

CARBENES

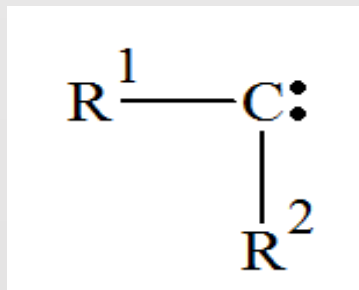
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Bs-1121

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CARBENES

Introduction

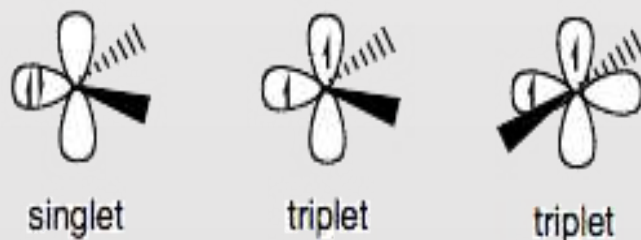


- A carbene is a molecule containing neutral carbon atom with a valence of two and two unshared valence electrons.
- Carbenes are uncharged, electron deficient molecular species that contain a divalent carbon atom surrounded by a sextet of electrons, and two substituents.

Types of Carbenes

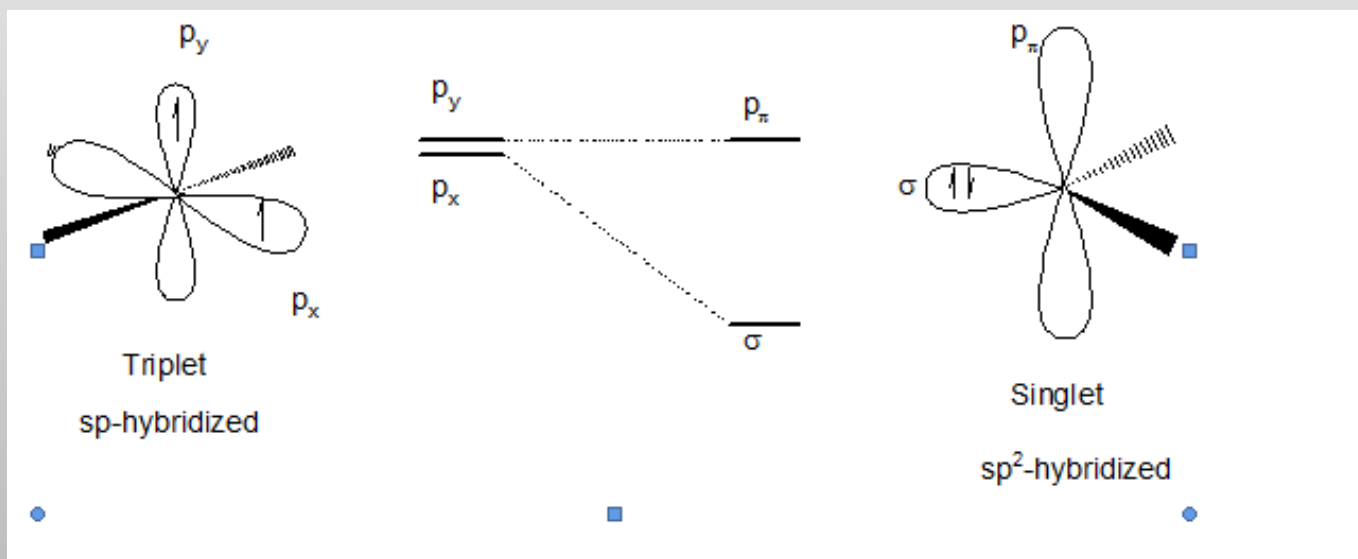
- Carbenes are called singlet or triplet depending on the electronic spins they possess.
- Triplet carbenes are paramagnetic. The total spin of singlet carbenes is zero while that of triplet carbenes is one.
- Bond angles are $130-150^\circ$ for triplet methylene and $100-110^\circ$ for singlet methylene.
- Triplet carbenes are generally stable in the gaseous state, while singlet carbenes occur more often in aqueous media.

Structure and bonding



- Singlet carbenes are spin-paired. This molecule adopts an sp^2 hybrid structure.
 - Eg- $:CH_2$ $:CHPh$ $:CHPh_2$ $:CHR$
- Triplet carbenes have two unpaired electrons.
- Most carbenes have a nonlinear triplet ground state, except for those with nitrogen, oxygen, or sulfur atoms, and halides directly bonded to the divalent carbon.
 - Eg:- $:CCl_2$ $:CHCl$ $:C(OMe)_2$

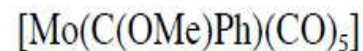
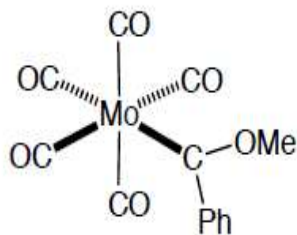
- Singlet state: carbocation-like in nature, trigonal planar geometry, electrophilic character. Singlet carbenes generally participate in cheletropic reactions as either electrophiles or nucleophiles.
- Triplet state: diradical-like in nature, linear geometry and participate in stepwise radical additions. Triplet carbenes have to go through an intermediate with two unpaired electrons whereas singlet carbene can react in a single concerted step.



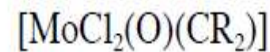
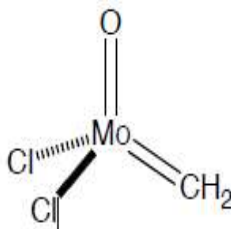
Cont.....

- Metal carbene complexes have been classified into two broad classes:
 - “Fischer-type” and “Schrocktype”.

