

Introduction to Radicals

The idea of a substituted carbon atom with 7 valence electrons being a reactive intermediate was established and accepted in around the 1930's.

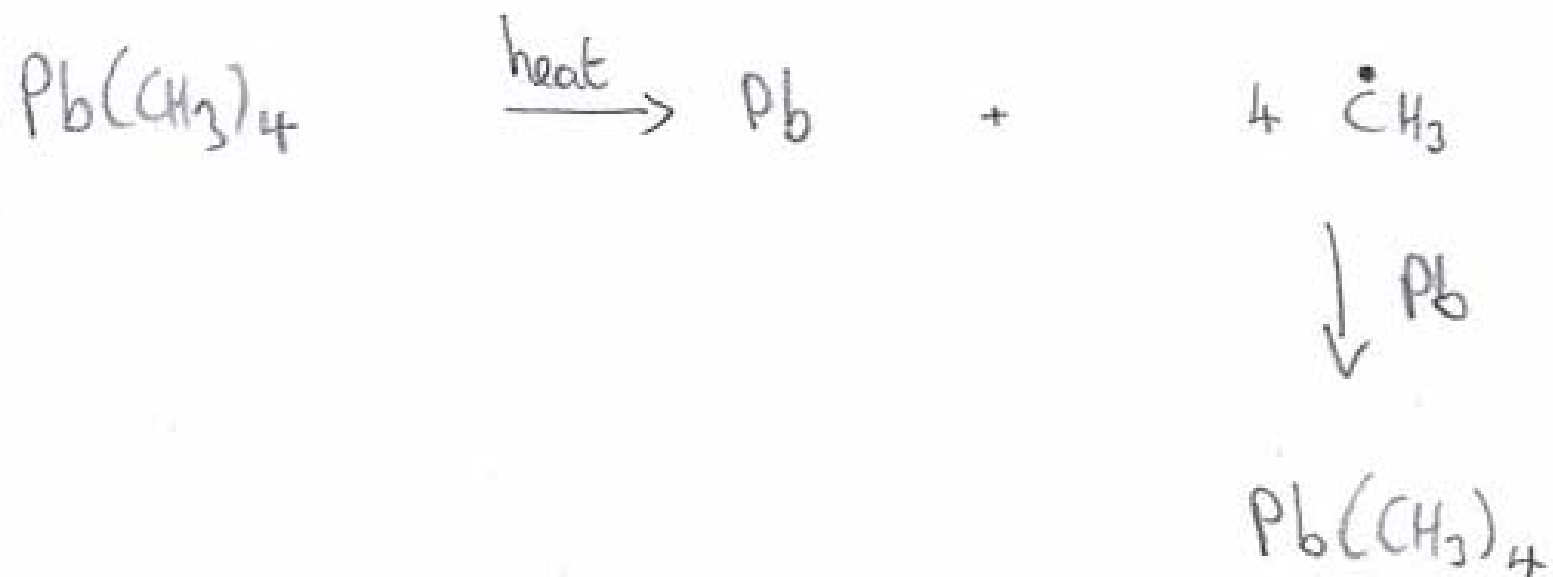
The two most famous "radical" breakthroughs were the work of Gomberg (in the 1900's) and Paneth (in 1929).

(Long story cut short...) Gomberg worked with triphenyl methyl chloride and was able to generate the $\text{Ph}_3\text{C}^\bullet$ radical.

