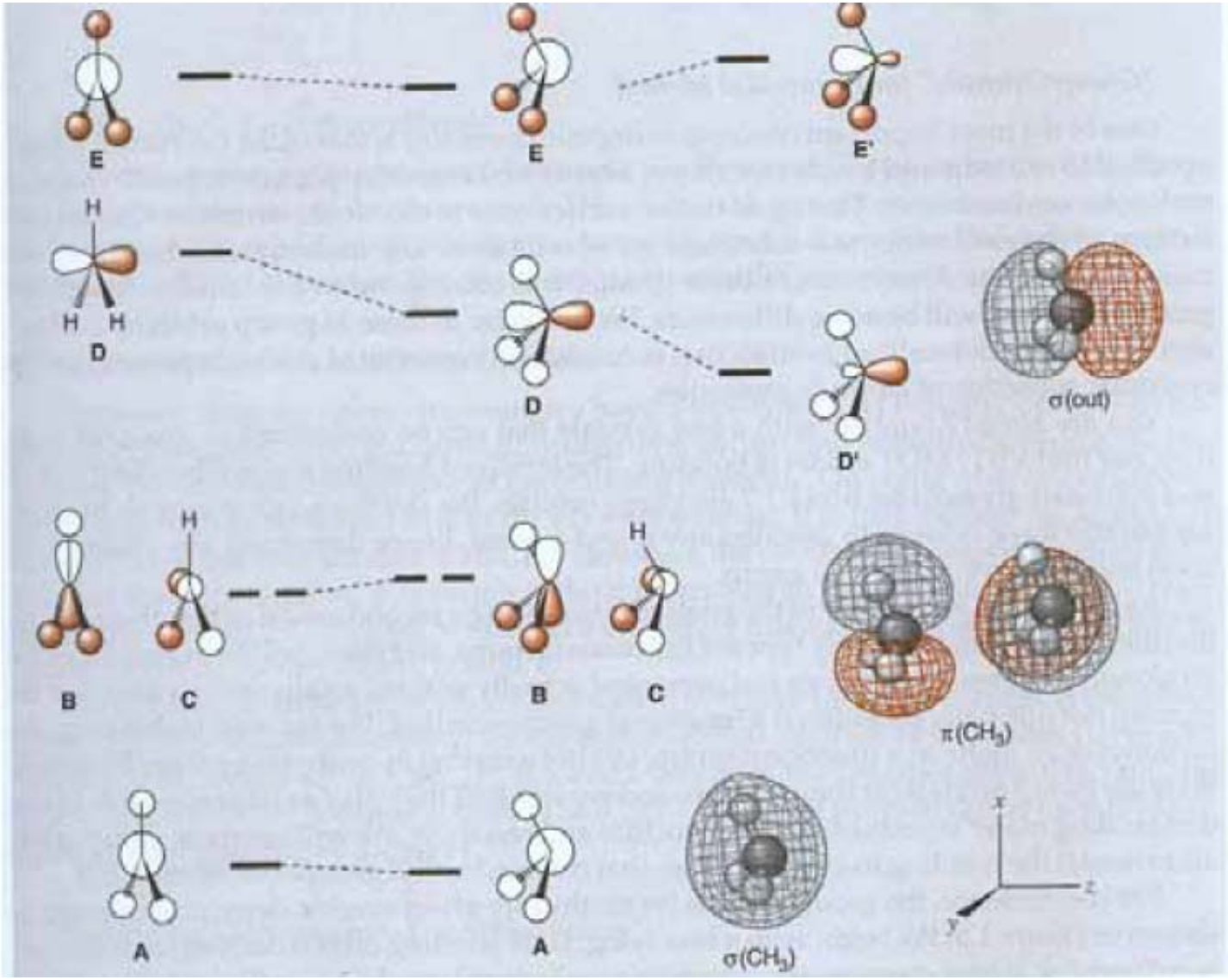
1. alkyl gps are electron-donating. (Inductive effect)

2. hyperconjugation { VB description → PMO description

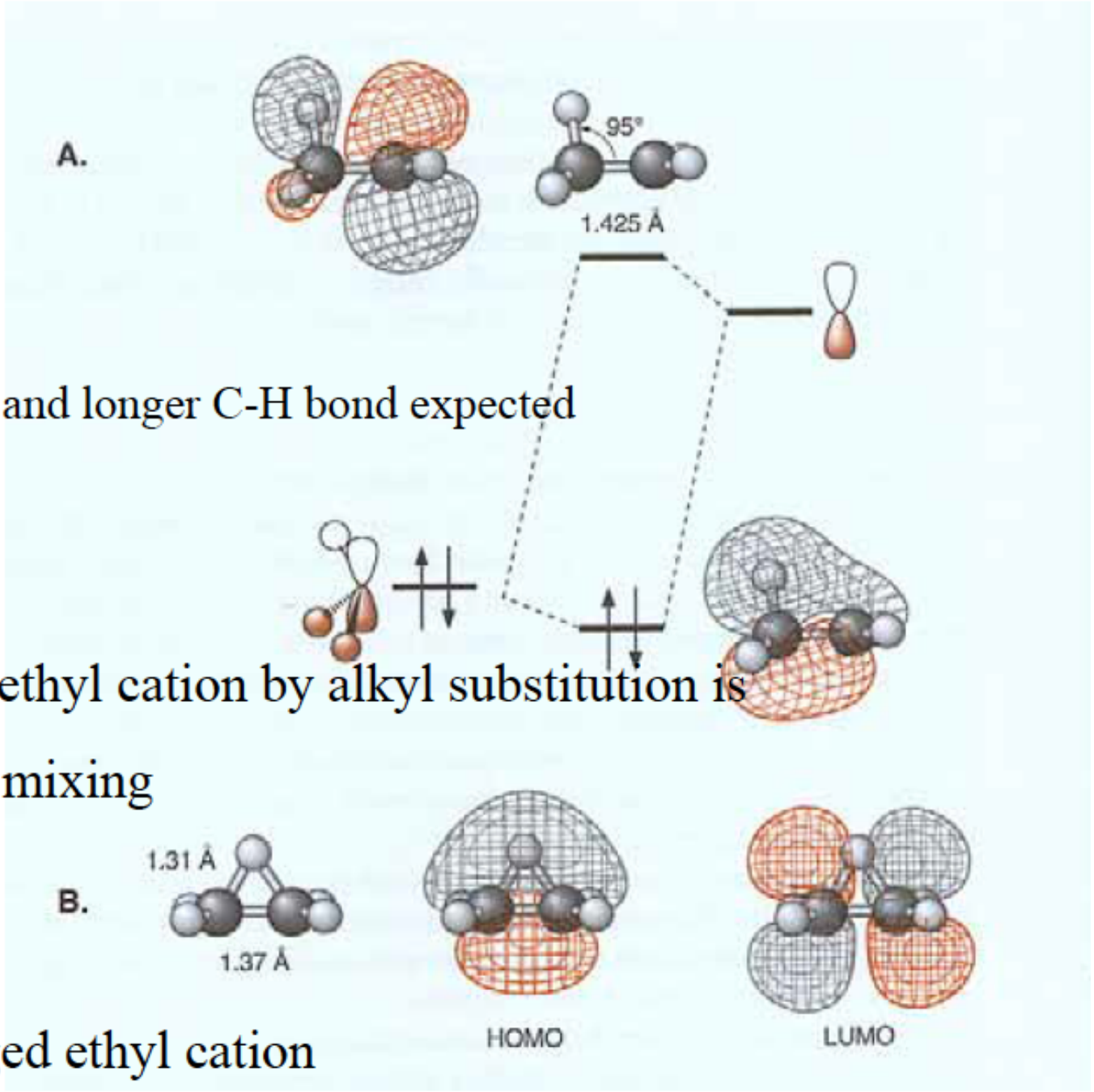




QMOT version



methyl cation with 6 valence electrons is planar

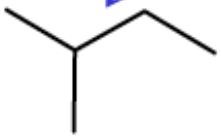


A shorter C-C bond and longer C-H bond expected

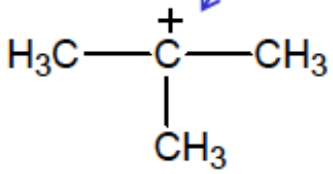
stabilization of methyl cation by alkyl substitution is a result of orbital mixing

Bridged ethyl cation

Detection of carbocation, by NMR

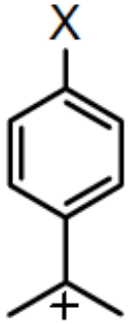


25.2 ppm



330.0 ppm (in SO_2ClF-SbF_5)(from TMS)

large shift due to deshielding with low electron density

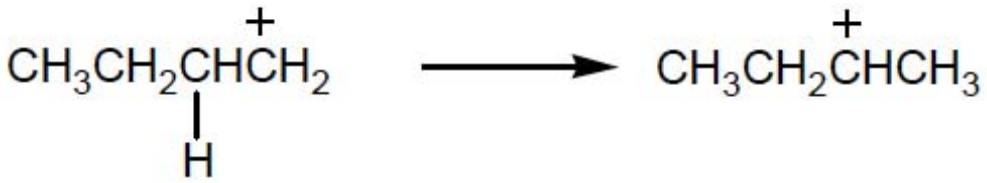


X	$\delta^{13}C$
OCH_3	219
CH_3	243
H	255
CF_3	269

stabilized by e^--donor

more shielded

Rearrangement of carbocation



1° 2°

NMR shows singlet for ^{1}H at -70° in super acid

^{13}C one peak that couple to 9 H →

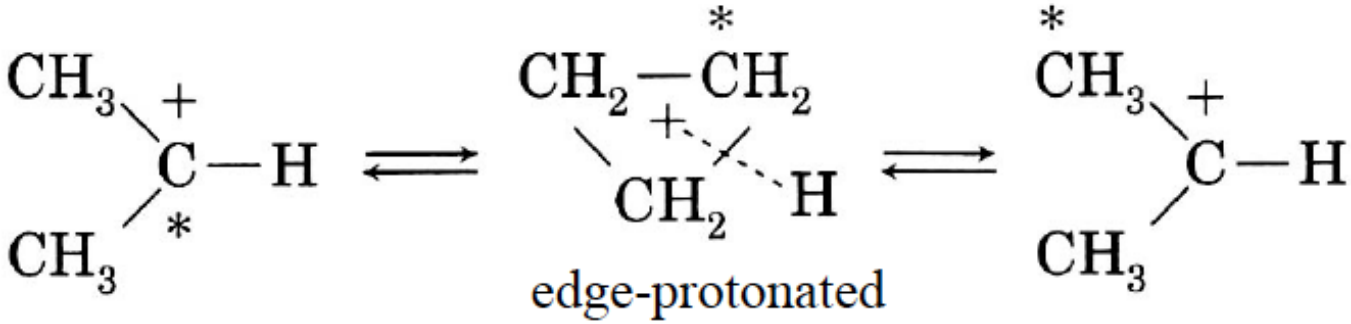
9 H become equivalent by fast rearrangement.