Fischer



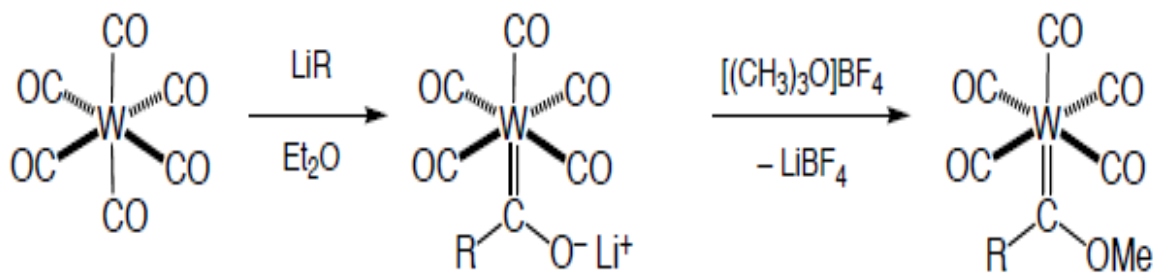
Schrock



Fischer Carbenes

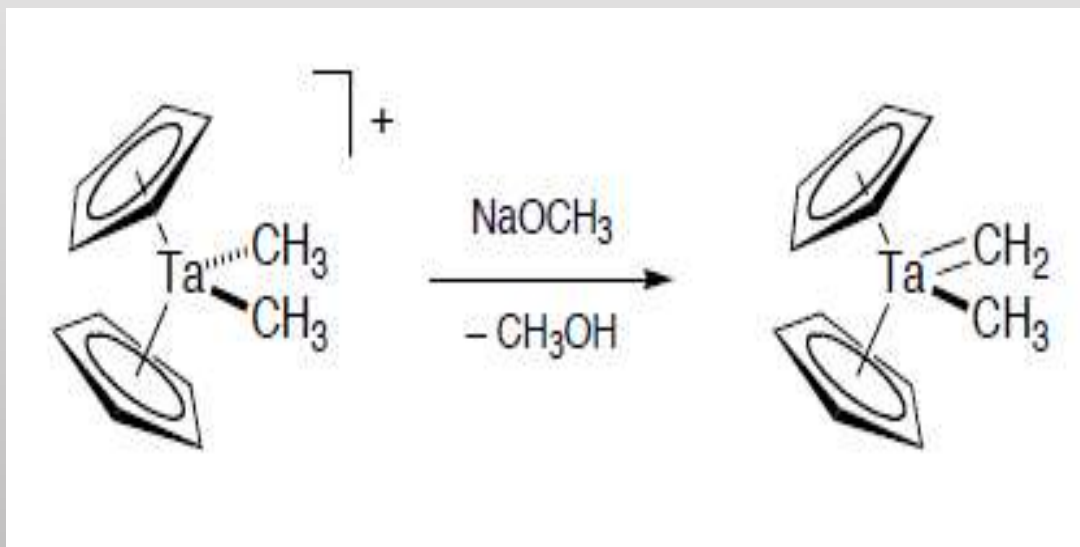
- The Fischer-type carbene complexes are low-valent complexes stabilized by strong π -accepting ligands (often CO).
- One or two heteroatoms (O, N, or S) are bonded to the carbene carbon atom and stabilize it by delocalizing the positive formal charge. The carbene is formally regarded as a neutral ligand.
- Accordingly, Fischer carbenes are relatively inert, but tend to react as electrophiles. In general, Fischer carbenes are 18 e⁻, coordinatively saturated complexes. Therefore, nucleophilic attack at the metal is not possible.

Fischer Carbenes

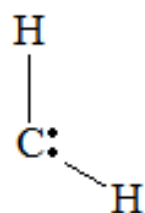


Schrock Carbenes

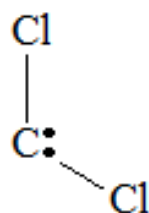
- The Schrock-type carbene complexes contain an early transition metal in a formal high oxidation state (often in the d⁰ electron configuration) stabilized by strong π -donor ligands.
- Most of these complexes have an electron count below 18 and are, thus, coordinatively unsaturated.
- Therefore, nucleophilic attack at the metal is possible because of the electron deficiency.