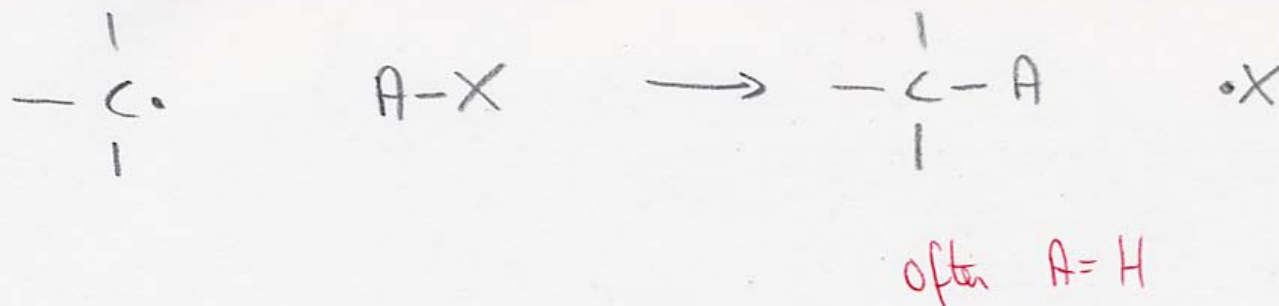
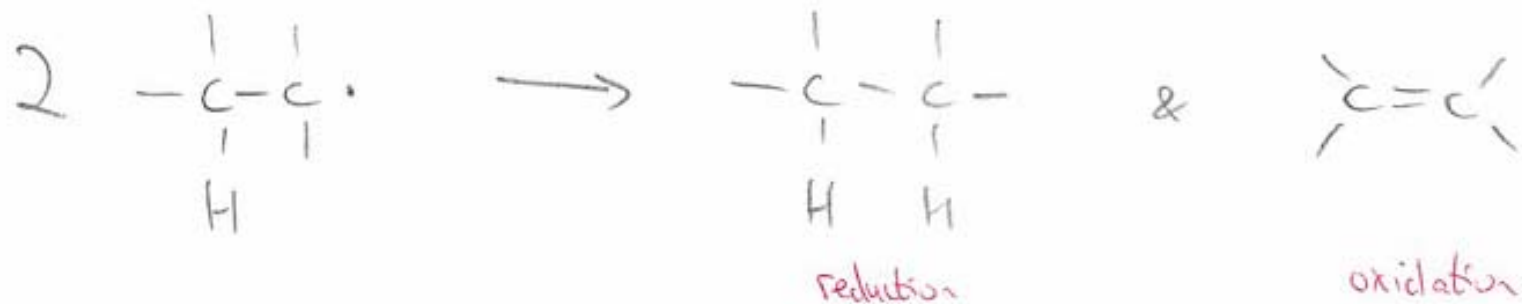
A species that did not display reactivity and behaviour of a normal hydrocarbon, or its derived cations/anions (e.g. it underwent dimerization).



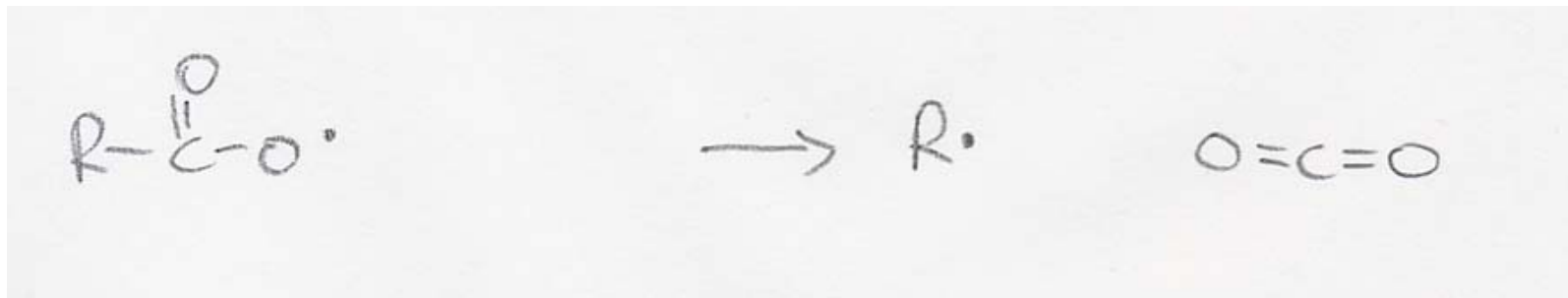
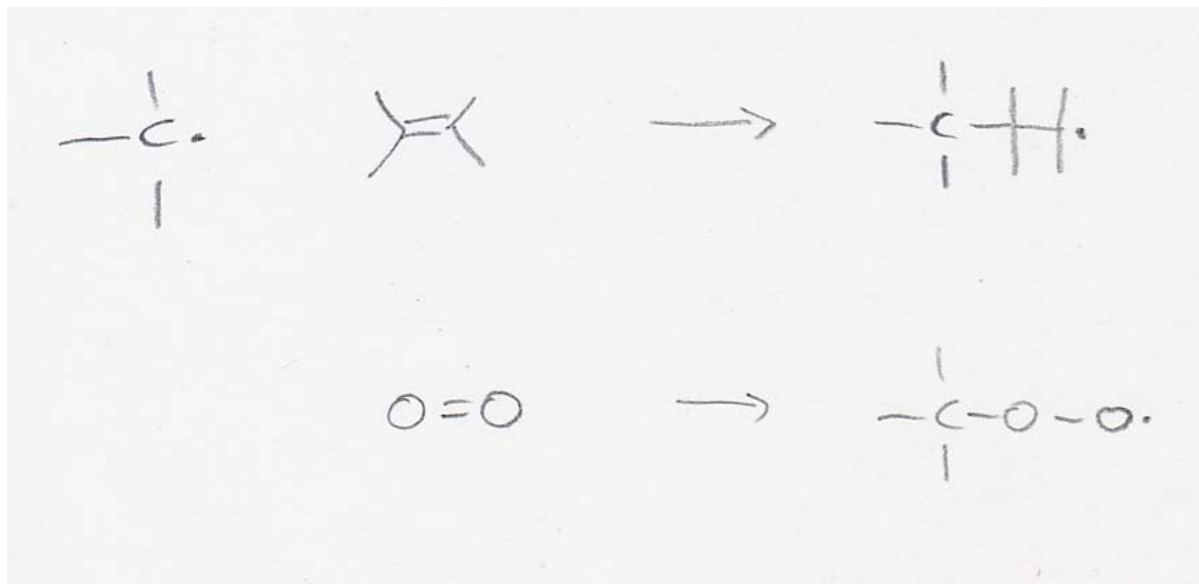
Paneth's experiments used tetramethyl lead, which generated methyl radicals, and he revealed that these radicals existed long enough to be transported down a tube, and would also react with elemental lead to reform $\text{Pb}(\text{CH}_3)_4$.