ESCA shows 4 uncharged carbon and one positively charged carbon

The contradiction is due to different time scale of NMR and ESCA

Rearrangements possible from 2° → 1°

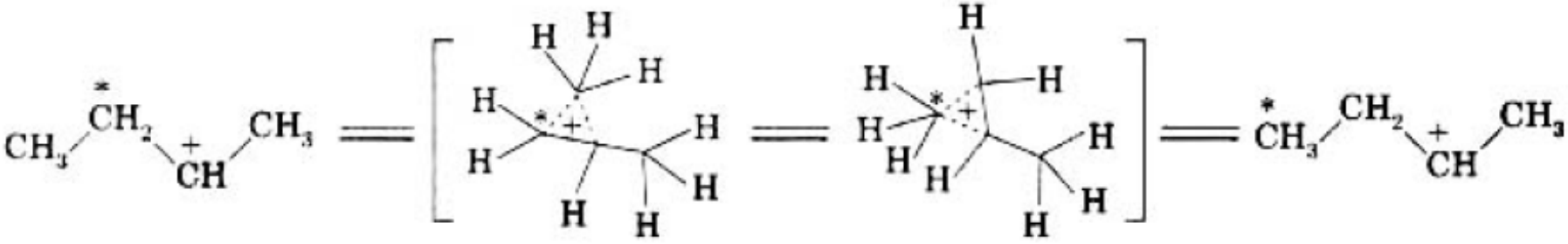
The H can scramble in isopropyl cation,
Carbon-atom also scramble.



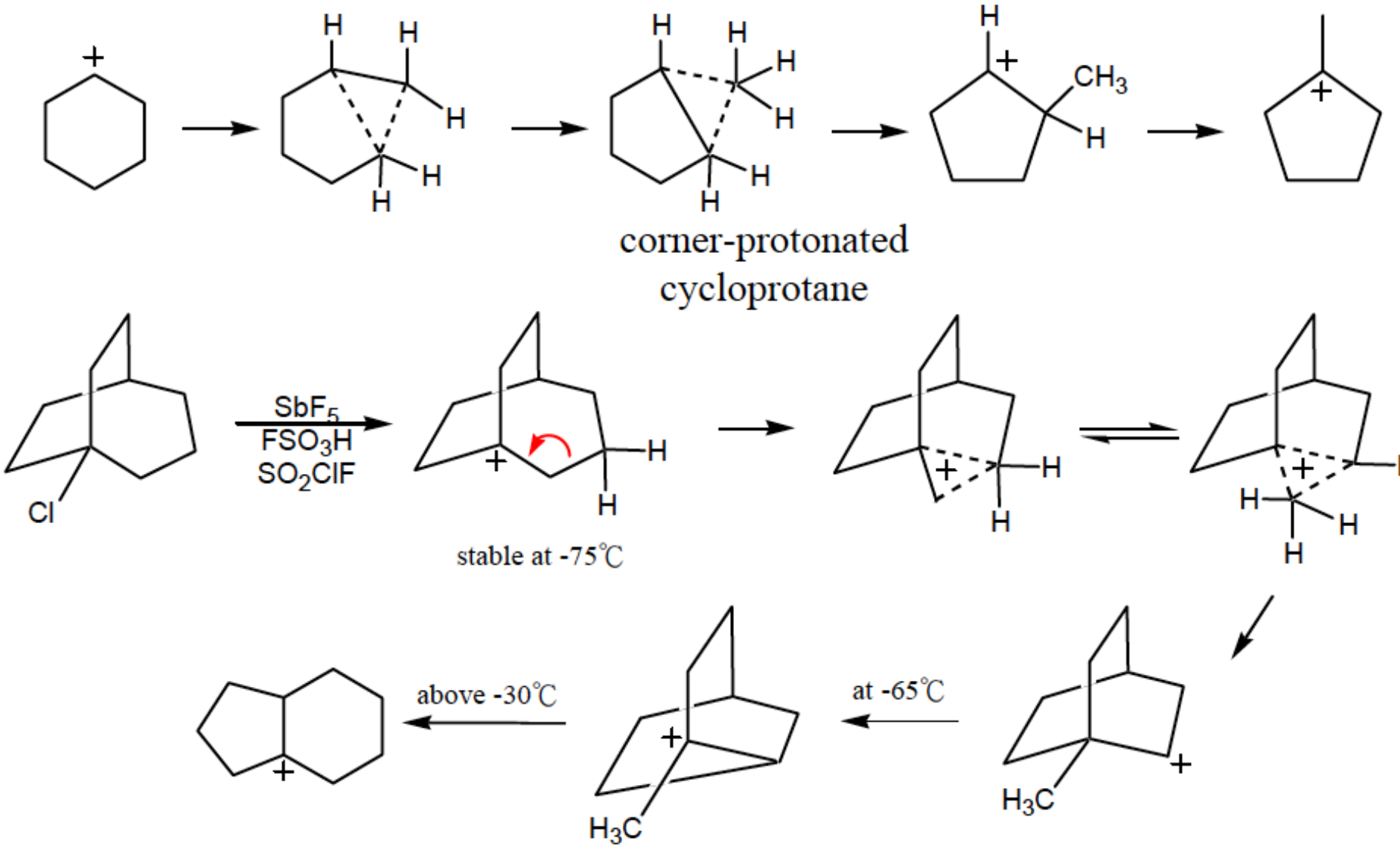
edge-protonated

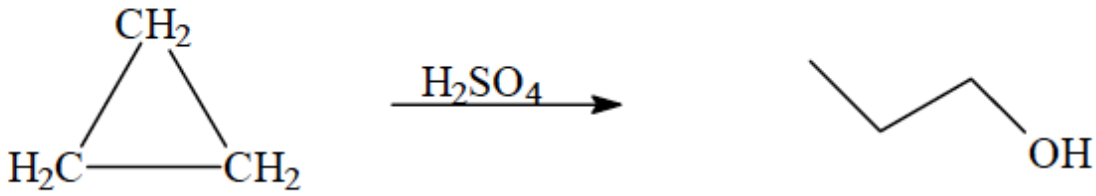
at -78℃ , $t_{1/2}$ = 1hr, ^{13}C scramble to all C

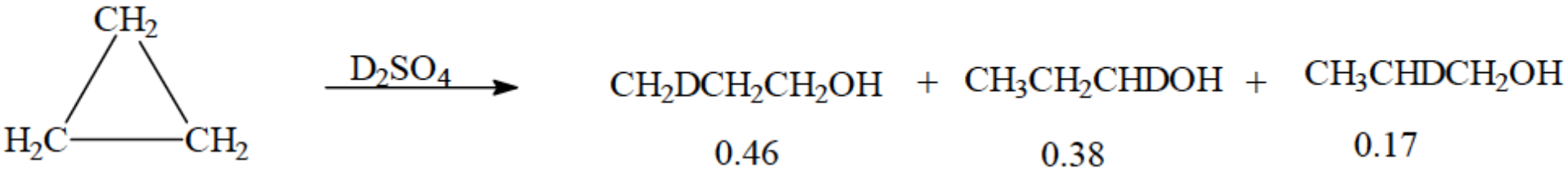
corner-proronated (methyl bridged)



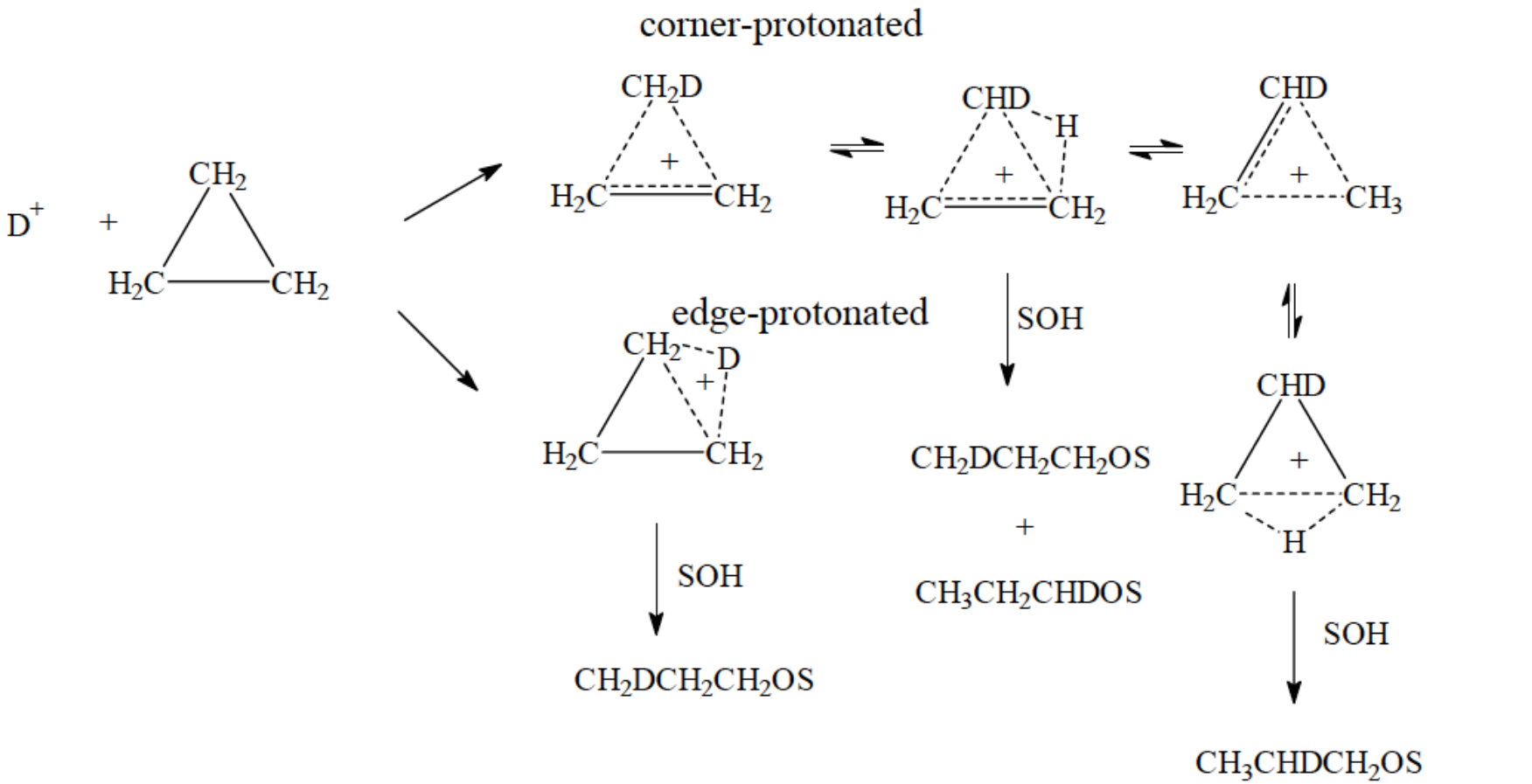
at -110℃ , 2 sets of peak
at -40℃ , one peak only