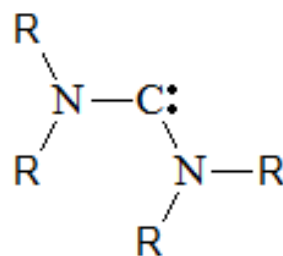
Carbene Examples



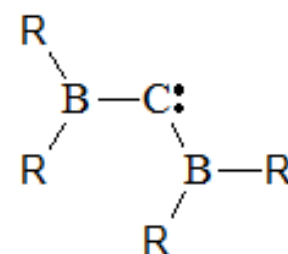
methylene



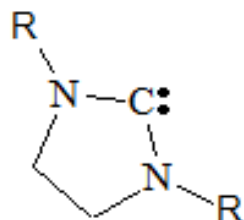
dichlorocarbene



diaminocarbenes



diborocarbene



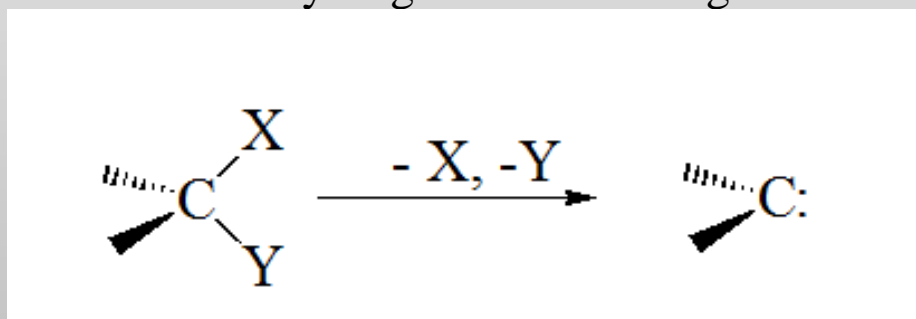
cyclic diaminocarbenes

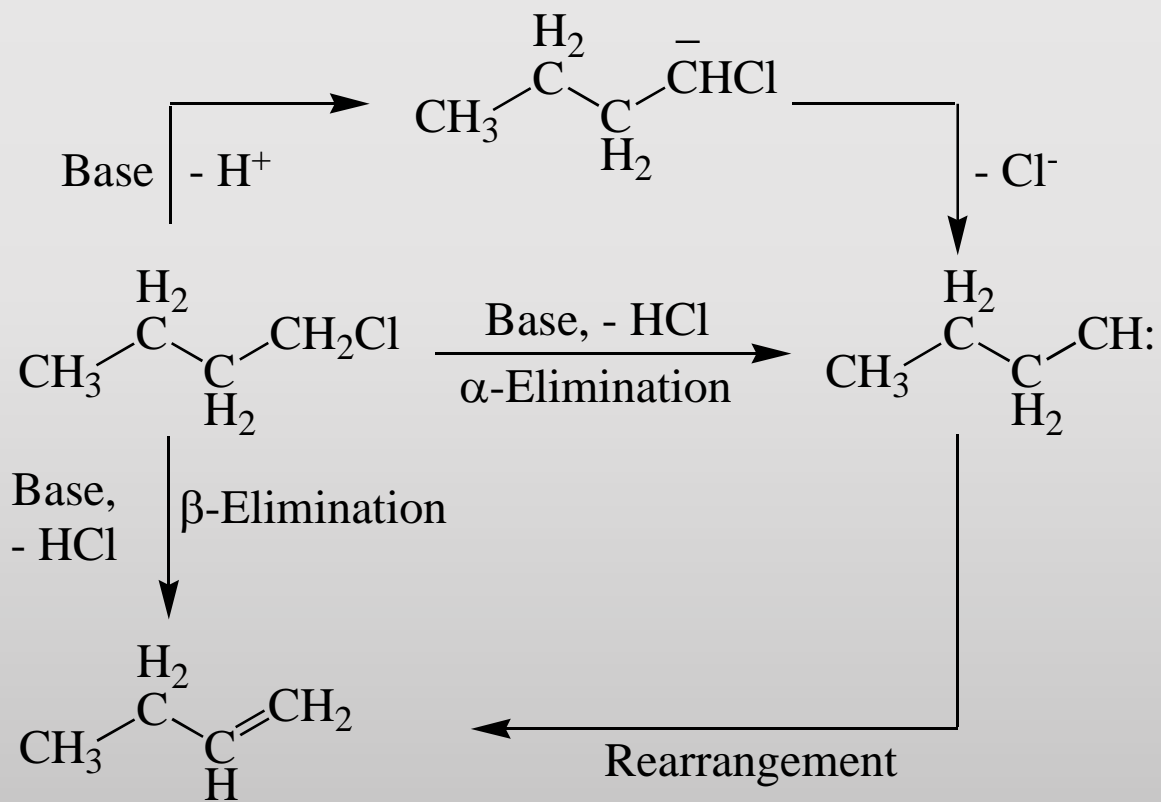
Formation of carbenes

- Carbenes are formed by reactions of halogenated compounds with bases.
 1. α elimination of chloroform with base
 2. Thermal decomposition of diazo compounds
 3. Metal(Rhodium or copper – catalysed decomposition of diazo carbonyl compound
 4. From tosylhydrazones

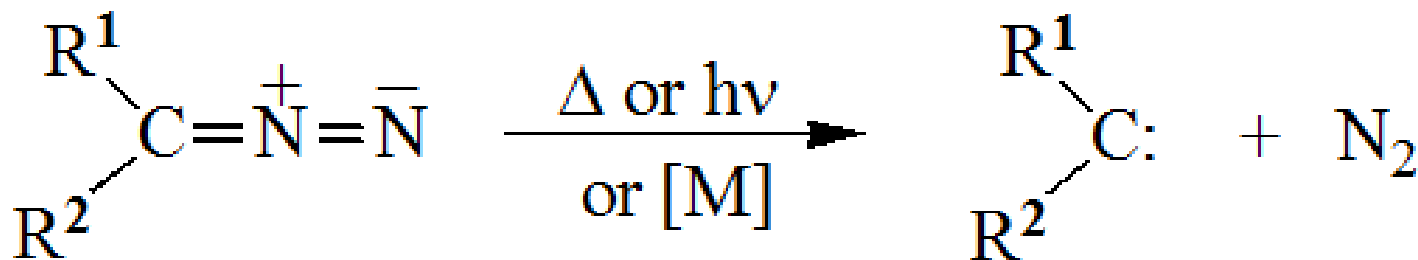
α -elimination of HX or X₂ from an organic halide

- α elimination means the eliminations in which both the proton and the leaving group are located on the same atom.
- A strong base removes an acidic proton adjacent to an electron withdrawing group to give a carbanion.
- Loss of a leaving group from the carbanion creates a carbene.
- One of the best known elimination reactions occurs when chloroform is treated with base, forming a dichlorocarbene.
- The more common dehydrogenations (to form alkenes) are called beta(β) eliminations because the hydrogen and the halogen are lost from adjacent carbon atoms.