Most organic free radicals are very reactive, with very short life times. Typical reactions include **dimerization**, **disproportionation**, **atom abstraction**, addition and fragmentation.



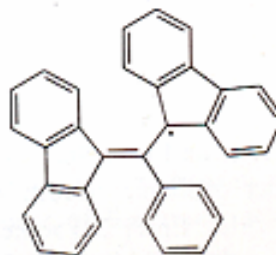
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There are certain structural features that can increase stability, (such as resonance stabilization / delocalization) and steric hindrance)

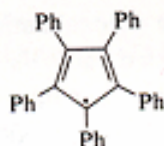
and in certain special and famous cases, “stable” free radical species can be formed.

1^a



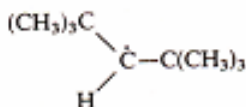
Indefinitely stable as a solid, even in the presence of air.

2^b



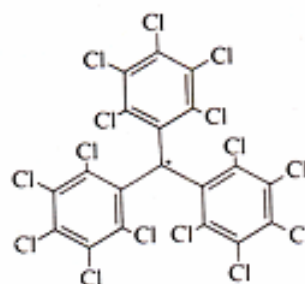
Crystalline substance is not rapidly attacked by oxygen, although solutions are air sensitive; the compound is stable to high temperature in the absence of oxygen.

3^c



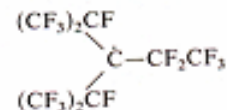
Stable in dilute solution ($<10^{-5} M$) below $-30^{\circ}C$ in the absence of oxygen, $t_{1/2}$ of 50 sec at $25^{\circ}C$.

4^d



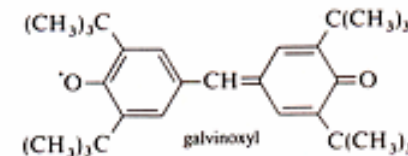
Stable in solution for days, even in the presence of air. Indefinitely stable in solid state. Thermally stable up to $300^{\circ}C$.

5^e



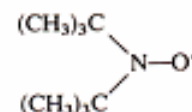
Stable to oxygen; thermally stable to $70^{\circ}C$.

5^f



Stable to oxygen; stable to extended storage as a solid. Slowly decomposes in solution.