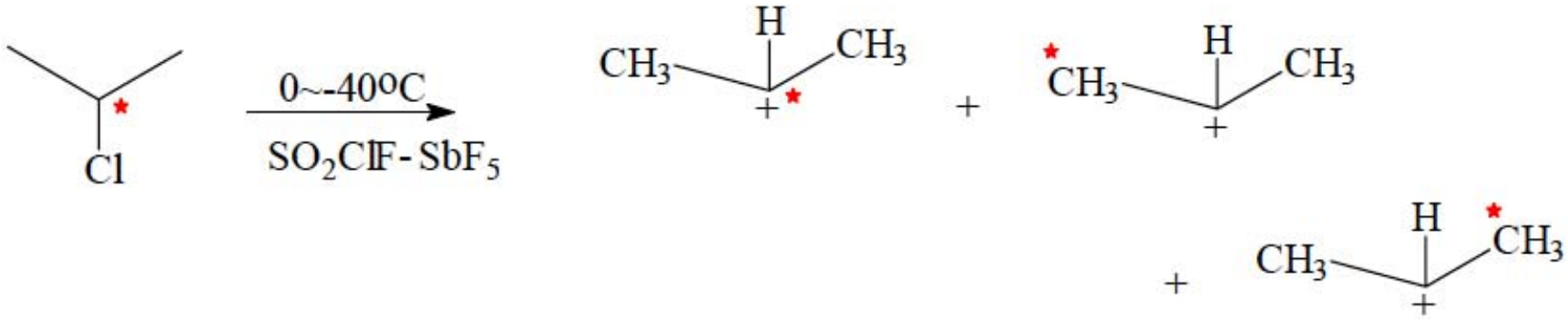

corner-protonated
cycloprotane
Cl
SbF5
FSO3H
SO2ClF
stable at -75℃
at -65℃
above -30℃
H3C
H3C
CH3





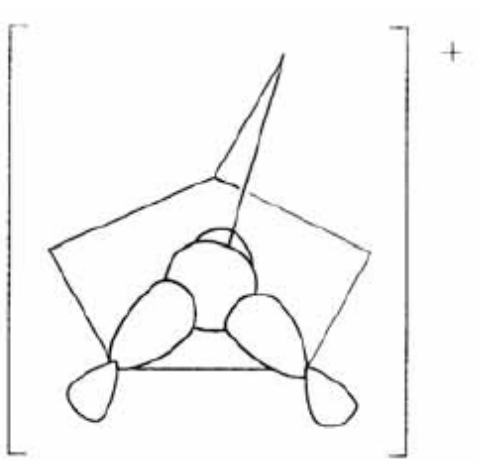
D scrambled to all carbons

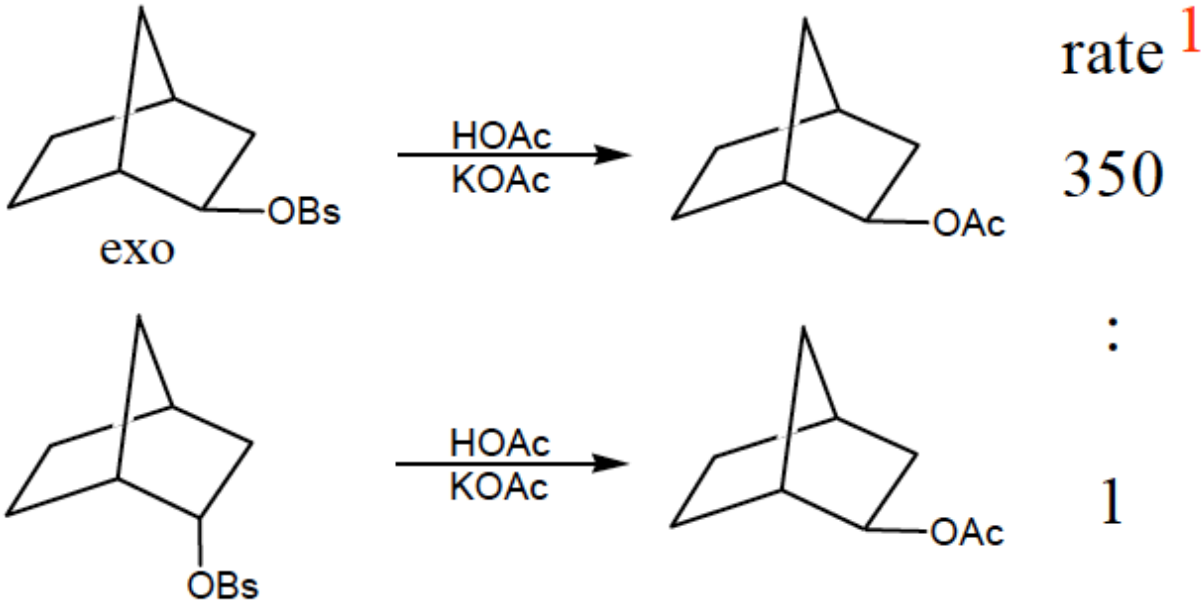

corner-protonated
edge-protonated
SOH
SOH
SOH
CH2DCH2CH2OS
CH2DCH2CH2OS
CH3CH2CHDOS
CH3CHDCH2OS


0~-40°C
SO2ClF-SbF5

Nonclassical Ion

Bridged structure with delocalized σ bond
→ a pair of e^- shared by three nuclei.



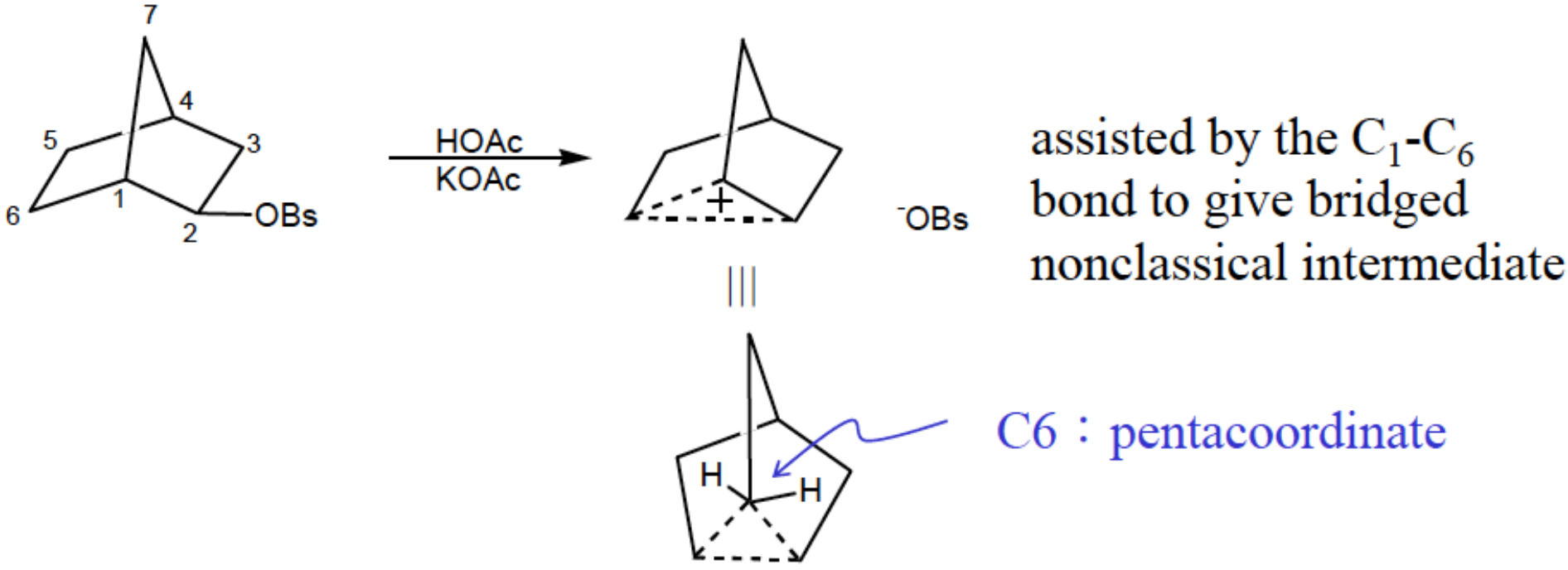


2 Optically active exo → racemic exo

3 Optically active endo → 93% racemic exo

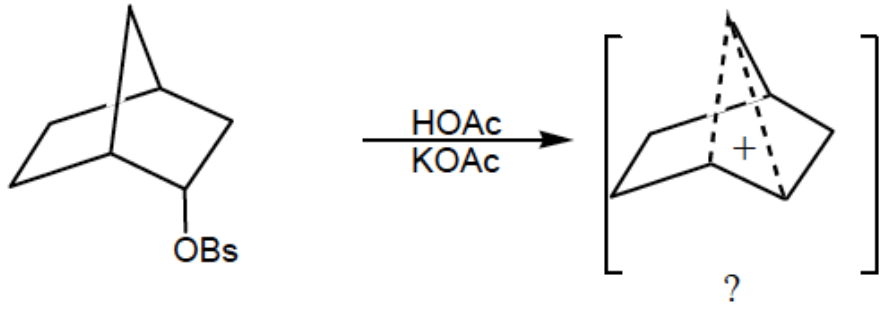
4 For chiral exo S.M., recovered S.M. partially racemized.