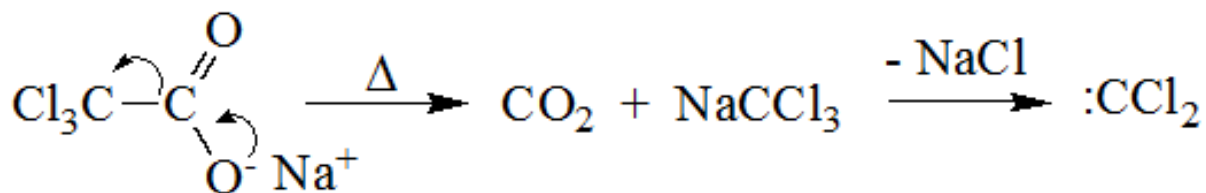


α -elimination of N₂ from diazo-compounds

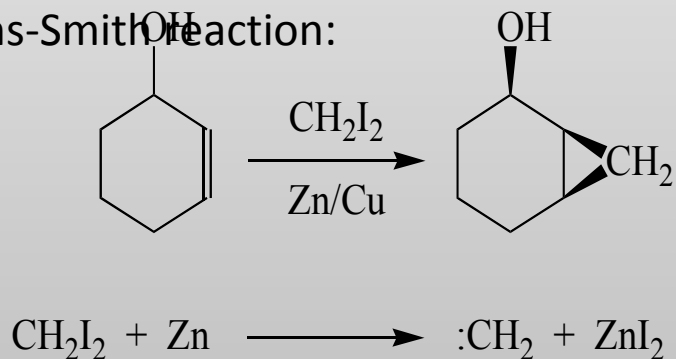


Carbene generation via α -elimination under mild non-basic conditions:

- Thermolysis of sodium trichloroacetate:

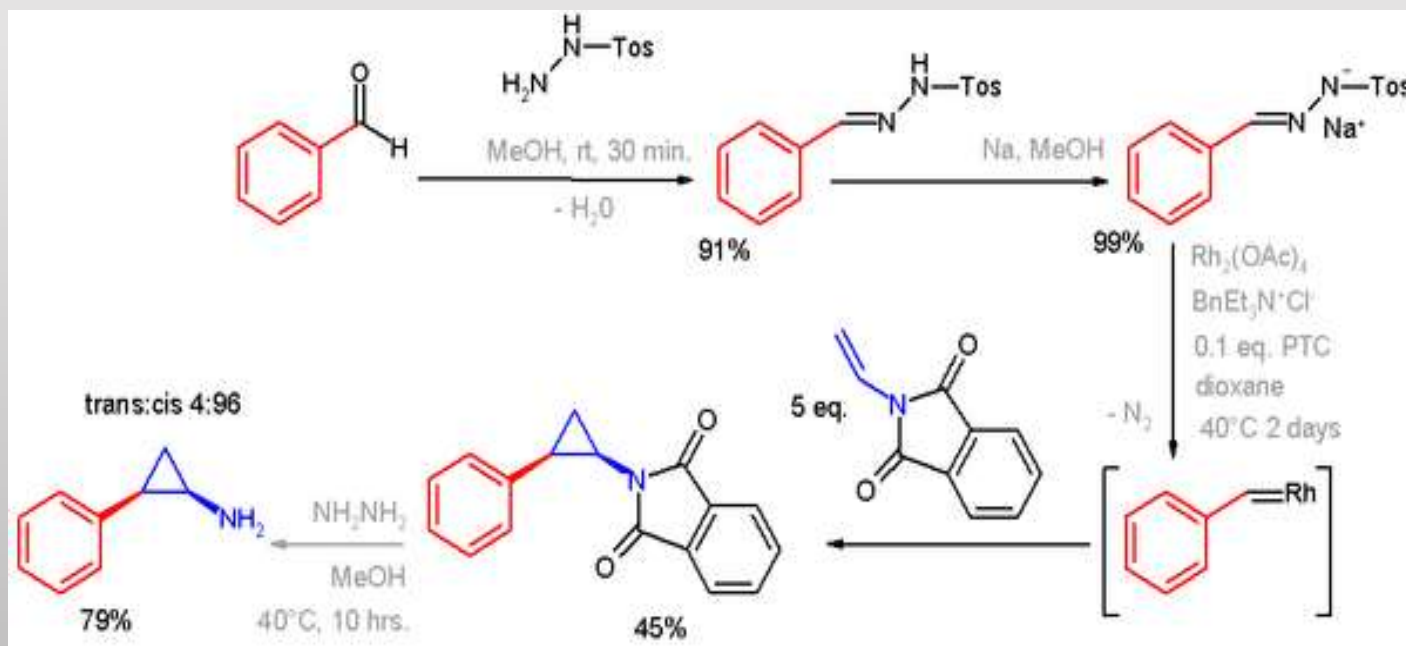


- The Simmons-Smith reaction:

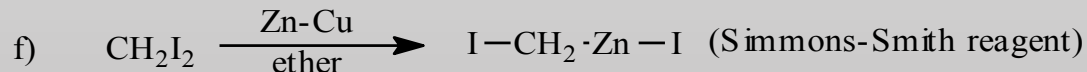
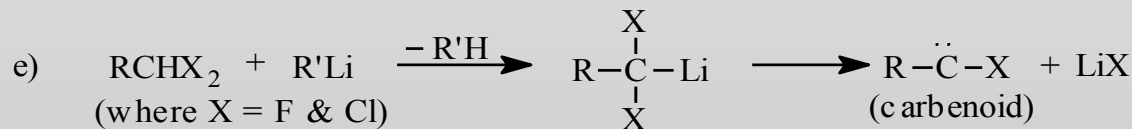
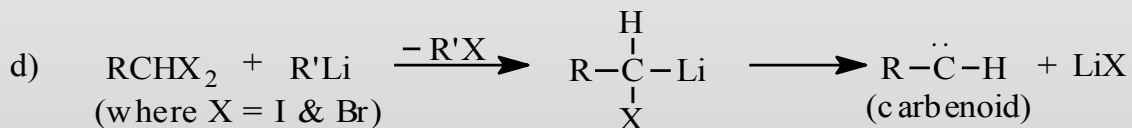
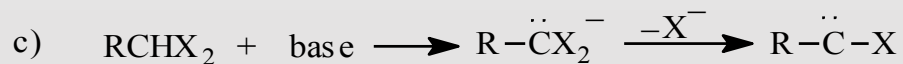
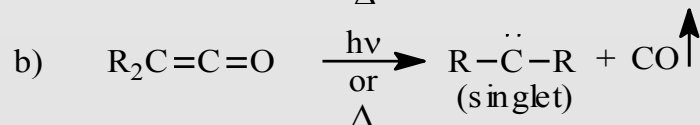
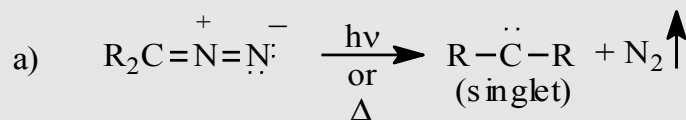


Formation of carbenes from tosylhydrazone

- Tosylhydrazone salts can react with metals to form metal carbenes and used in cyclopropanations and epoxidations.
- An example of a transition metal-catalyzed cyclopropanation is a synthesis of transylcypromine, in which the sodium salt of benzaldehyde tosylhydrazone is converted to a rhodium metal carbene through the diazo intermediate.



Formation reactions of carbenes

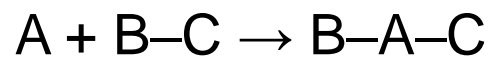


a carbenoid species that reacts stereospecifically with alkenes to give cyclopropanes but does not insert into alkane C-H bonds

Reactions of carbenes

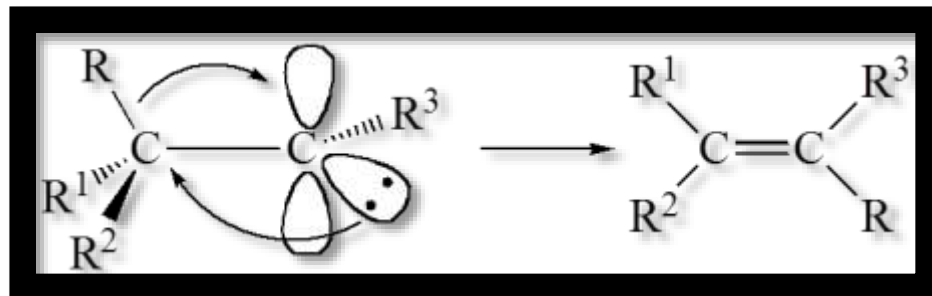
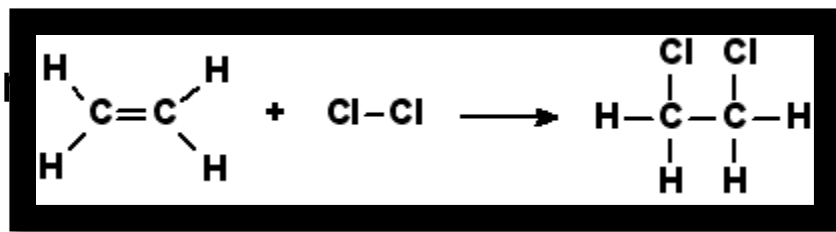
- Carbenes are highly electrophilic species.
- Three major classes of carbene reactions.
 - (1) Carbene insertions
 - (2) Carbene additions
 - (3) Carbene rearrangements

- Insertion



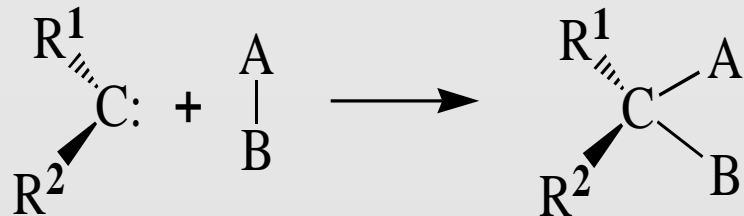
- Addition

- Rearrangement

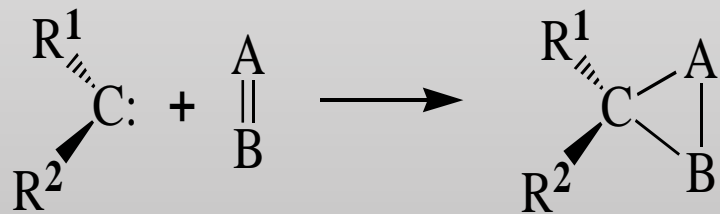


Carbene.....