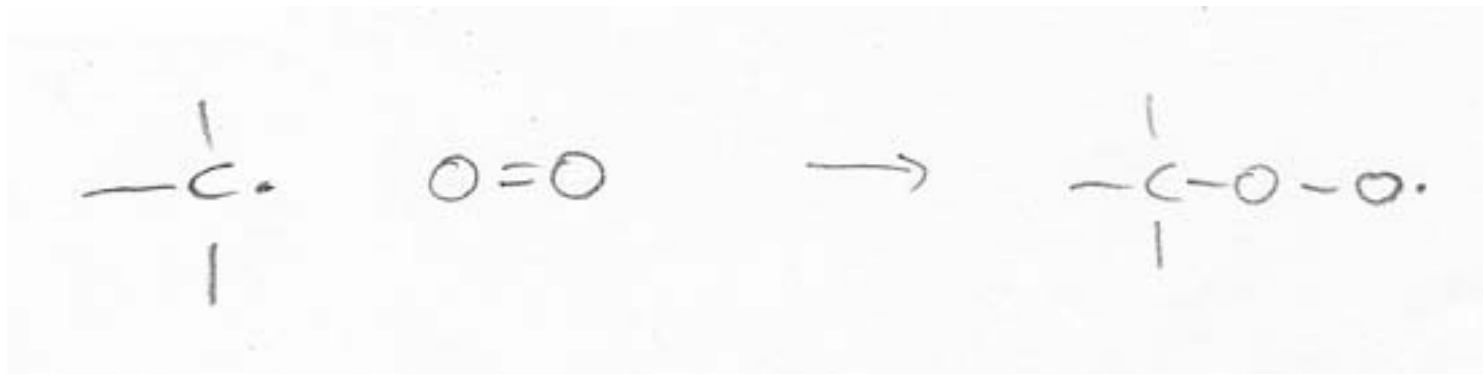
6^f



Stable to oxygen even above $100^{\circ}C$.

a. C. F. Koelsch, *J. Am. Chem. Soc.* **79**, 4439 (1957).
 b. K. Ziegler and B. Schnell, *Justus Liebigs Ann. Chem.* **445**, 266 (1925).
 c. G. D. Mendenhall, D. Griller, D. Lindsay, T. T. Tidwell, and K. U. Ingold, *J. Am. Chem. Soc.* **96**, 2441 (1974).
 d. M. Billester, J. Riera, J. Castañer, C. Badia, and J. M. Monsó, *J. Am. Chem. Soc.* **93**, 2215 (1971).
 e. K. V. Scherer, Jr., T. Ono, K. Yamanouchi, R. Fernandez, and P. Henderson, *J. Am. Chem. Soc.* **107**, 718 (1985).
 f. G. M. Coppinger, *J. Am. Chem. Soc.* **79**, 501 (1957); P. D. Bartlett and T. Funahashi, *J. Am. Chem. Soc.* **84**, 2596 (1962).
 g. A. K. Hoffmann and A. T. Henderson, *J. Am. Chem. Soc.* **83**, 4671 (1961).

Oxygen is very reactive to radicals. Hence air is often troublesome to radical reactions, and inert atmospheres have to be used.

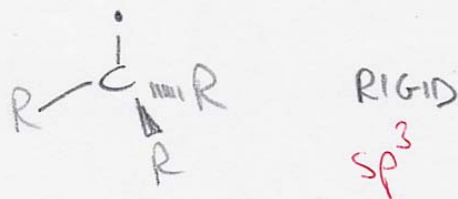


However, even though there are examples of stable and /or persistent free radicals, **THESE ARE SPECIAL CASES**, and most free radicals are highly reactive intermediates that have very short lifetimes and can only be generated and studied in relatively low concentrations

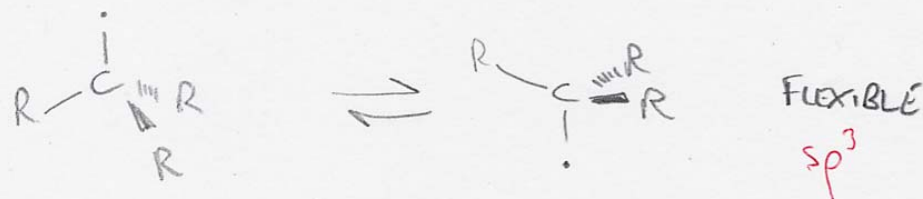
Structural and Stereochemical Aspects

If we limit our discussion to alkyl radicals, then our possibilities for structures are:

Rigid pyramidal



Flexible pyramidal



Planar



From electron Spin Resonance (ESR or EPR), and from stereochemical reaction studies, it has been established that:

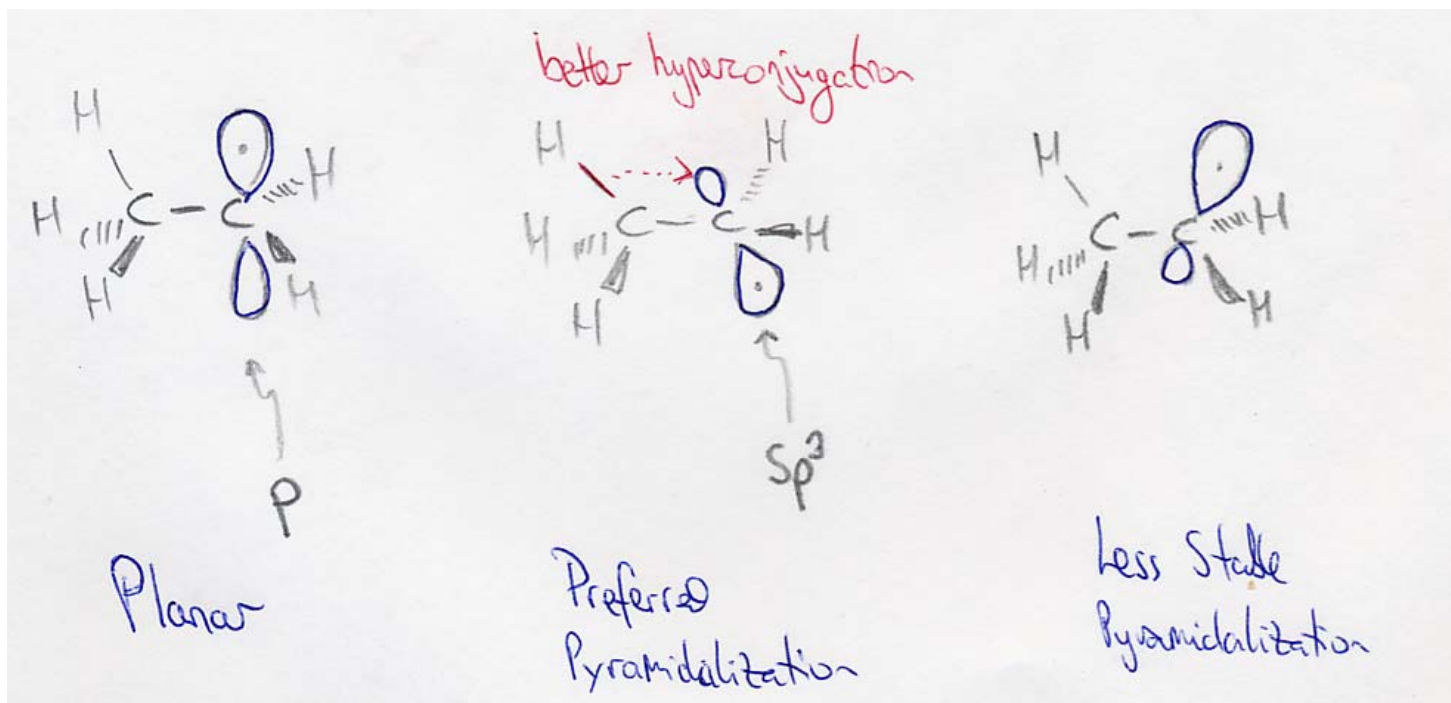
For the methyl radical, the structure is either planar or a very shallow pyramid. At low temperatures there is only a 5° deviation from planarity.

For the ^tbutyl radical, almost all the experimental and theoretical considerations point towards a very slight pyramidal structure, which can easily invert.

Notice that a pyramidal structure requires the radical electron to be in an sp³ hybrid orbital, whereas planar means it is in a p orbital.