5 For chiral endo S.M., recovered S.M. did not racemized.

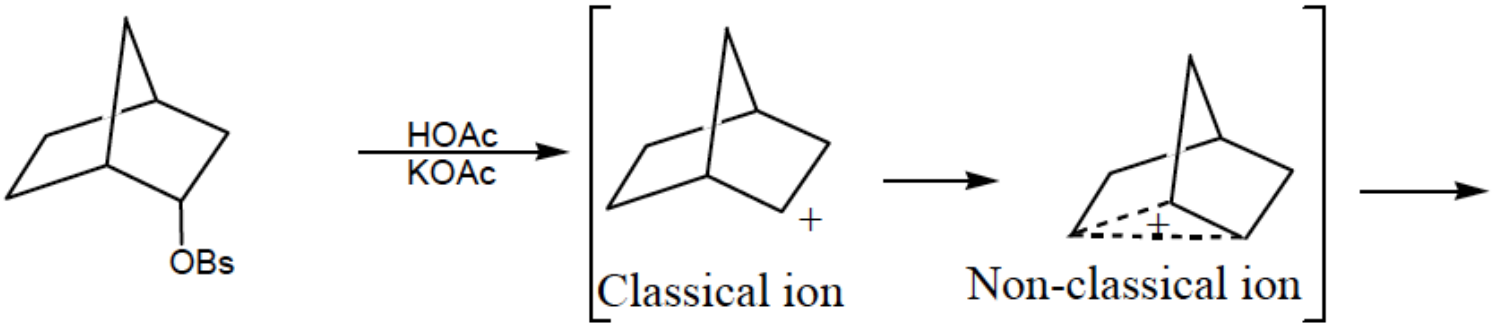


The rate enhancement was due to proper anti-alignment of the C(1)-C(6) bond and the leaving gp at C(2).
The stereochemical outcome is due to a symmetric intermed.

No backside assistance in endo compound



The endo S.M. undergoes a classical ion intermediate then nonclassical ion



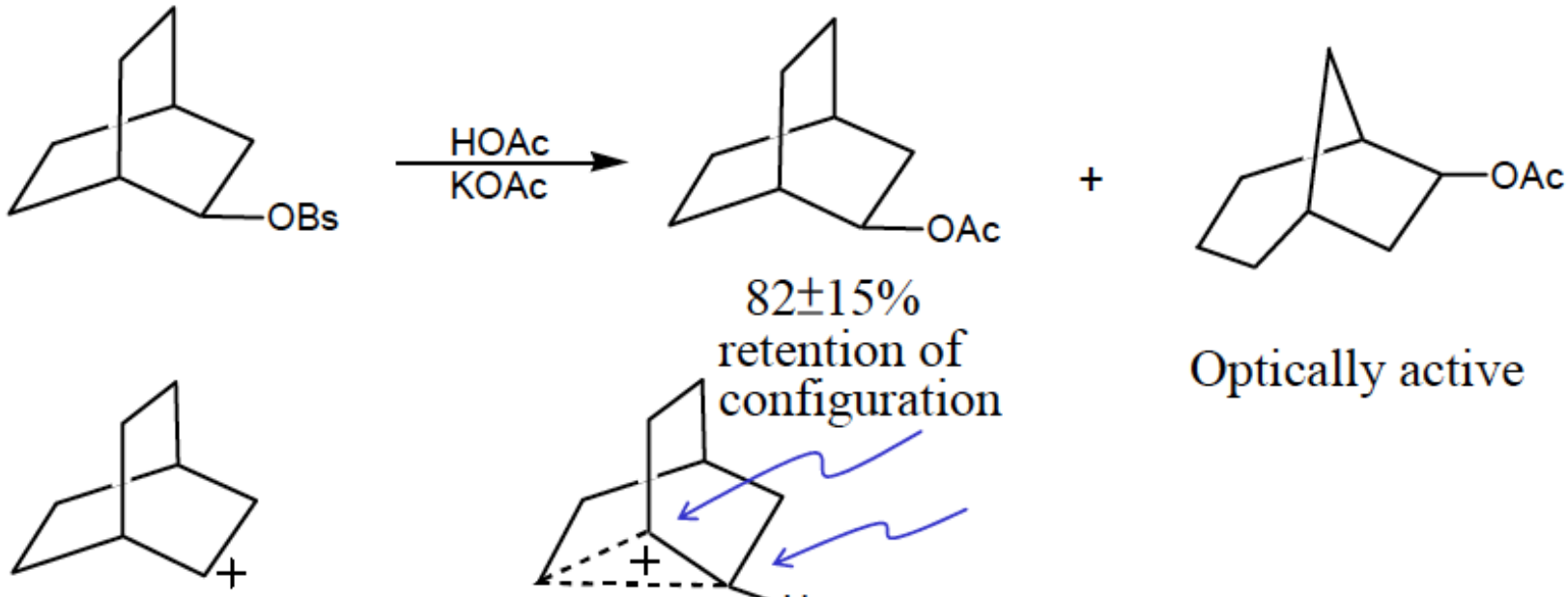
Two steps, the classical ion may be intercept by solvent to retain configuration , depending on the nuceophilicity of the solvent.

Thus, in acetone, → 87% racemization

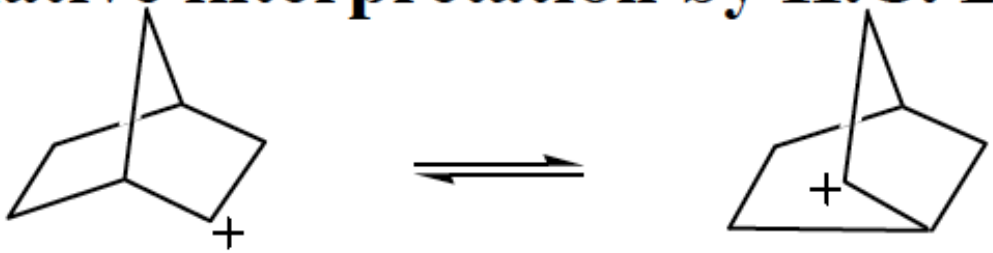
HOAc, → 93% racemization

HCOOH → 97% racemization

Observation in recovered S.M. is due to internal return of symmetrical Intermediate for exo S.M.



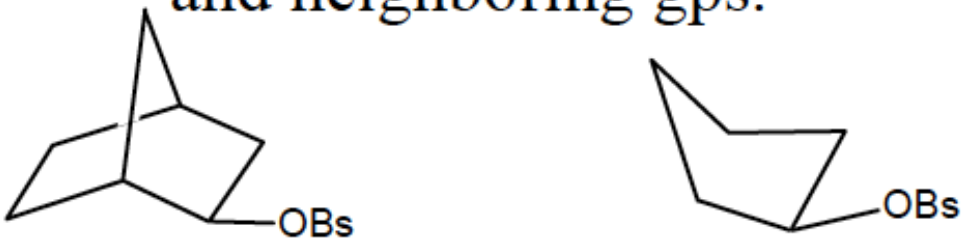
Alternative interpretation by H.C. Brown



fast equilibrium of classical ions

rate enhancement：release of torsional strain of leaving gp and neighboring gps.

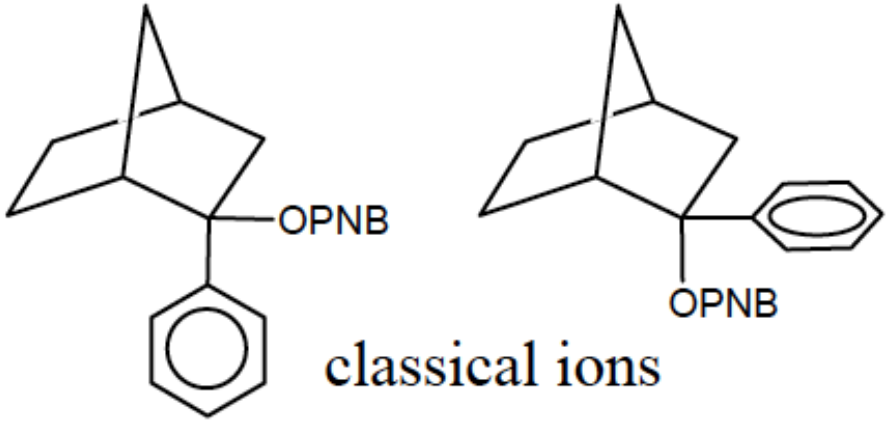
e.g.



rate 14 : 1

high exo/endo ratio：steric hindrance

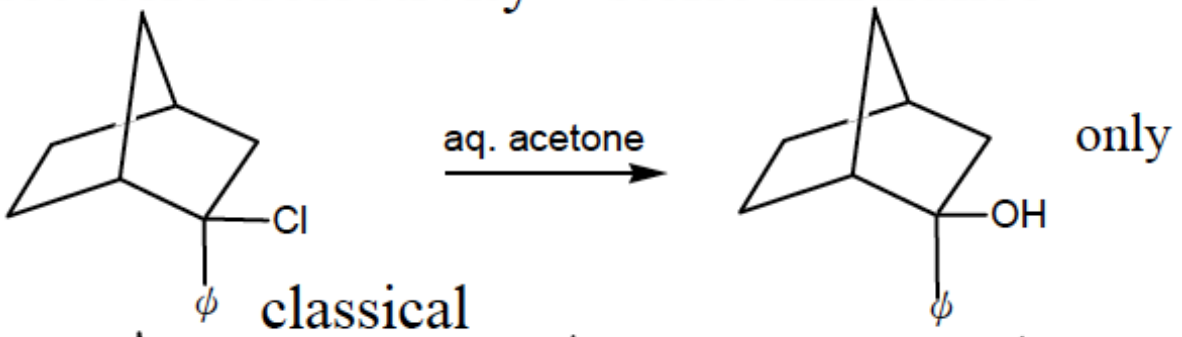
e.g.