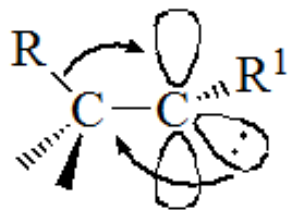
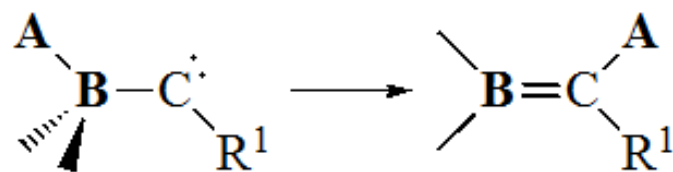
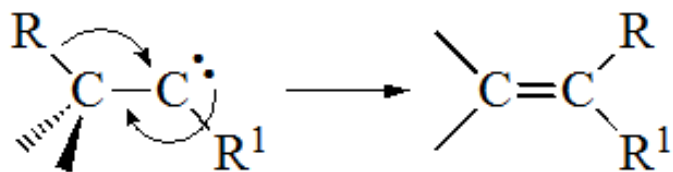
- Insertion



- Addition to multiple bonds

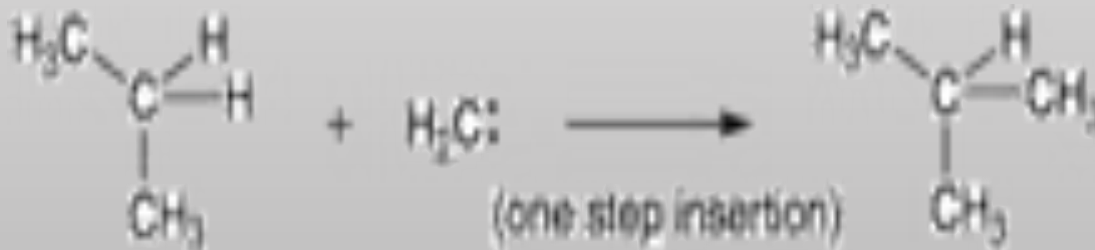


Rearrangement



1. Carbene insertions

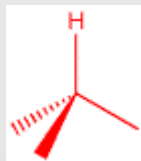
- common type of carbene reactions.
- The order of preference is commonly:
 - 1. X–H bonds where X is not carbon
 - 2. C–H bond
 - 3. C–C bond.
- Insertions may or may not occur in single step.



- Carbocation usually react with the HOMO of a molecule.
- It will be much more selective about which HOMOs will do.
- For carbenes ,any HOMO will do a lone pair,a C=C or even a C-H bond.

Type of nucleophile

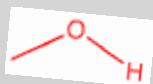
Method of insertion



[Insertion in a C-H bond](#)

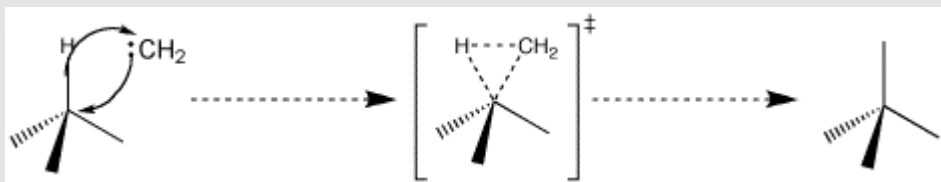


[Insertion in a C=C bond](#)



[Insertion in an O-H bond](#)

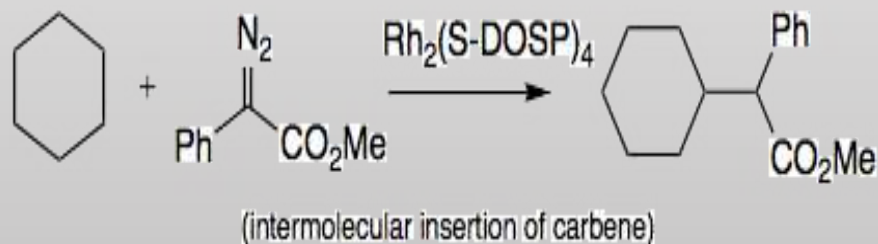
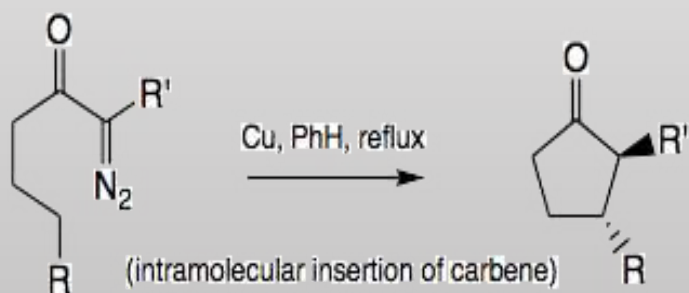
- Simple C-H insertion:



- Carbenes can undergo insertion into a C-H bond.
- These insertion reactions create new bonds at completely unfunctionalized centres.

intramolecular insertion and intermolecular insertion

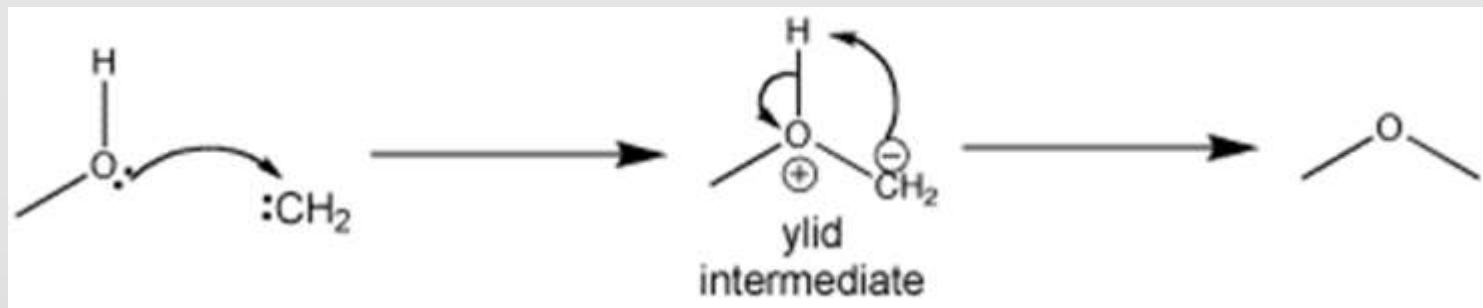
- Intramolecular insertion reactions present new synthetic solutions.
- When an intramolecular insertion is possible, no intermolecular insertions are seen.