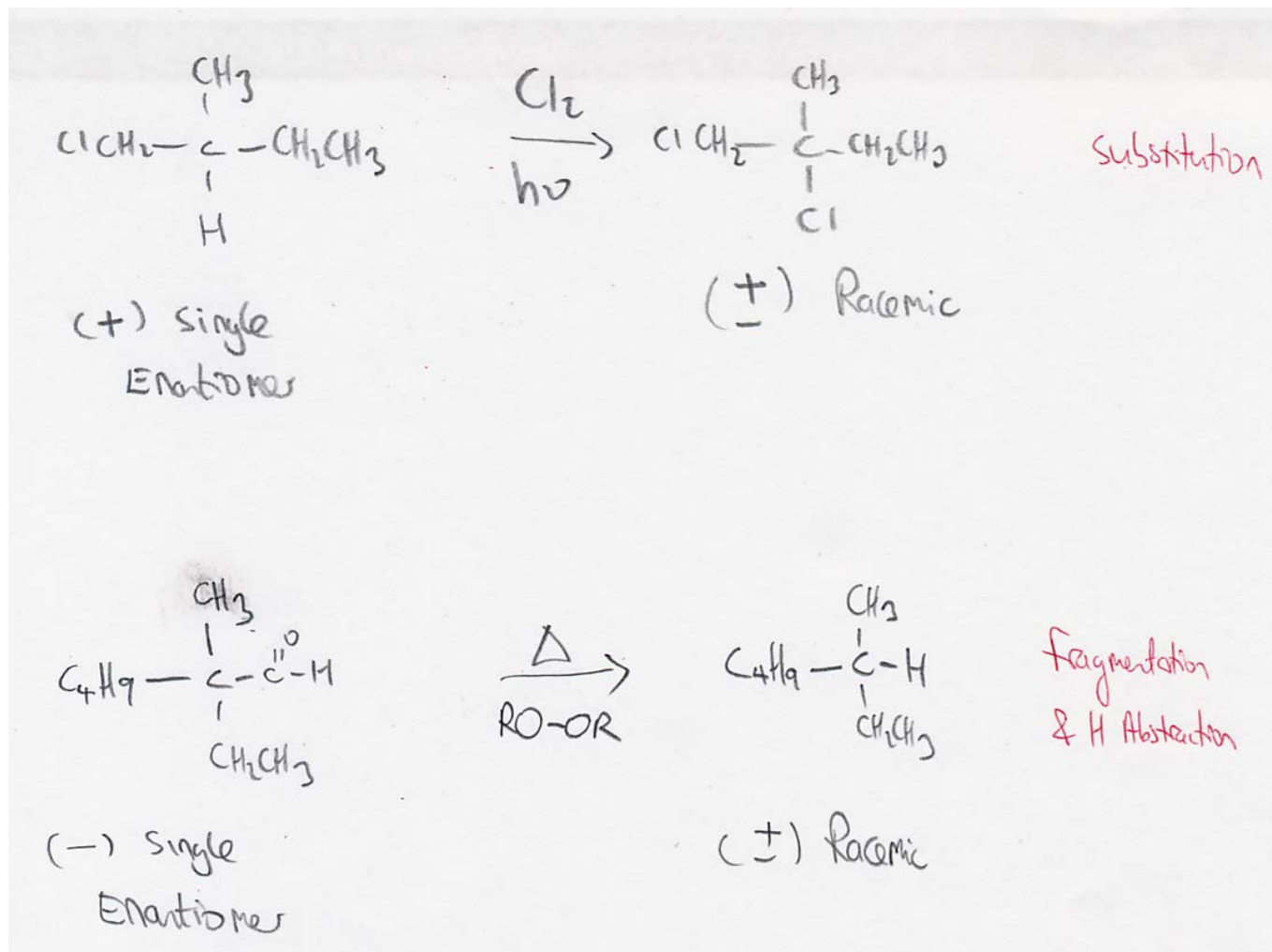
Calculations suggest that simple radicals prefer slight pyramidalization.

The radical center prefers a staggered conformation relative to its substituents. This minimized eclipsing interactions, and allows for superior **hyperconjugation** from the full C-H to the half filled radical orbital.



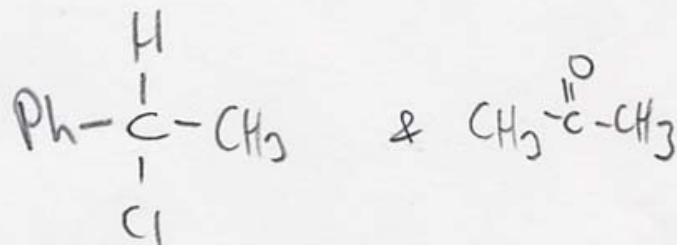
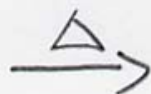
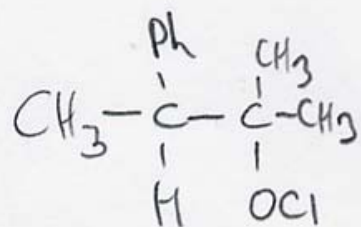
FOR MOST RADICALS WE ARE ONLY TALKING ABOUT 1 – 2 KCAL/MOL BARRIER TO INVERSION, SO RAPID INVERSION IS OCCURRING.

Stereochemical reactions have been used to demonstrate the geometry of radicals. One would expect racemization to occur if the radicals that are generated are either planar or rapidly inverting.



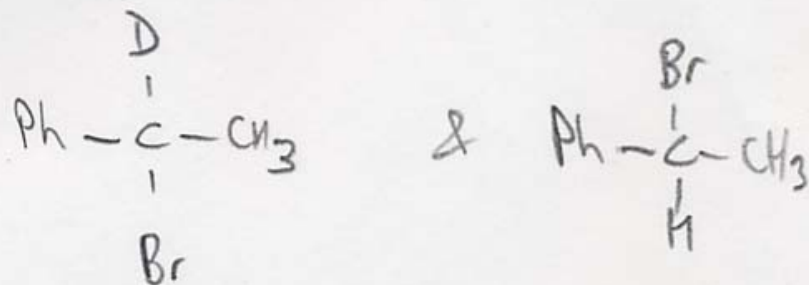
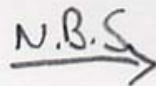
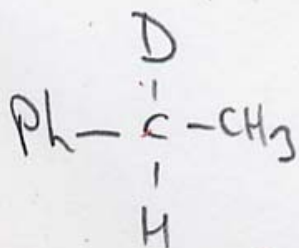
These reactions from the 1940 and 1950's demonstrate that the radicals produced are not rigid pyramidal structures (implying planarity, or close to planarity / rapidly inverting).

Same thing here, implying planarity, or close to planarity / rapidly inverting.



(+) Single Enantiomer

(+) Racemic



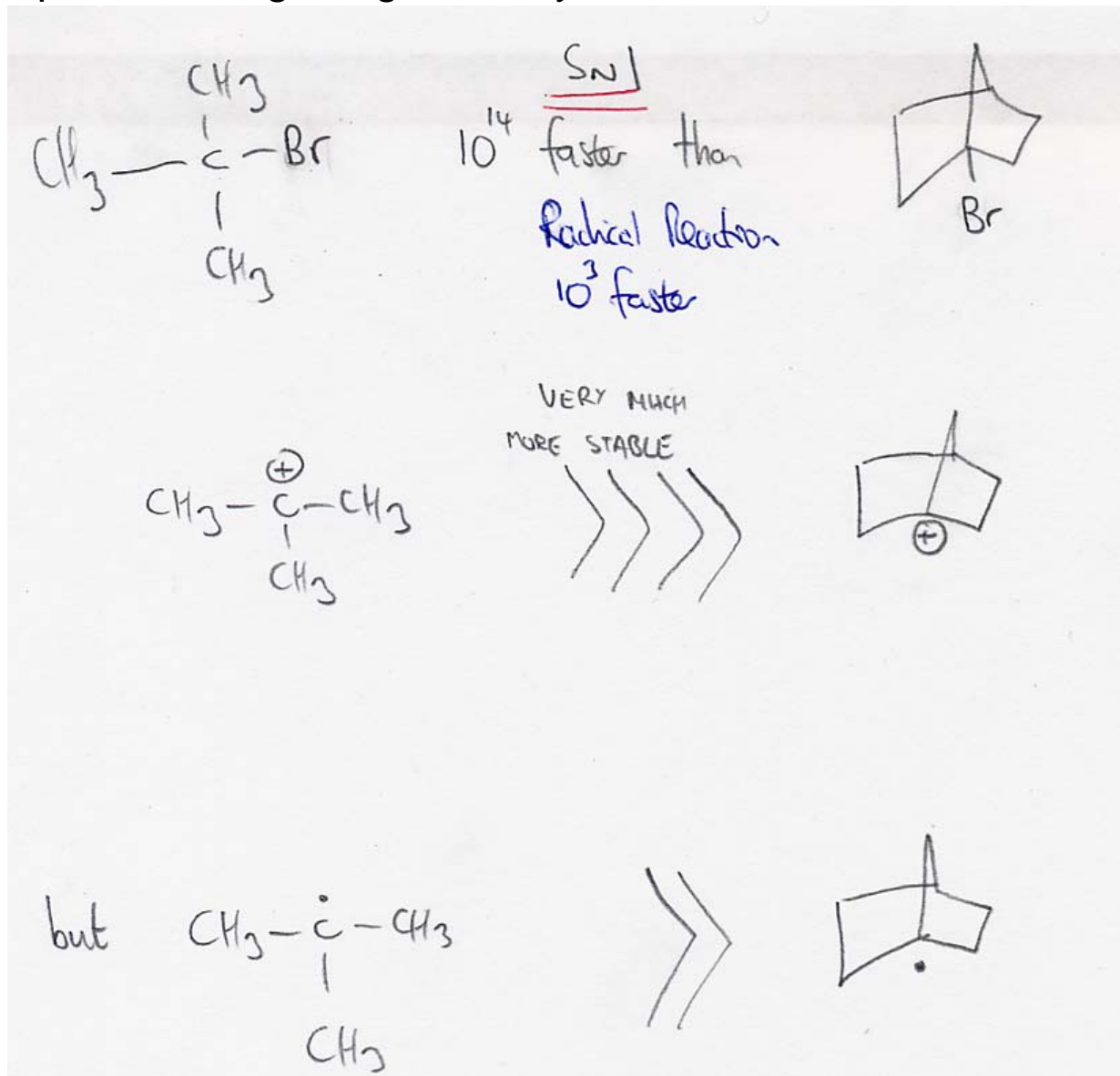
single Enantiomer

Racemic

Racemic

Geometric requirements can be probed using bridgehead systems:

E.g. in S_N1 reaction rates
tButyl 10^{14} faster than
norbornyl



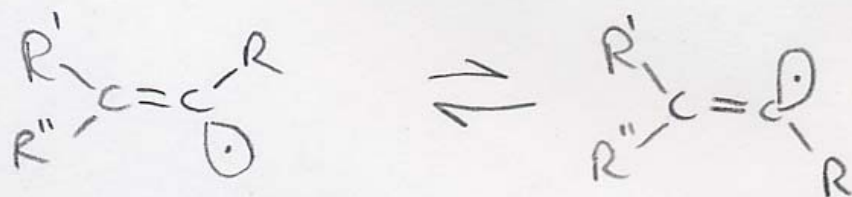
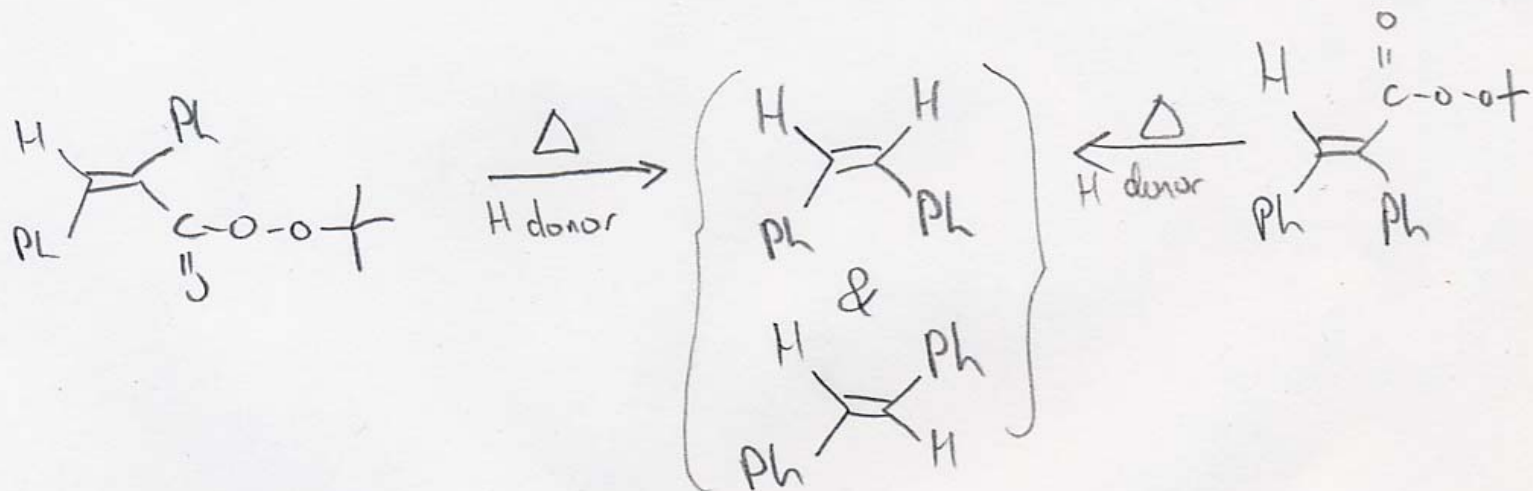
But for radicals

tButyl (only) 500 – 1000
faster than norbornyl.

So radicals are happier (more tolerant) with pyramidalization (sp^3) than cations.

Vinyl free radicals also have been shown to undergo rapid inversion.

e.g.

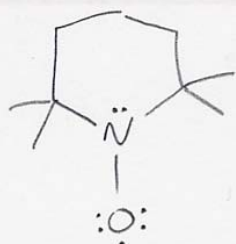


Typical barriers to inversion are around 2 kcal/mol, with lifetimes of individual isomers are on the scale of 10^{-9} seconds.

Radical reactions have certain characteristics:

-Rates not largely dependant on reaction media polarity (polar or non-polar solvent does not significantly affect the rate).

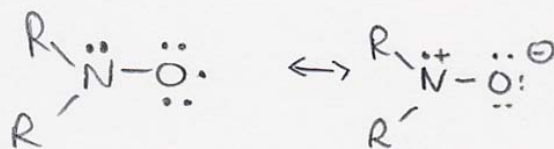
-Reactions slow down or do not work in the presence of **free radical inhibitors** such as oxygen in the air, or deliberately added like TEMPO or dinitrobenzene.



TEMPO

2,2,6,6-Tetramethyl piperidine -1-oxyl

Nitroxides = (relatively) stable Free Radical Functional Group



-Often require initiation of some sort (thermal, chemical, photochemical).

-Can be chain processes.

-Radical reactions often lead to additional side products.