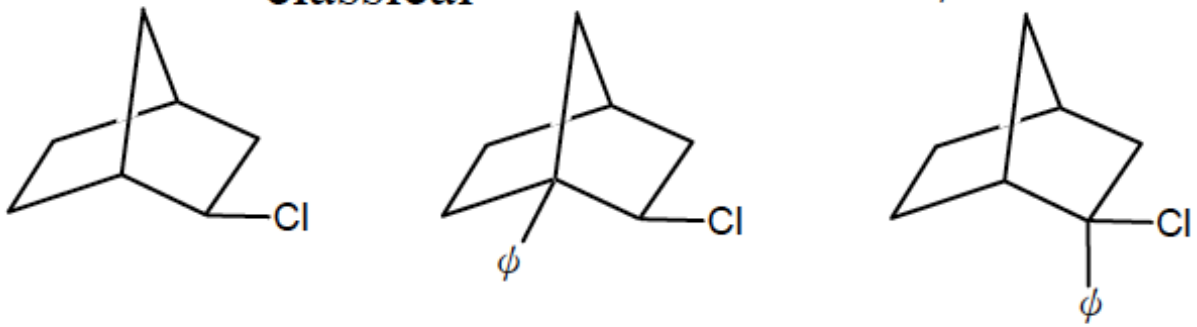


k_{exo}/k_{endo}=140

classical ions

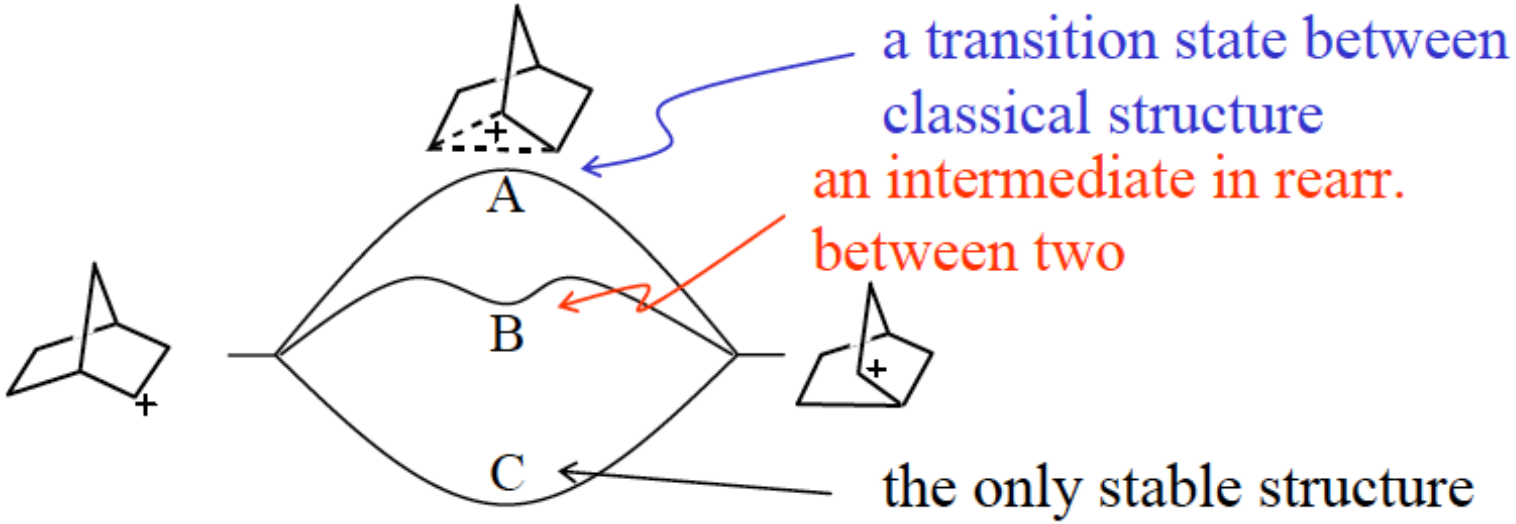
product stereoselectivity：steric hindrance





rate 1 3.9 3.9×10^7

potential energy for stable and unstable bridged ion



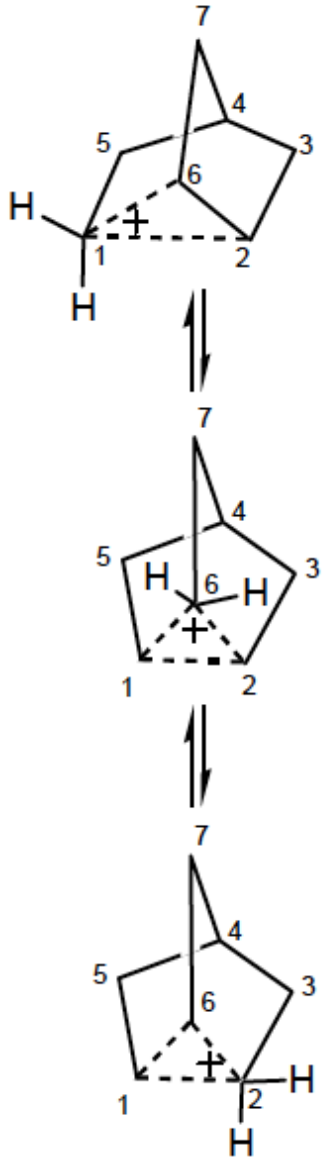
Direct Observation of Norbornyl cation by NMR: Olah

^{13}C NMR in SO_2-SbF_5 (super acid)

at -70℃, 101.8 ppm C-1,2,6
162 ppm C-3,5,7
156.1 ppm C-4

at -150℃ and → 5°K
78.5 ppm C-1,2
171.4 ppm C-6
160.4 ppm C-4
145.8 ppm C-3,7
165.8 ppm C-5

at -150℃, the hydride shift frozen

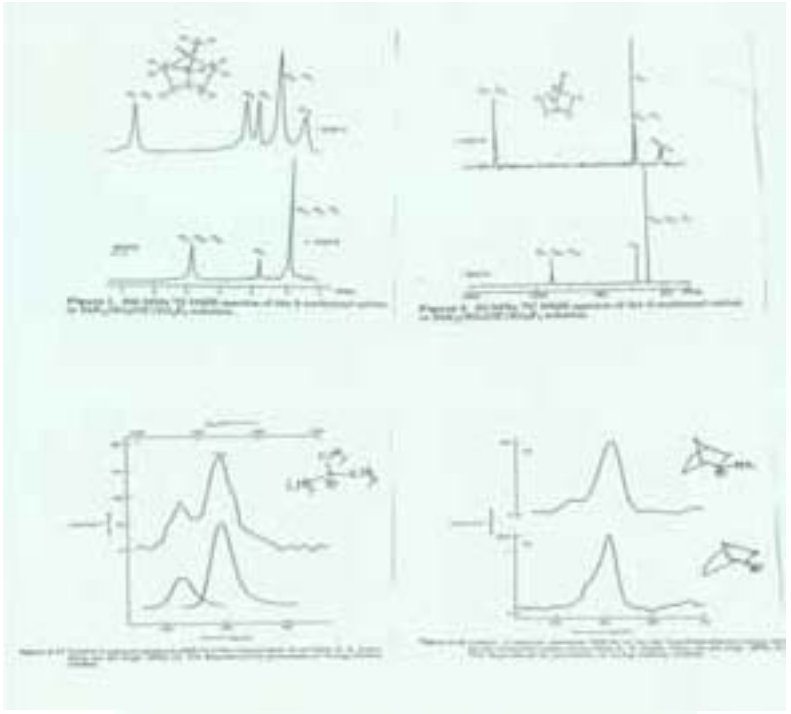


^1H at -60 ℃,
5.35 ppm (4H)
3.15 ppm (1H)
2.20 ppm (6H)

at -150℃, the hydride shift frozen

→ the NMR confirm the existence of norbornyl cation as non-classical.

or a equilibrating intermediate with barrier < 0.2kcal



Summarize:

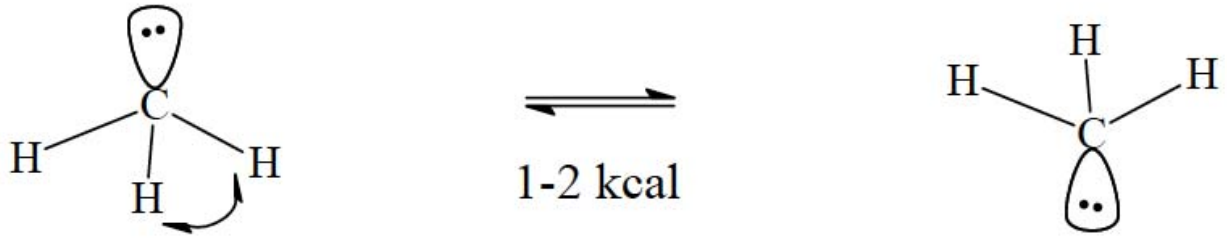
Nonclassical or bridged structure are readily attainable intermediate or transition state for many cations.

For norbornyl cation, the bridged structure is an intermediate. tertiary cation is nearly always classical cation.

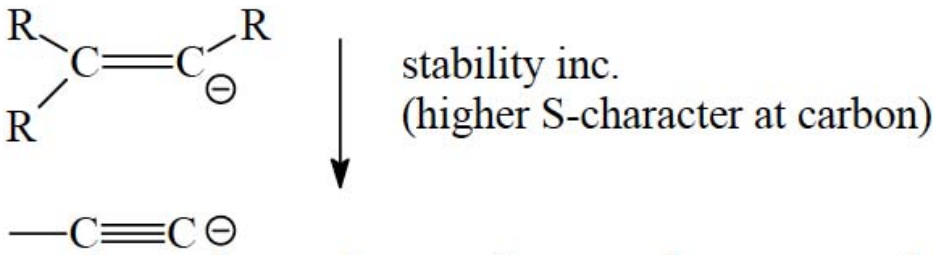
primary cation can rearrange to more stable secondary or tertiary carbocation, with bridged structure as T.S..

§ Carbanions:

intermediates with formal charge of –1 on carbon, 8 valence electrons



less than 109.5°



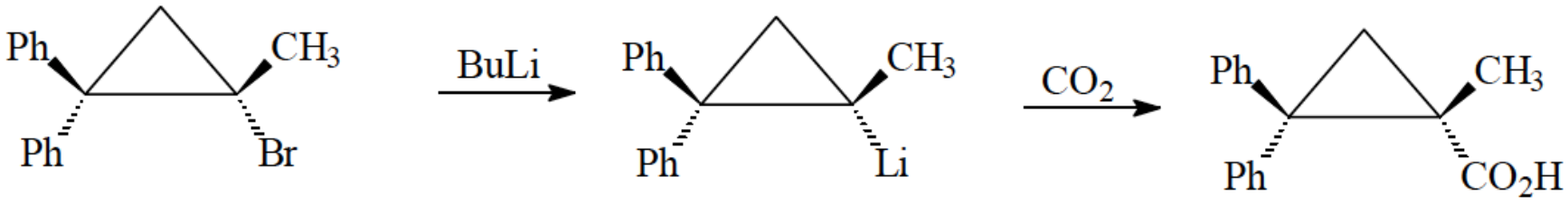
Metal-carbon bond can be polar-covalent, such as C-Li

Organometallic species can be associated species(oligomeric)

The barrier of inversion at carbanion carbon can be increased by incorporation of small ring, attaching electronegative substituent,

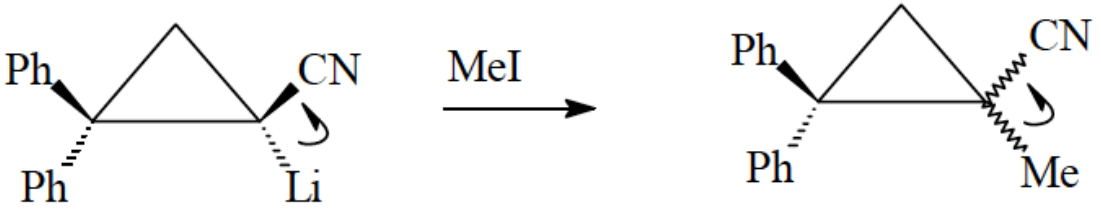
cyclopropyl anion is stable pyramidal

Inversion barrier for NH_3 ~5kcal, for NF_3 ~50kcal



100% retention of conformation

Substituent that allows π-delocalization favors planar structure



stabilized by resonance
less interaction with metal ion

racemic → a fast inverting tetrahedral carbanion center is indicated

Generation of carbanion

→reduction of carbon-halogen bond by metal

→deprotonation (acid/base rxn) by strong base

→reduction/addition of alkene

→…….

Stability of carbanion

Acidity $3^o < 2^o < 1^o$ in solution

(due to destabilization of e-donating alkyl groups?)

But in gas phase, measured acidity:

Ethene<propane(2^o-H)<methane<isobutane(3^o-H)

The solution acidity is complicated by solvation

The order of acidity of alcohol

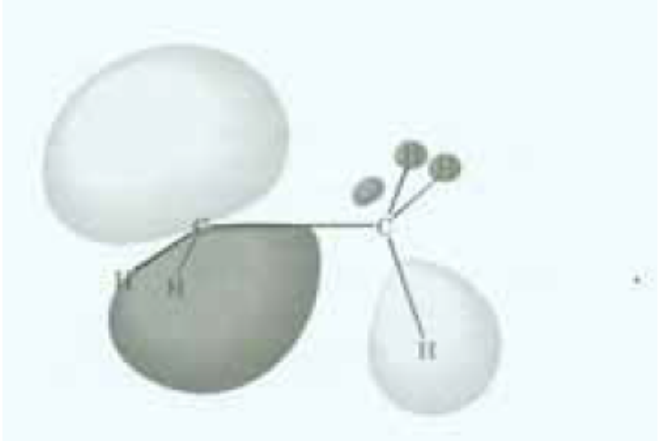
In gas phase

t-butyl > isopropyl>ethyl>methyl

In aqueous solution

methyl>ethyl>isopropyl>t-butyl

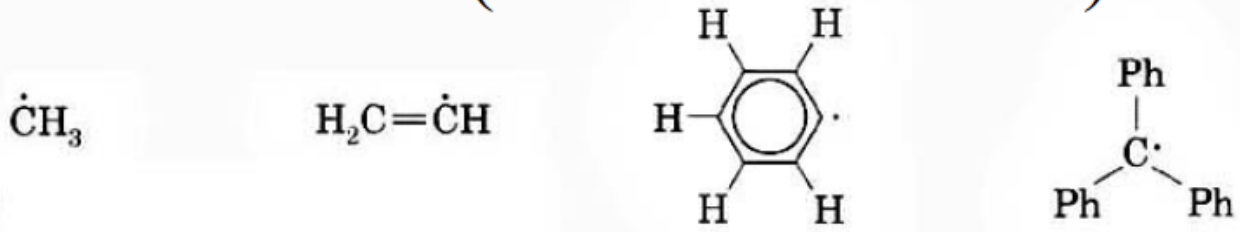
The alkyl group can polarize the electron away from the center of negative charge and stabilize it.



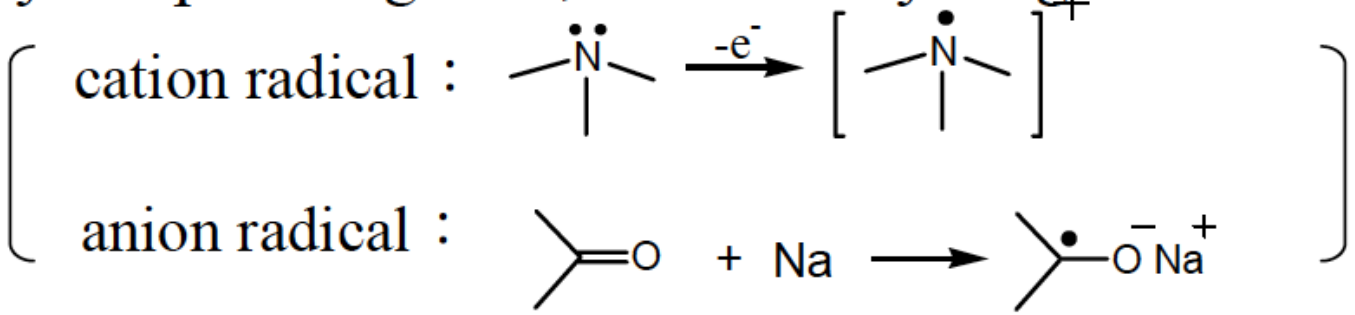
§ Free Radicals

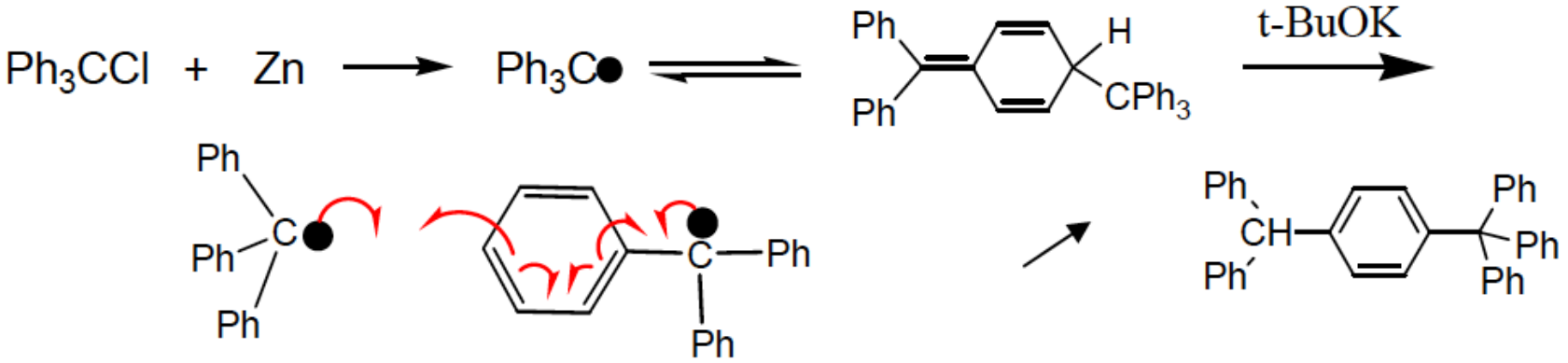
Structure with unpaired electron and zero formal charge

7 valence electrons (for neutral radical)

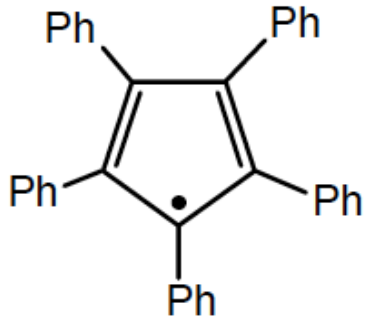


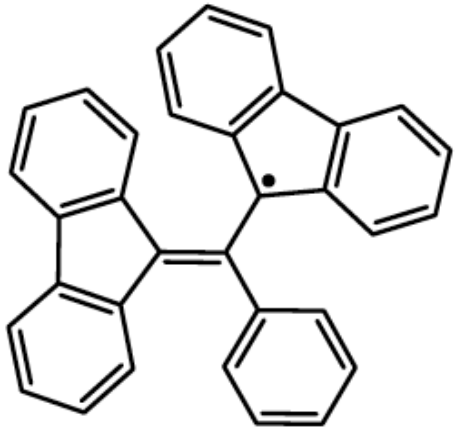
They are paramagnetic, attracted by magnetic field.



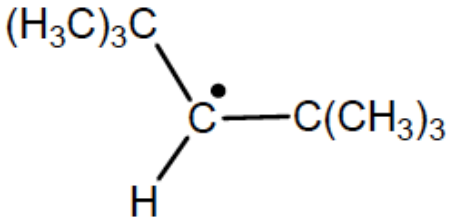


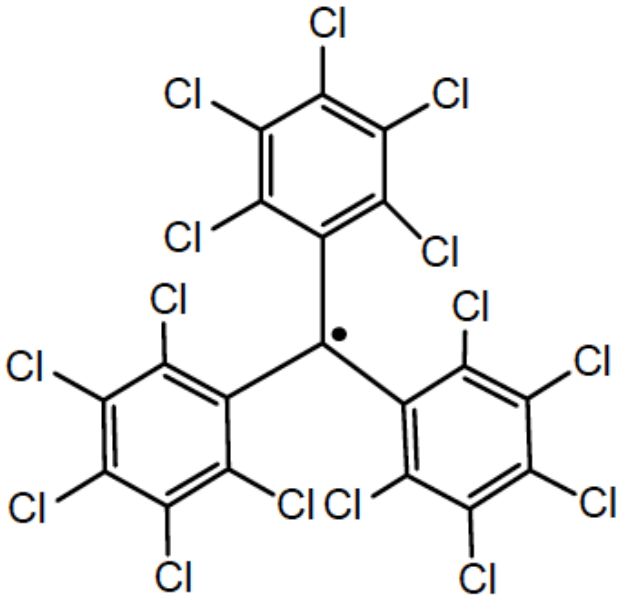
Radicals are in general reactive intermediate, but can be stablized via delocalization of the radical：such as



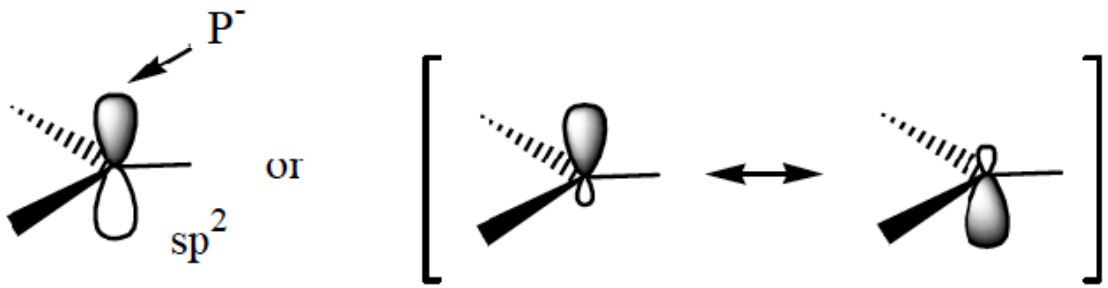


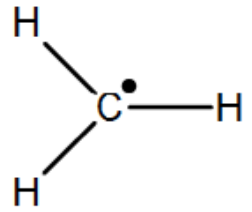
or by steric hindrance



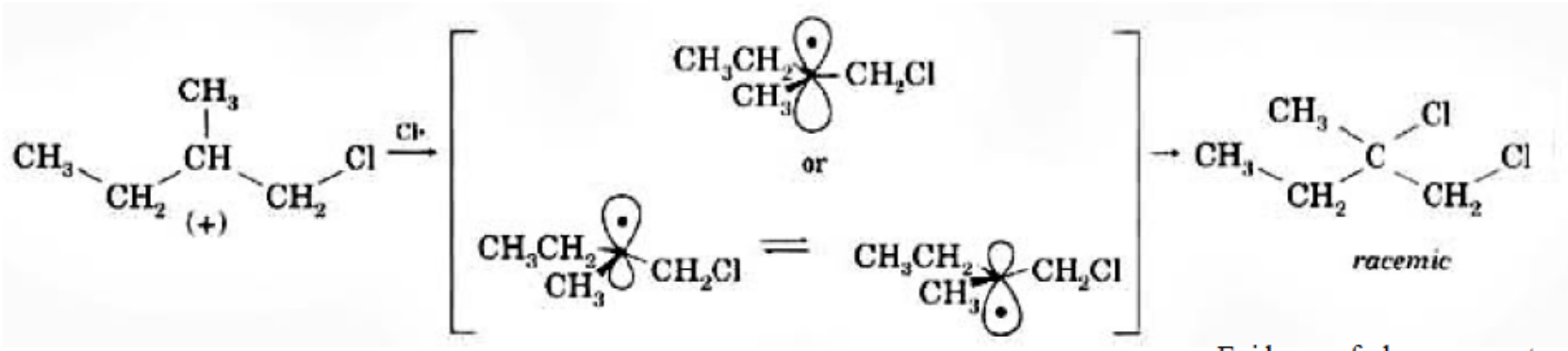


alkyl radical



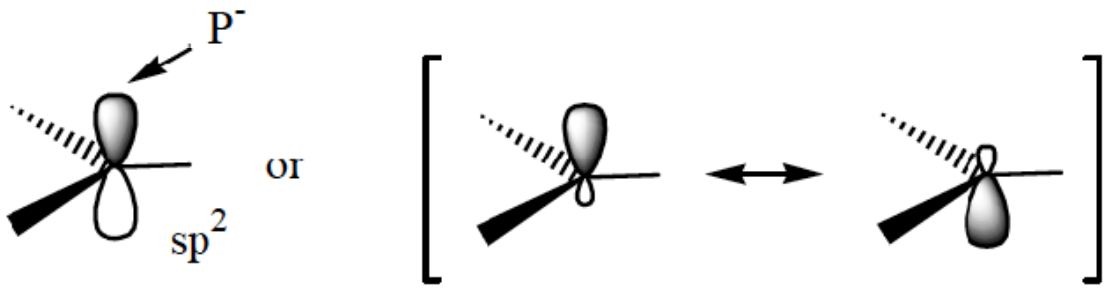


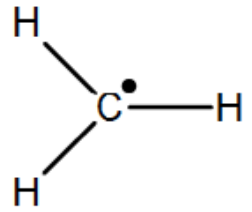
is planar



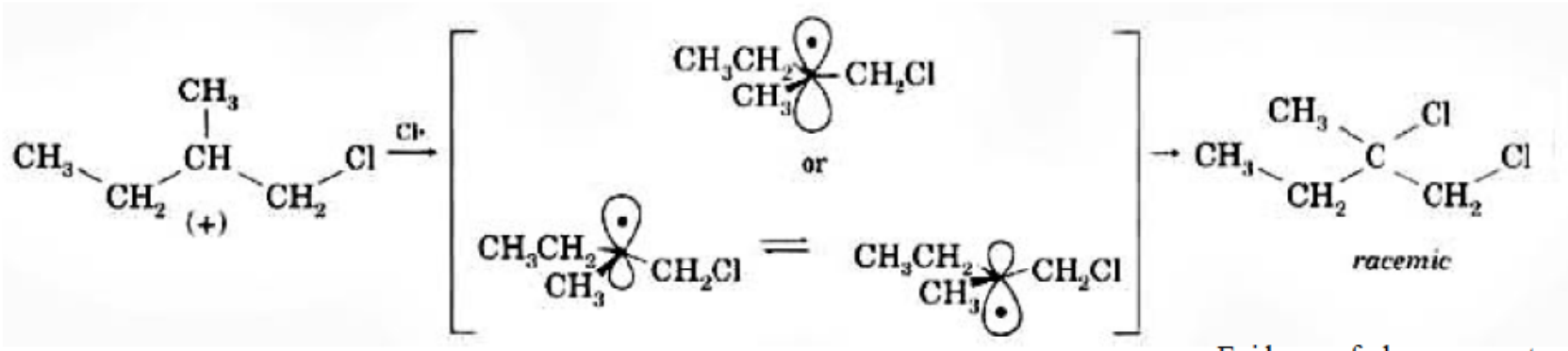
Evidence of planar geometry

alkyl radical

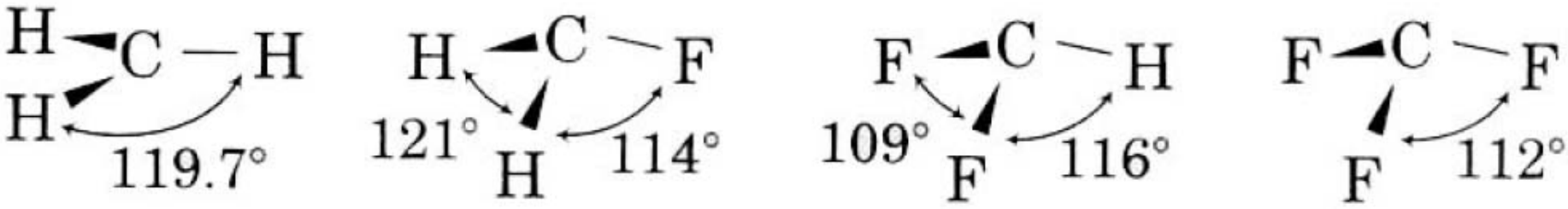




is planar



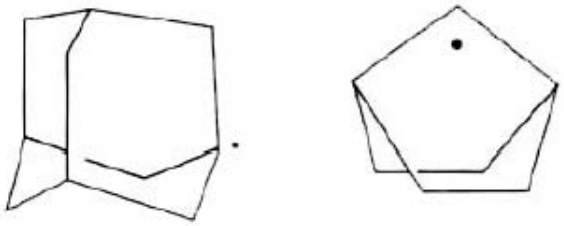
Evidence of planar geometry



⟶

Methyl radical is planar, with very small barrier for pyramidalization. All other radicals are non-planar. Electronegative substituent shifts the shape to pyramidal.

bridgehead radical are less strained, as compare to planar carbonium ion



stability of radical

Table 5.1 ΔH_f^0 values for selected radicals and bond dissociation energies for selected alkanes.

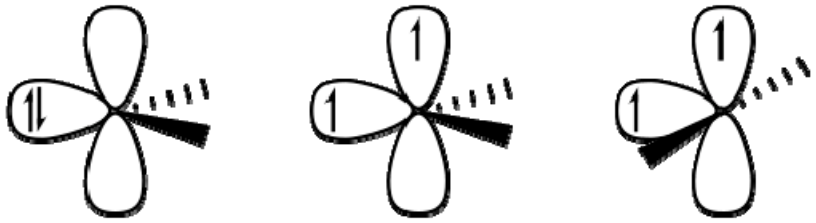
Radical ($R^{\cdot}$)	ΔH_f^0 (kcal/mol)	BDE (R-H) (kcal/mol)
H	52.1[a]	104.2[a]
Methyl	34.9 ± 0.2[b]	104.9[c]
Ethyl	28.3 ± 0.4[b]	100.6[c]
n-Propyl	24.0 ± 0.5[c]	100.9[e]
i-Propyl	22.3 ± 0.6[c]	99.3[c]
	21.3 ± 0.7[b]	
sec-Butyl	16.7 ± 0.5[c]	99.0[c]
t-Butyl	11.7 ± 0.4[d]	95.9 − 0.4[d]
	12.4 ± 0.5[c]	

[a]Data from reference 65. [b] Data from reference 67. [c]Data from reference 68. [d]Data from reference 69. [e]Calculated from ΔH_f^0 values of the radicals and the alkane.

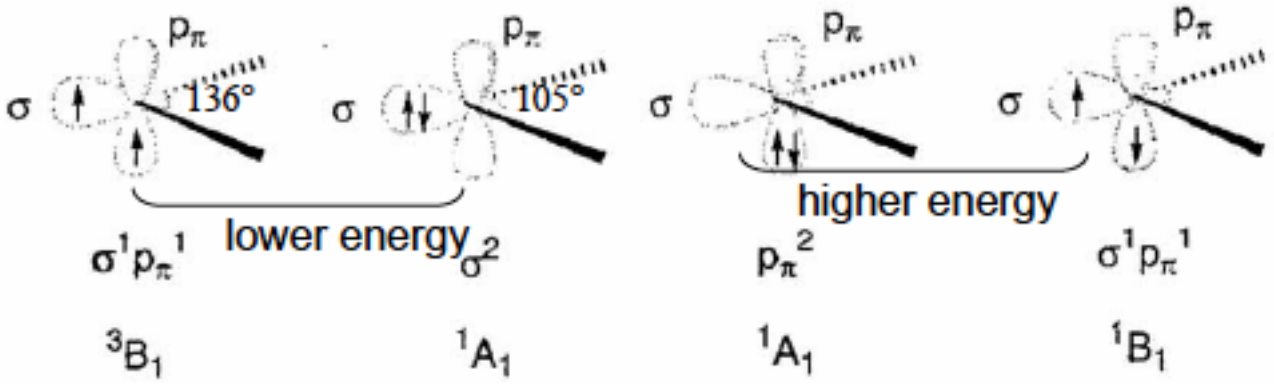
methyl < 1° < 2° < 3°

due to hyperconjugation

§ carbenes



Ground state for simple carbene



Ground state multiplicity affects reactivity (e.g. singlet has ambiphilic character; triplet reacts as diradical)

Large σ -p π separation => singlet ground state

Smaller σ -p π separation => triplet ground state.

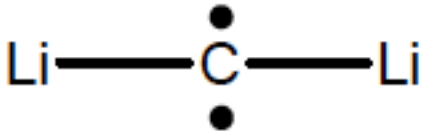
The substituents affect the ground state multiplicity

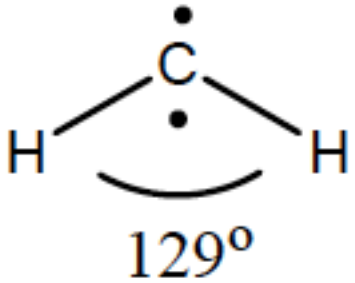
The substituents affect the ground state multiplicity

Inductive effect: (inductively stabilize σ by increasing its S-character)

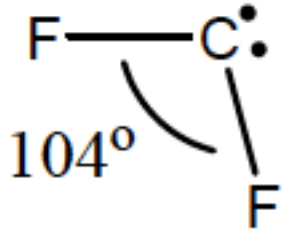
σ -withdrawing group favors singlet

σ -donating group favors triplet





triplet



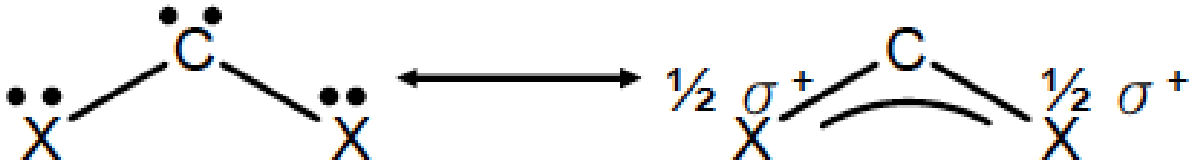
singlet

Resonance Effect:

X: +R (-F, -Cl, -Br, -I, -NR2, -PR2, -OR, -SR)

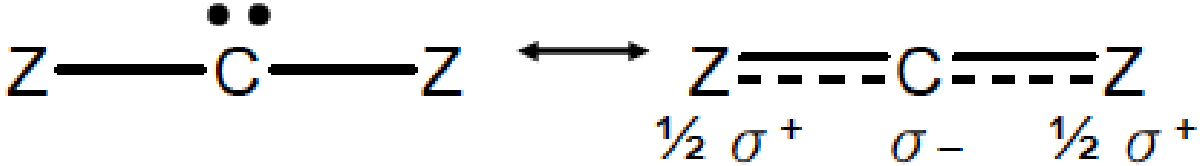
Z: -R (-COR, -CN, CF3, -BR2, -SiR3, -PR3+)

(X,X) –carbene => bent singlet



e.g, dimethoxycarbene, dihalocarbene

(Z,Z) – carbene => linear singlet carbene



e.g. diborylcarbene, dicarbomethoxycarbene

(X,Z) – carbene => linear singlet

e.g. phosphinosilylcarbene

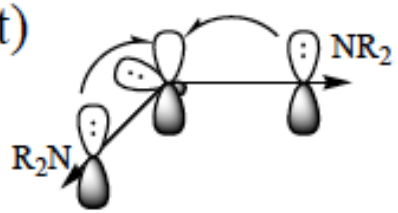
Steric effect:

increasing steric bulkness -> increase the bond angle =>
favor triplet

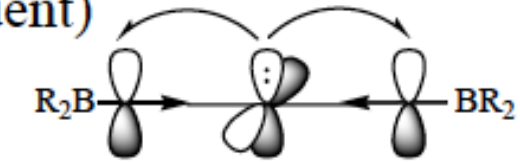
Dimethylcarbene,	di(t-butyl)carbene	diadamantylcarbene
Bent singlet, 111°	triplet, °	triplet, 152°

To stabilize a carbene:

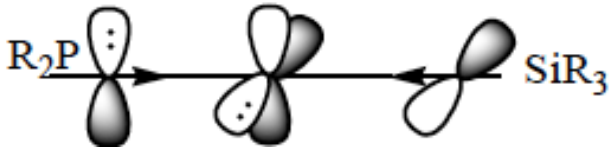
two π-donor, σ -attractor substituents (push push resonance, pull pull inductive substituent)



Two π-attractor, σ -donor substituents (pull pull resonance, push push inductive substituent)



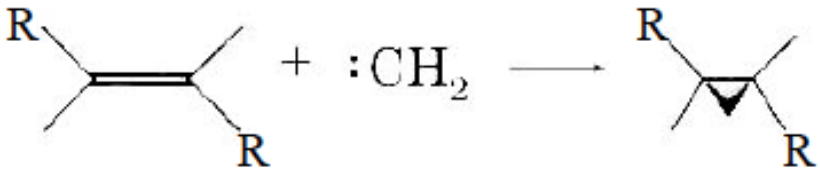
A π-donor, π-acceptor (push pull resonance substituent)



Reaction of Carbene

triplet carbene behaves as diradical
singlet carbene behaves as both carbocation and carbanion.

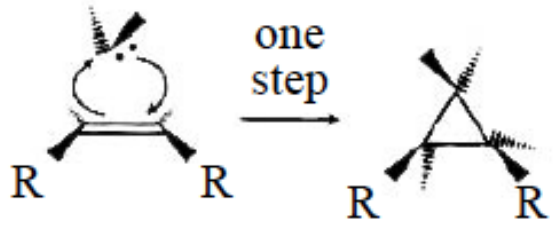
Addition



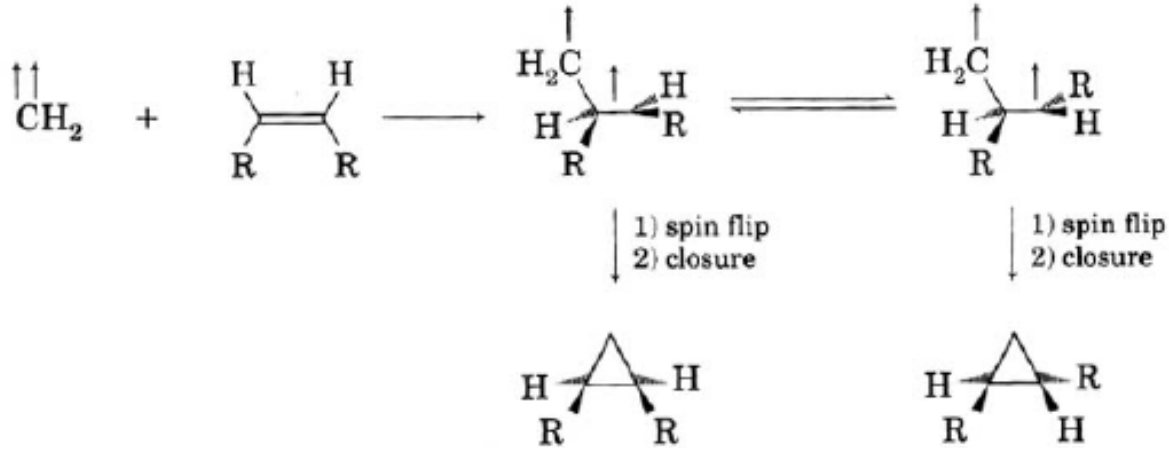
Singlet carbene inserts stereospecifically

triplet carbene inserts non-stereospecifically

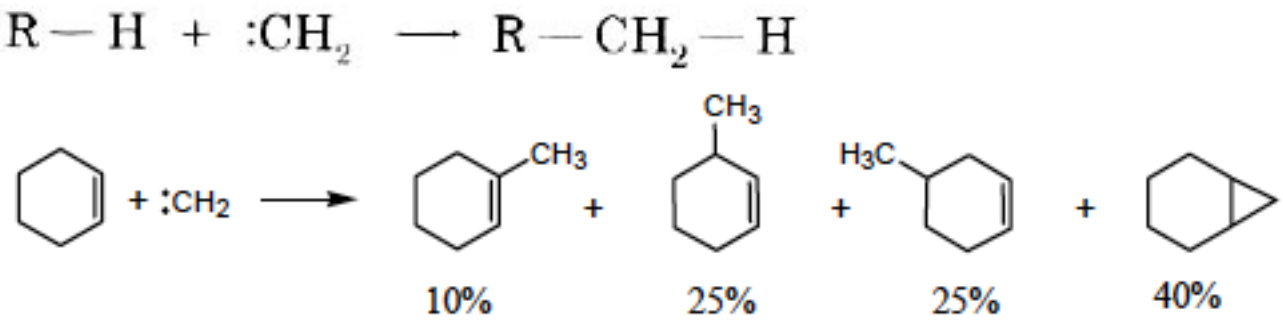
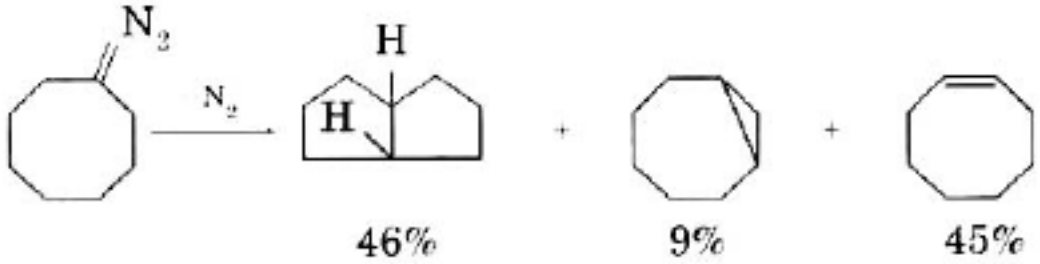
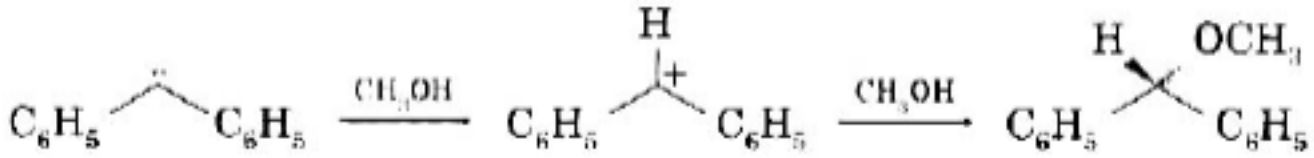
Singlet



Triplet



Insertion



Rearrangement