Carbenes will also insert into other bonds

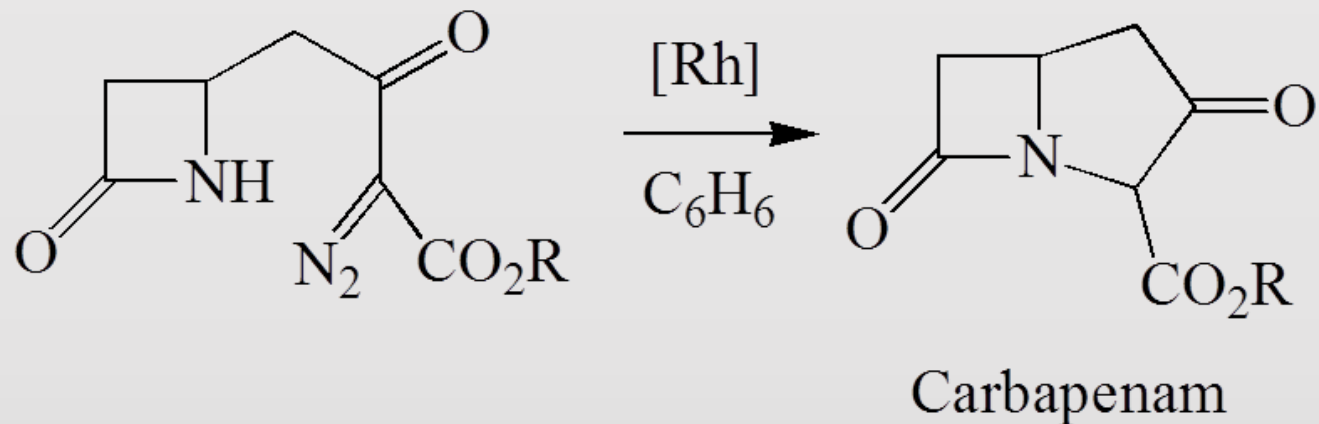
- Carbene insertion into an O-H bond

Initial attack on the lone pair of hetero atom



- The mechanism involves addition of the oxygen lone pair into an empty p-orbital on the carbene, followed by proton transfer to generate a neutral molecule

Carbene insertion into an N-H bond - Merck industrial synthesis of a β -lactam antibiotic.



A synthesis of the class of compound as carbapenam around a rhodium catalysed carbene insertion into a N-H bond.

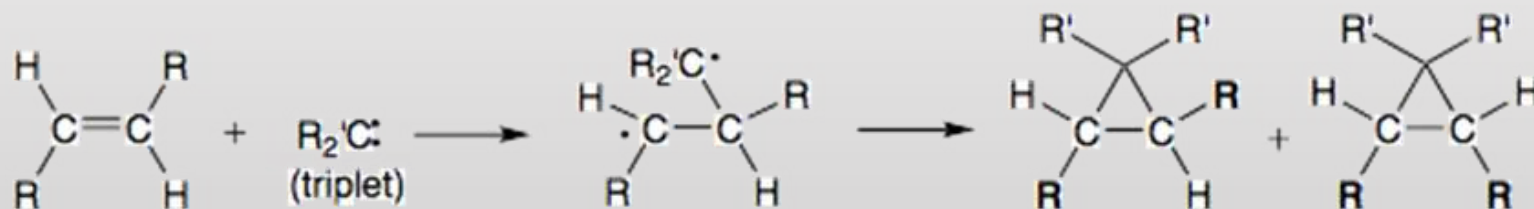
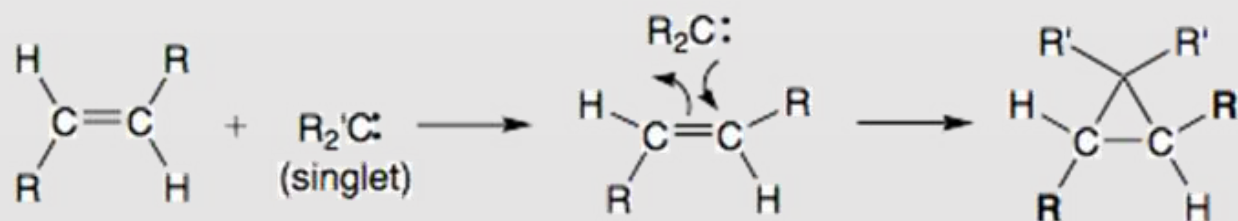
2. Carbene addition

- The stereochemistry of carbene addition to alkenes can be used as a test of whether the carbene is reacting via the singlet or the triplet spin state:

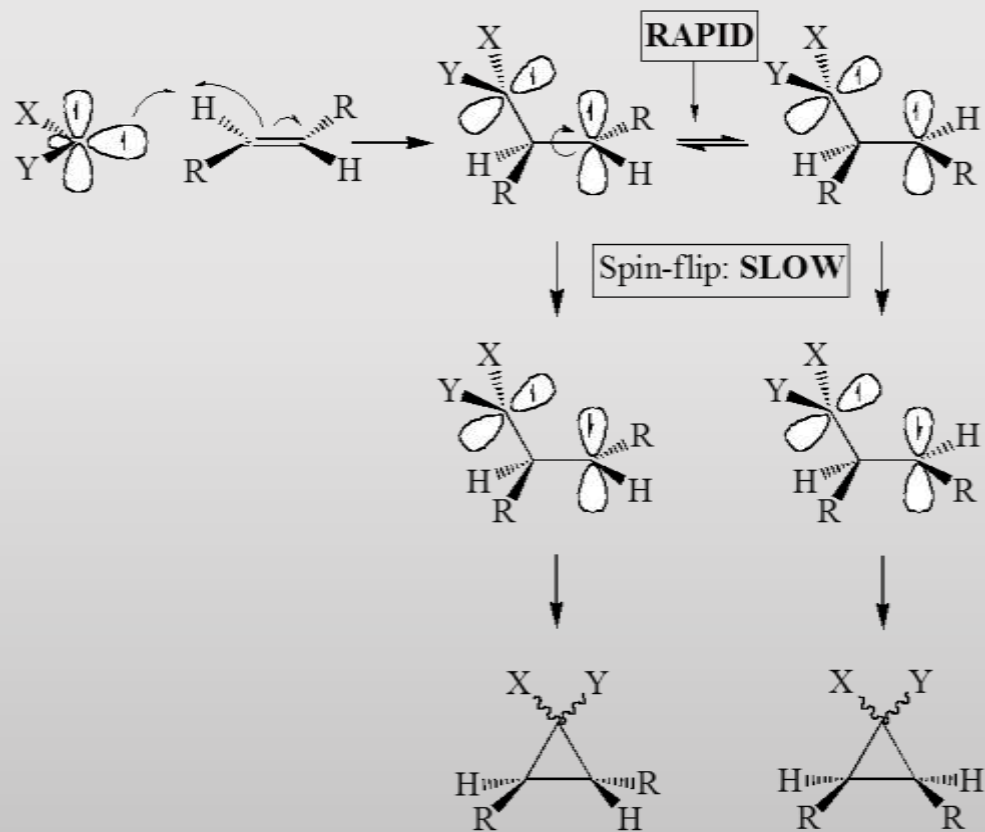
Addition of singlet and triplet carbenes to alkenes.

- Singlet and triplet carbenes do not demonstrate the same reactivity
- Triplet carbenes should be considered to be [diradicals](#), and participate in stepwise radical additions.
- Triplet carbenes have to go through an intermediate with two unpaired electrons whereas singlet carbene can react in a single concerted step.

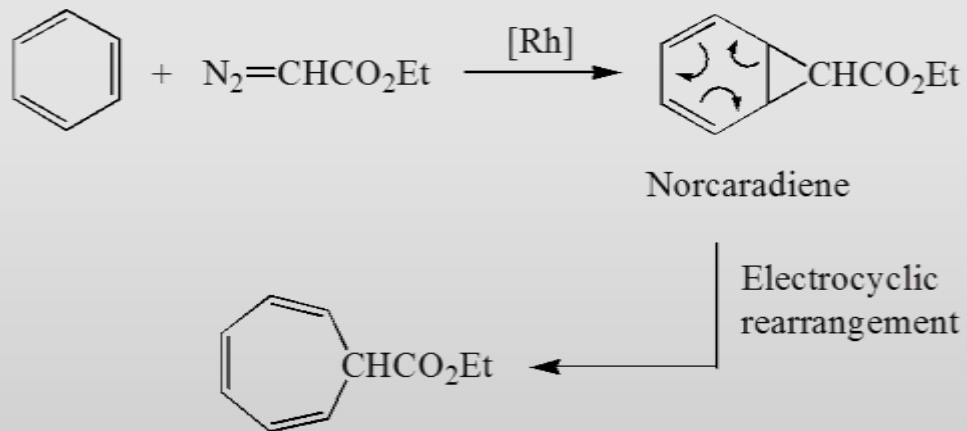
Alkenes react with singlet carbene in a concerted fashion - alkene stereochemistry is preserved in the cyclopropane product:



Alkenes react with triplet (i.e. diradical) carbene in a **stepwise** fashion - the alkene stereochemistry is lost in the cyclopropane product:



Carbene additions to arenes: 6 \rightarrow 7 ring-expansion to yield cycloheptatrienes:



- Step 1:
- The reaction mechanism of a Buchner ring expansion begins with carbene formation from ethyl-diazoacetate generated initially through photochemical or thermal reactions with extrusion of nitrogen.
- The generated carbene adds to one of the double bonds of benzene to form the cyclopropane ring.

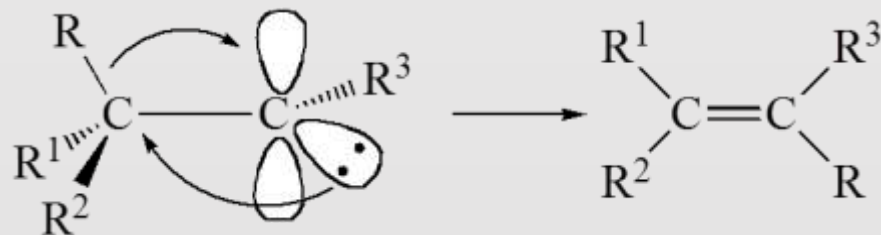
3. Carbene rearrangement

- **Wolff rearrangement**

- The Wolff rearrangement is a reaction in organic chemistry in which an α -diazocarbonyl compound is converted into a ketene by loss of dinitrogen with accompanying 1,2-rearrangement.
- The Wolff rearrangement yields a ketene as an intermediate product, which can undergo nucleophilic attack with weakly acidic nucleophiles such as water, alcohols, and amines, to generate carboxylic acid derivatives
- The Wolff rearrangement can be induced via thermolysis, photolysis, or transition metal catalysis.

(1) Carbene Rearrangement

Mechanism: 1,2 migration of hydride or a carbanion:



Migratory aptitude: R = H >> aryl > alkyl

Arndt-eistert reaction

- One important application of this reaction is the chain extension of acyl chlorides to their homologous esters known as the arndt-eistert reaction.

Arndt-Eistert Reaction - homologisation of carboxylic acid derivatives:

