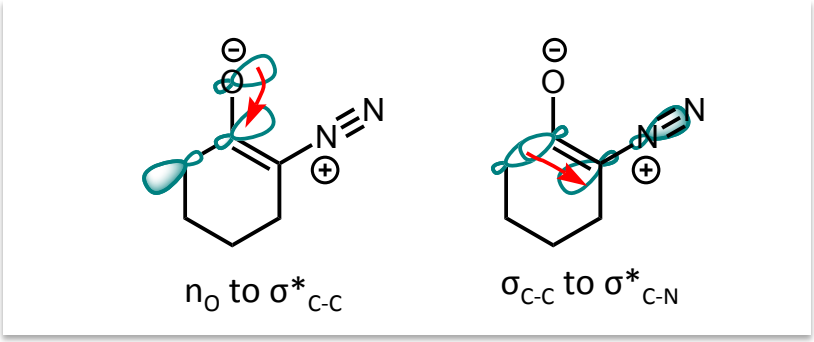
Rearrangements and Reactive Intermediates

1A Organic Chemistry

Handout 2 – Carbenes and Nitrenes



http://burton.chem.ox.ac.uk/teaching.html

Carbenes

- neutral divalent carbon species – 6 electrons around central carbon atom – highly reactive, generally electrophilic
- structure – singlet carbenes

singlet

- singlet carbenes have three electron pairs and an empty orbital to place around the central atom - a similar case to carbocations (carbenium ions)

- singlet carbenes are bent with the bond pairs and lone pairs in sp^2 hybridised orbitals, along with a vacant p-orbital

- typical bond angle range for singlet carbenes are 100° - 110°

- structure – triplet carbenes

triplet

- triplet carbenes are bent with a typical bond angle range of 130° - 150°

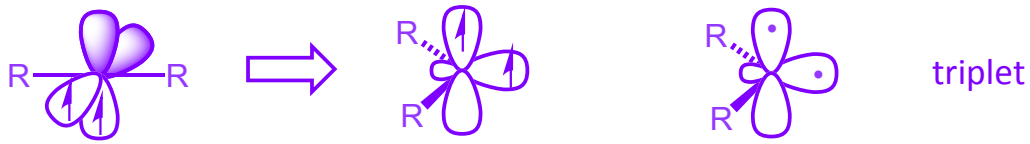
- carbene structures from spectroscopy, in low pressure gas, and in low temperature matrix (<77 K)

  - electronic spectra with rotational structure
  - infra red analysis
  - electron spin resonance (for triplets)

- Why are triplet carbenes bent?

- imagine a linear geometry for the triplet carbene
  - there will be a central sp hybridised carbon atom with the two bonding pairs of electrons are in sp-hybrid orbitals (50% s-character)
  - the unpaired electrons are in the two orthogonal 2p orbitals

- this linear arrangement means that the unpaired electrons have no s-character – the more s-character the more stable the electron



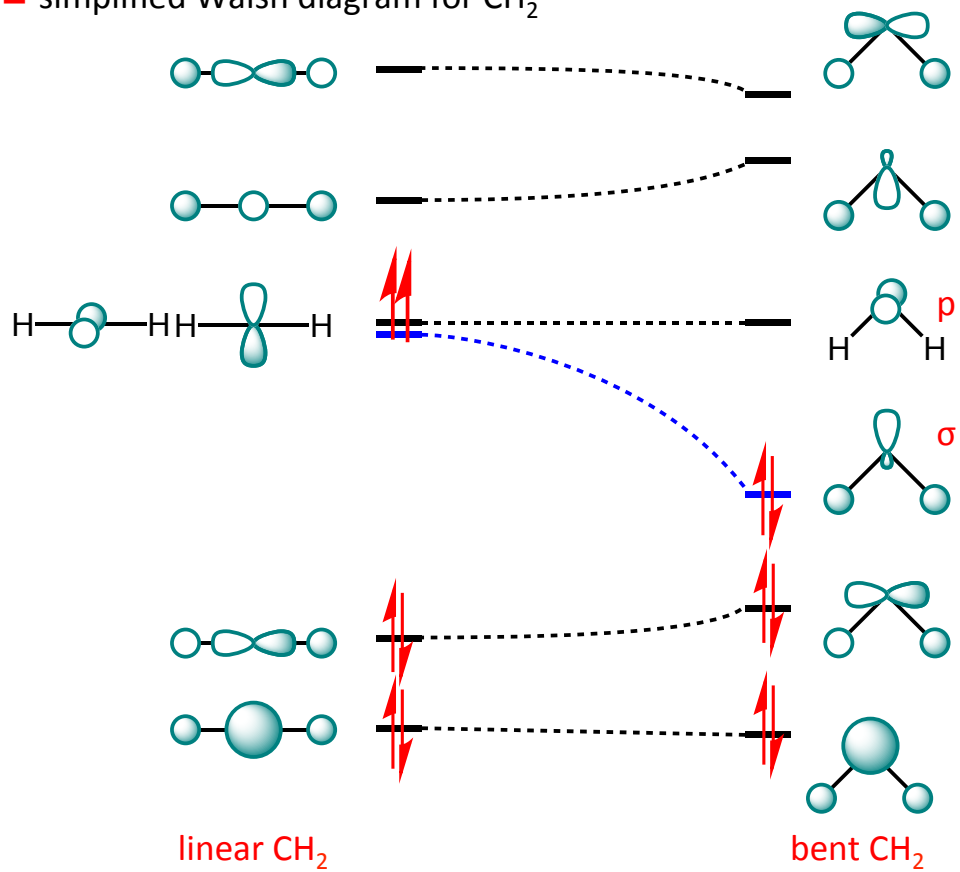
- bending the linear state leads to one of the unpaired electrons gaining some s-character and being lowered in energy – here one of the p-orbitals becomes an sp^n hybrid orbital (a σ-orbtial)

- the more bent the carbene is the greater the difference in energy between the p and σ-orbitals

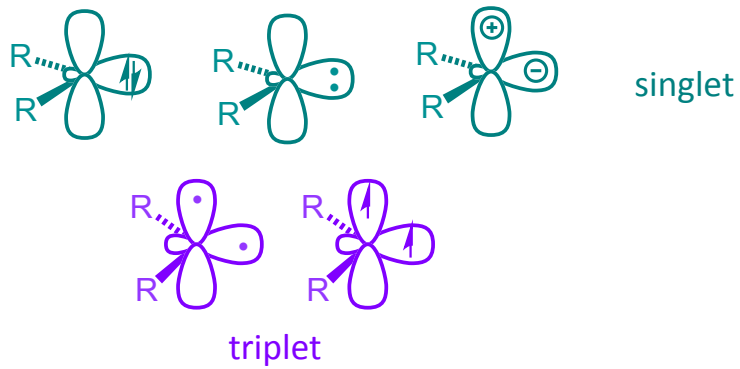
- due to electron electron repulsion there is an energy cost in pairing electrons (Hund's rule)

- if there is a small energy gap between σ and p-orbitals the electrons will remain unpaired i.e. triplet

- Walsh diagram for CH_2 gives a more sophisticated analysis and accounts for electronic structure of CH_2 – see Prof McGrady "Bonding in Molecules" course 2nd year
- simplified Walsh diagram for CH_2



- beginning with linear CH_2, MO diagram predicts a triplet ground state
- slight bending should be stabilising as one of the electrons is now in a bonding MO
- with further bending, the lower energy of the bonding MO overcomes electron-electron repulsion and the singlet carbene becomes more stable

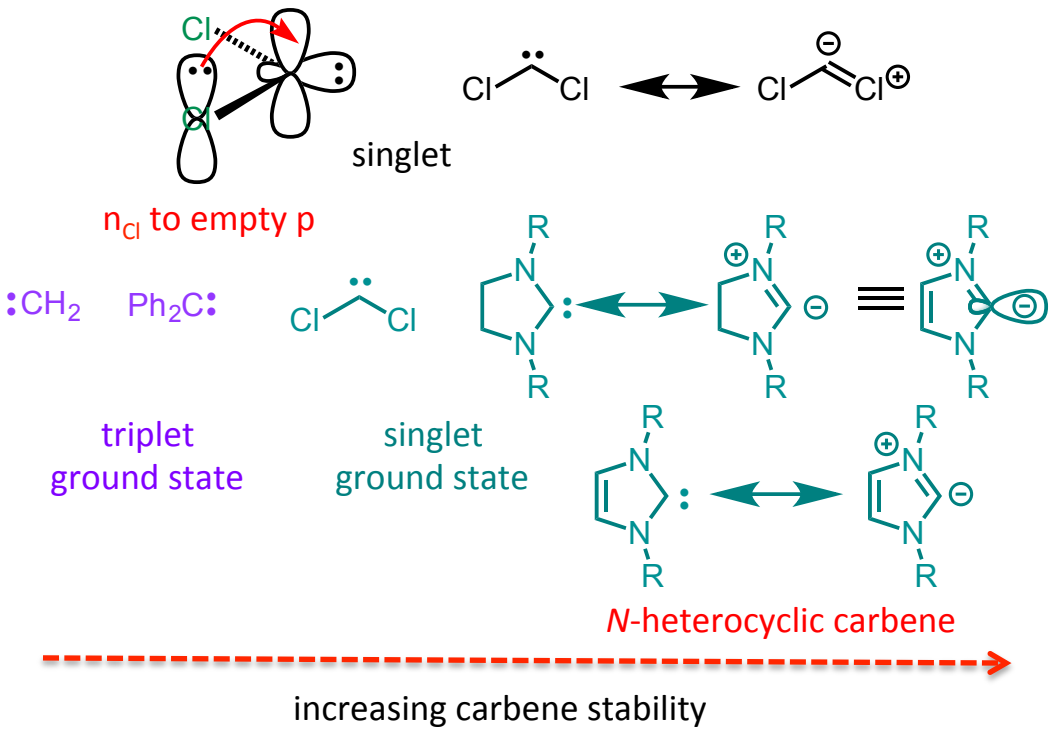


- *take home message* – triplet carbenes and singlet carbenes are bent – we will consider them both to be sp^2 hybridised
- triplet carbenes have a larger bond angle than singlet carbenes
- the above representations are adequate for our purposes
- neither Walsh diagram nor hybridisation allows us to predict the ground state for any particular carbene

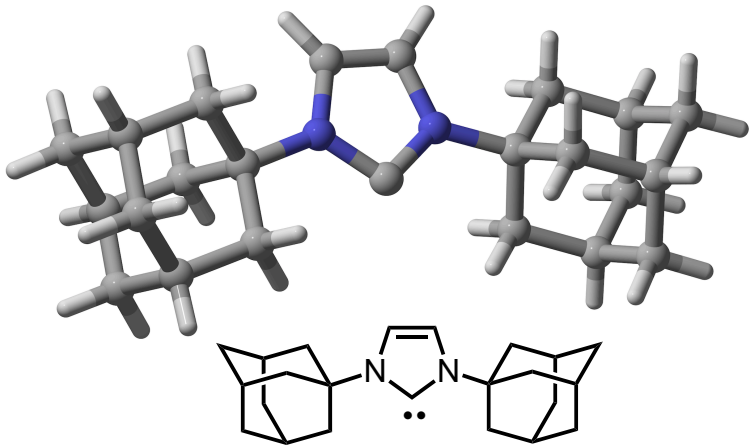
- methylene (CH_2) has a triplet ground state – the singlet state is ca. 38 kJmol^{-1} higher in energy

- dialkylcarbenes, arylalkylcarbenes and some diarylcarbenes have triplet ground states

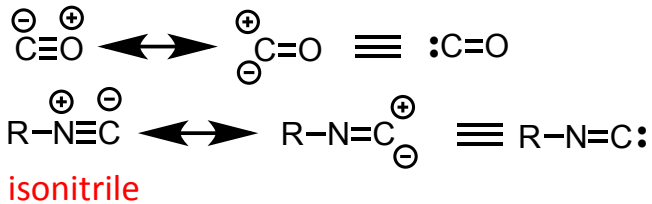
- heteroatom substituted carbenes have singlet ground states due to delocalisation



- first X-ray structure of a carbene (*J. Am. Chem. Soc.*, **1991**, *113*, 361).

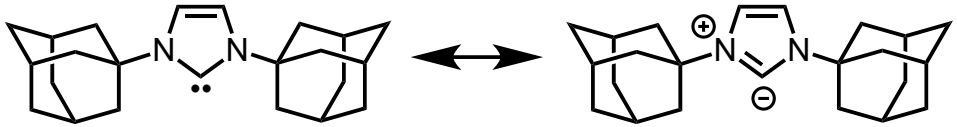


- carbene or ylid? c.f.

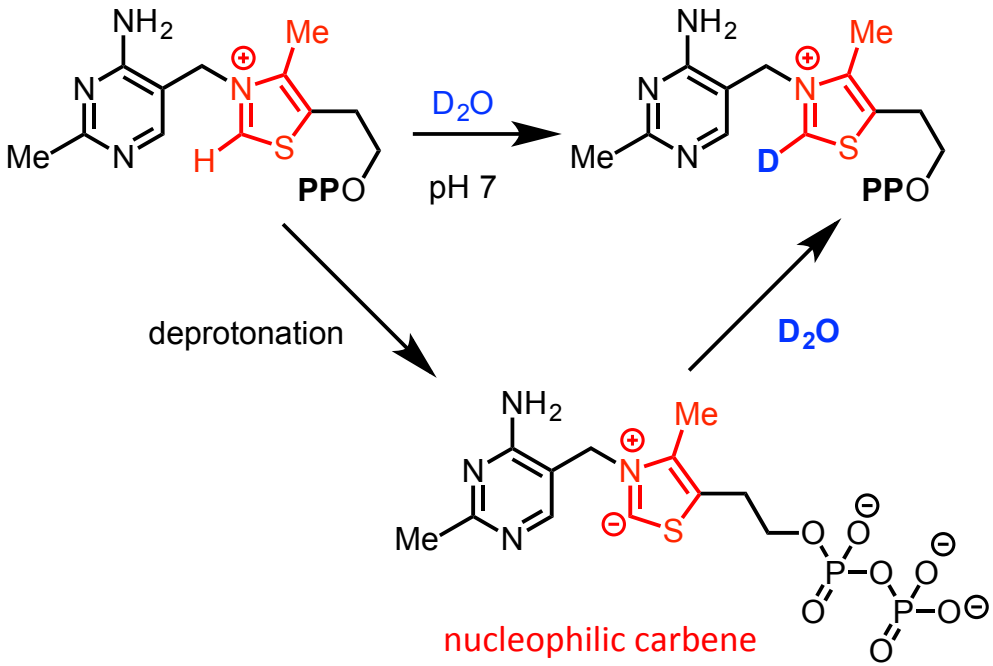


- the majority of carbenes are electrophilic – there are six electrons around the central carbon and hence they are electron deficient

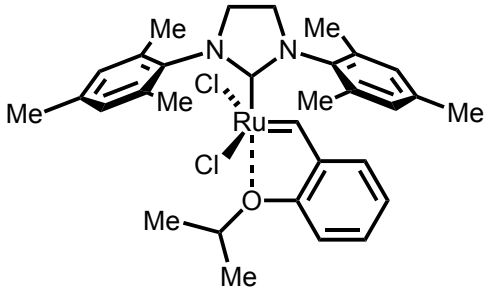
- *N*-heterocyclic carbenes (and related carbenes) are nucleophilic - they are widely used as ligands for transition metals

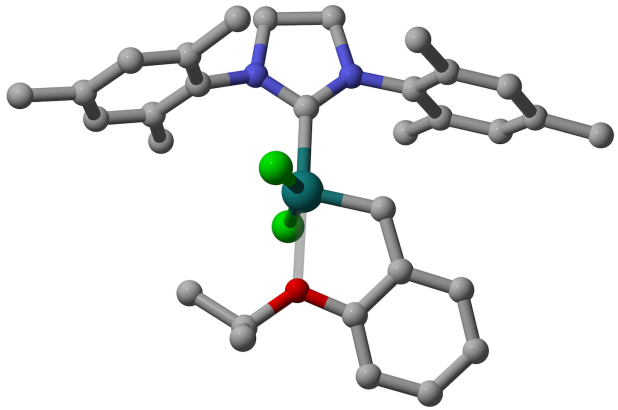


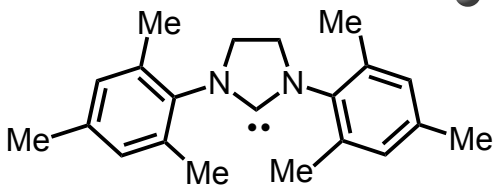
- Nature was here before us with nucleophilic carbenes – thiamine pyrophosphate (vitamin B1) – more next year



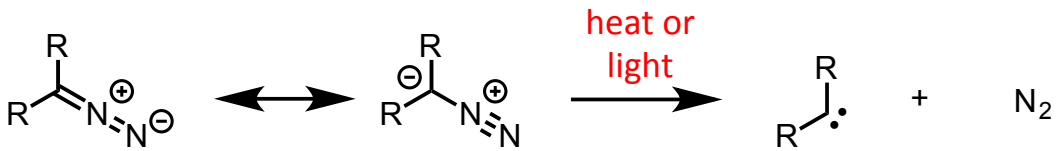
- Grubbs-Hoveyda 2nd generation metathesis catalyst (*J. Am. Chem. Soc.*, **2000**, *122*, 8168) – more next year

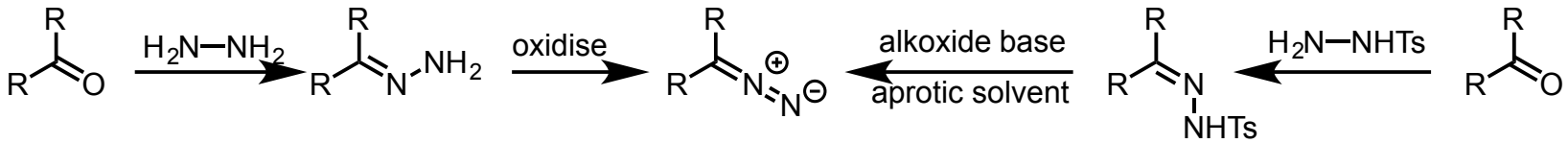


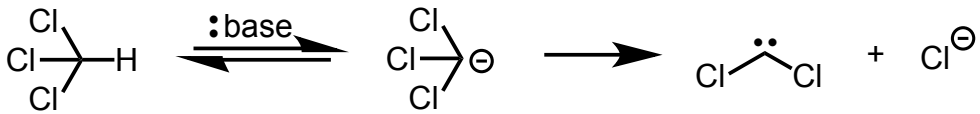


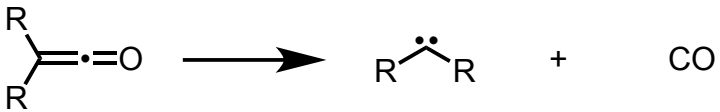


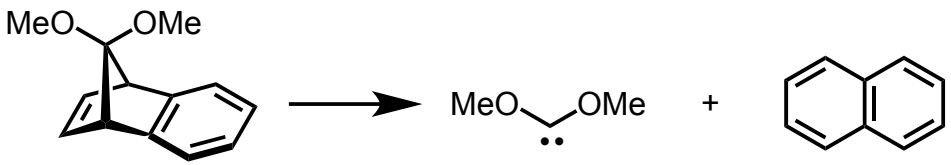
- some methods for carbene formation





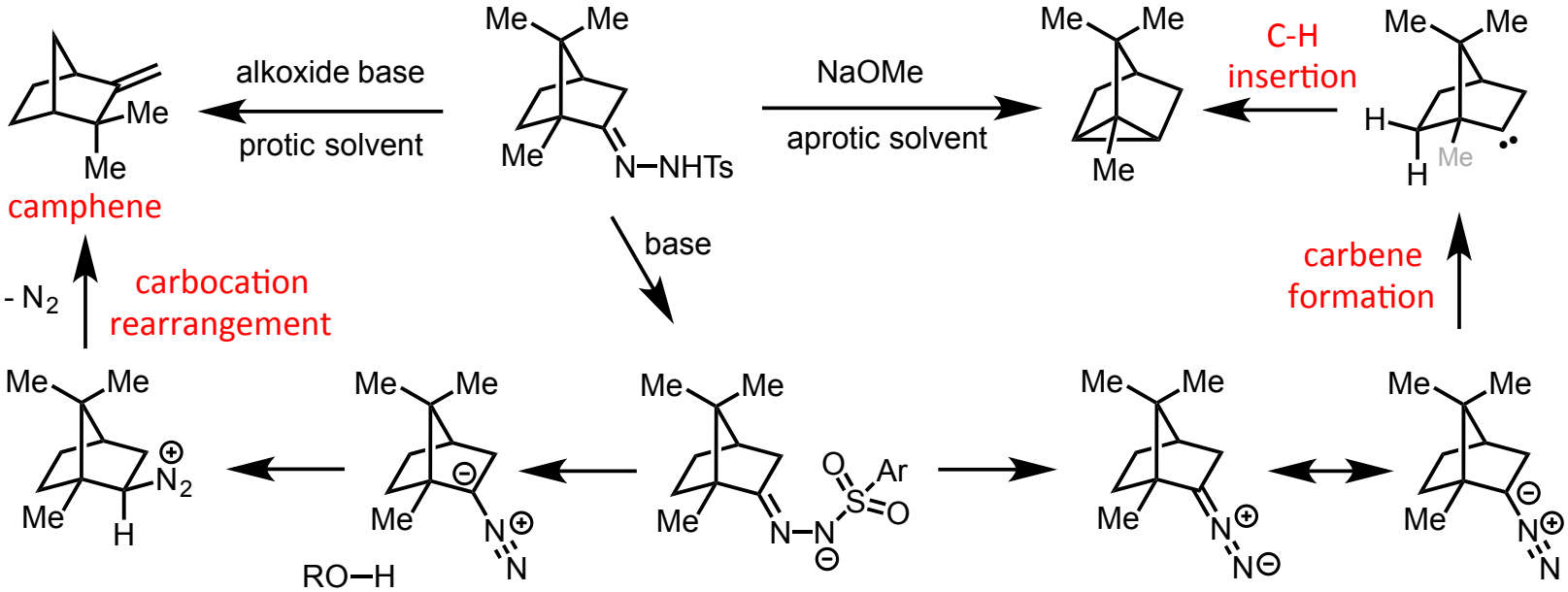




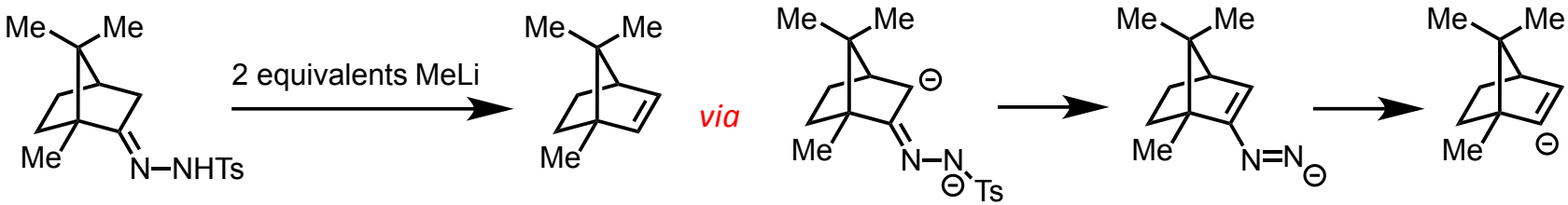


- direct irradiation normally produces a carbene in the singlet excited state
- irradiation or heating diazo or diazirine compounds forms singlet carbenes
- relaxation of the singlet state to the triplet state (if it is lower in energy) can occur but requires collision with other molecules
- direct formation of the triplet state can occur by irradiation in the presence of a triplet sensitiser

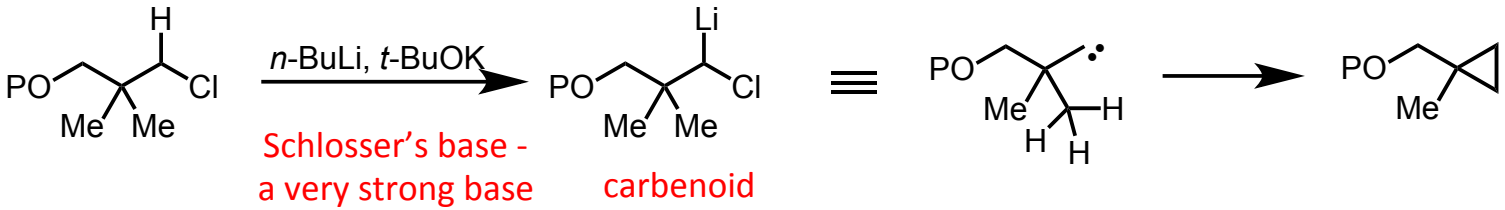
- reactions of carbenes
- insertion into C-H bonds – generally unselective, occurs with very reaction carbenes, not Cl_2C:
- for singlet carbenes reaction occurs with retention of configuration – with triplet carbenes stereochemistry is lost
- example – the Bamford Stevens reactions – solvent dependent product formation



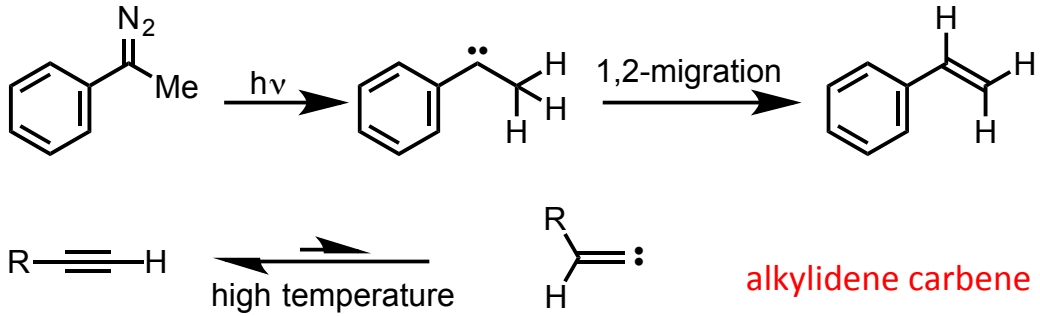
- remember on treatment with 2 equivalents of an alkyllithium, tosylhydrazones undergo the Shapiro reaction

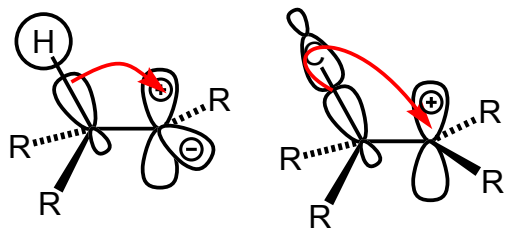


- insertion reactions



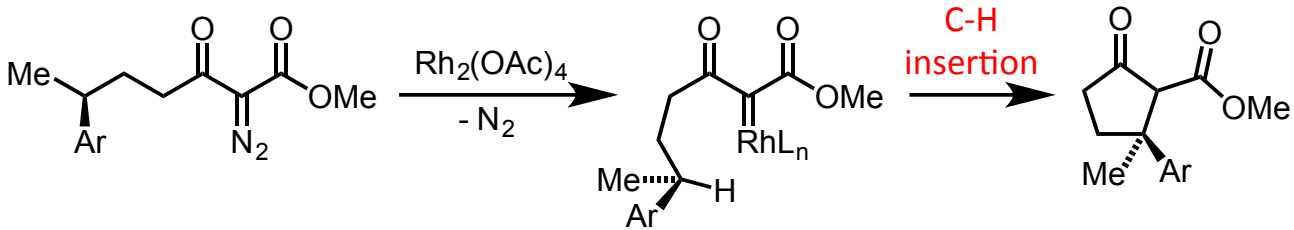
- insertion reactions into adjacent C-H bonds is the equivalent of a 1,2-shift



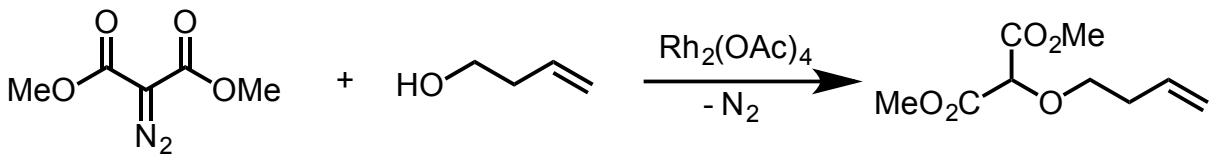


- carbene 1,2-shift
- cation 1,2-shift

- insertion into XH bonds is common using transition metal catalysis

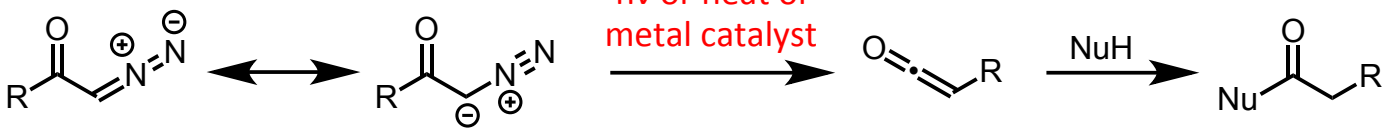


- rhodium carbenoid is equivalent to a carbene

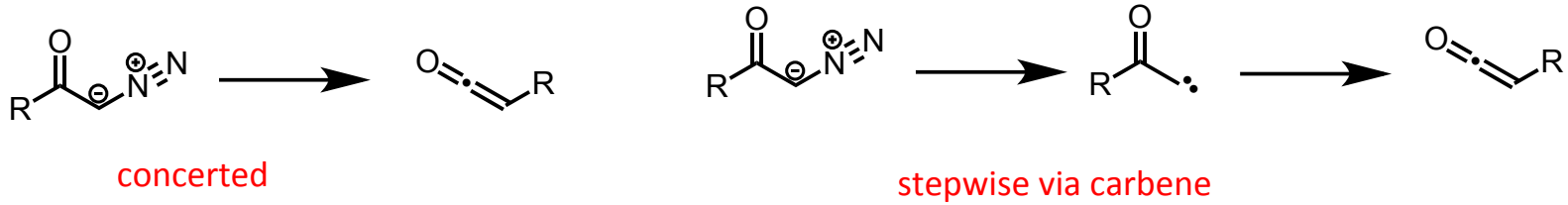


- here the (rhodium) carbene is attacked by the nucleophilic alcohol followed by proton transfer

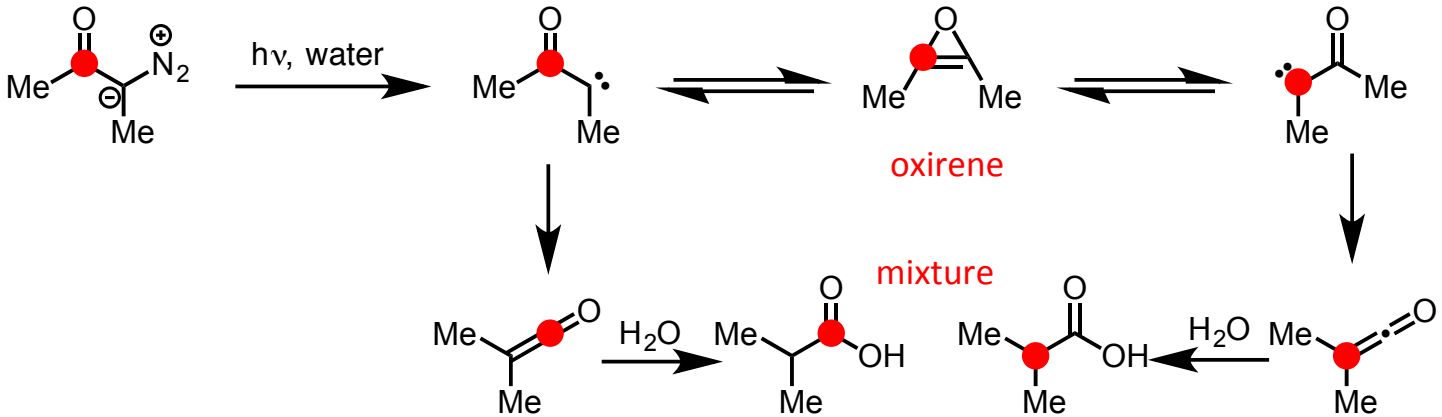
- Wolff rearrangement



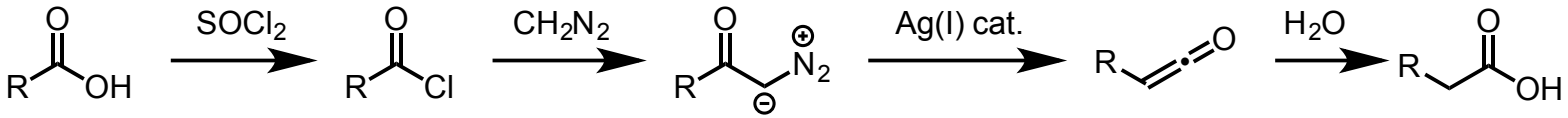
- concerted or stepwise mechanism – depends on substrate and reaction conditions
- as a rule of thumb, the thermal reactions are concerted and the photochemical reactions proceed via carbenes



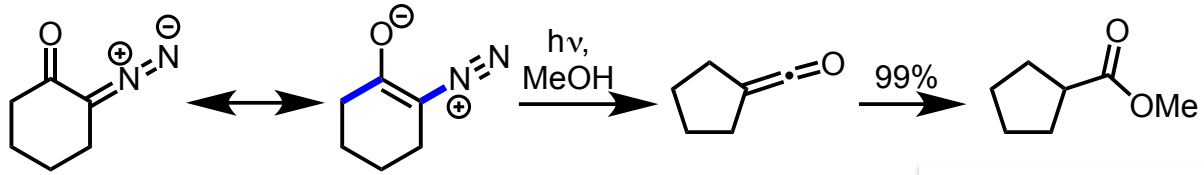
- the acyl carbenes are also in equilibrium with an oxirene in some cases (● = ^{13}C)



- Arndt-Eistert homologation

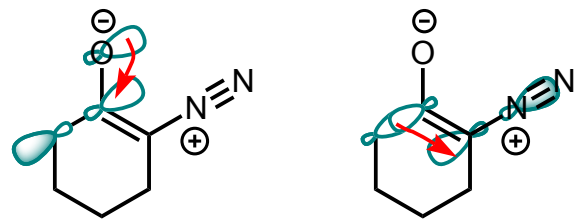


- Wolff rearrangement – a look at the orbitals
- with cyclic ketones the reaction is likely to be concerted under most conditions



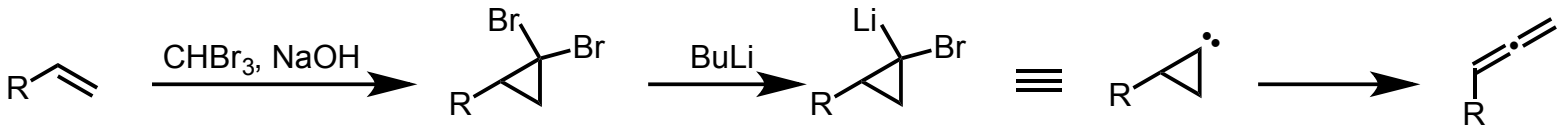
antiperiplanar bonds

- mechanism in more detail correct orbital overlap required for migration

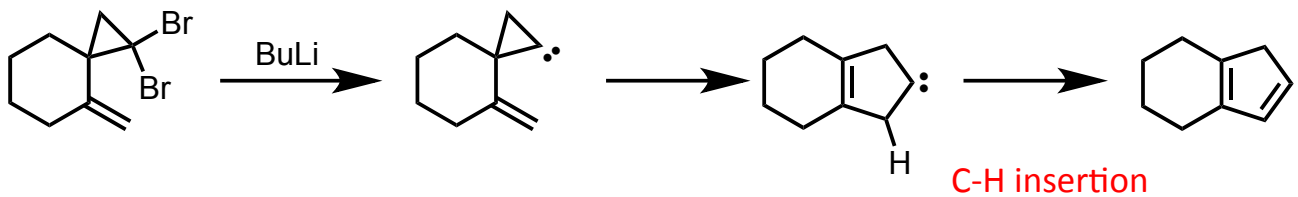


n_O to $\sigma^*_{C\text{-}C}$ $\sigma_{C\text{-}C}$ to $\sigma^*_{C\text{-}N}$

- migration with retention of configuration
- some other rearrangements
- Doering-LaFlamme allene synthesis



- Skattebol rearrangement

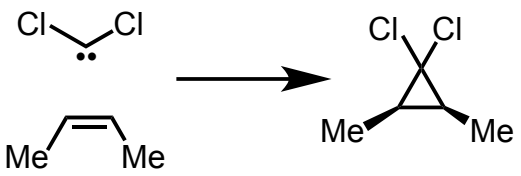


C-H insertion

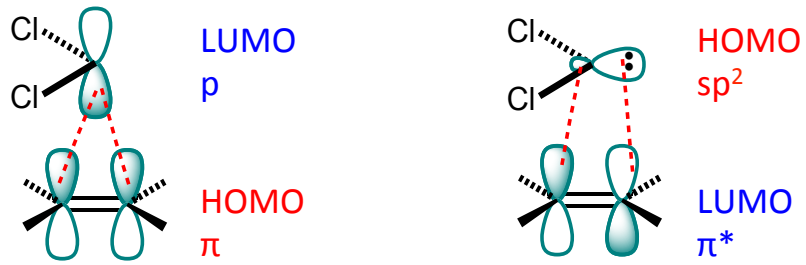
- carbene addition reactions

- addition to C=C bonds: i) stereospecific for singlet carbenes; ii) non-stereospecific for triplet carbenes; iii) distinguishes between triplet and singlet carbenes

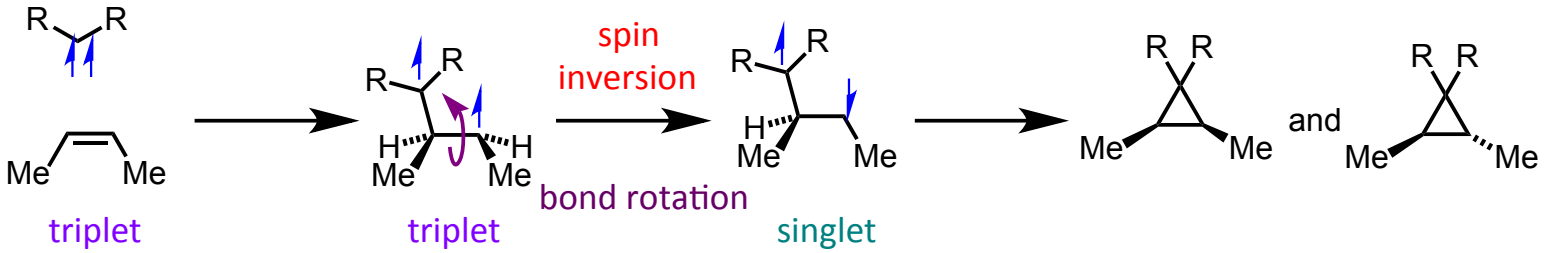
- singlet carbene – concerted reaction



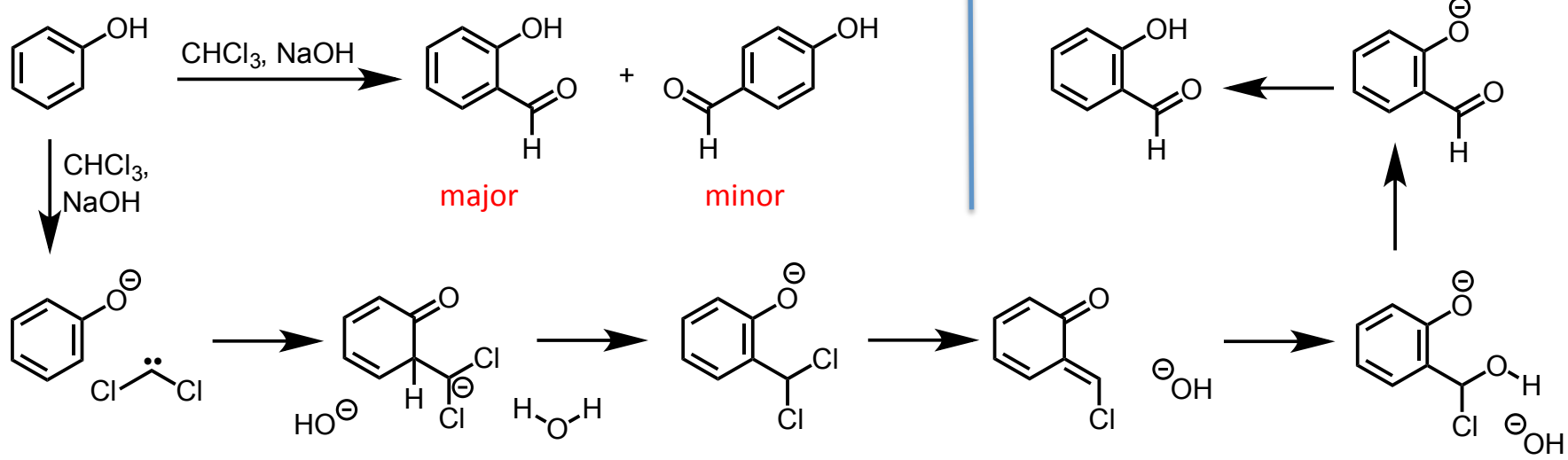
- orbital picture



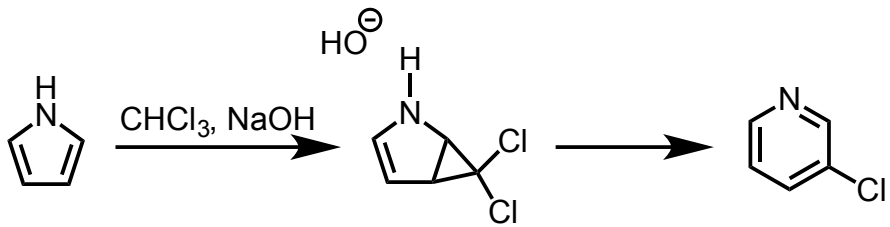
- triplet carbene – non-concerted radical reaction – spin inversion (requires molecular collision) may be slower than bond rotation leading to stereochemical scrambling



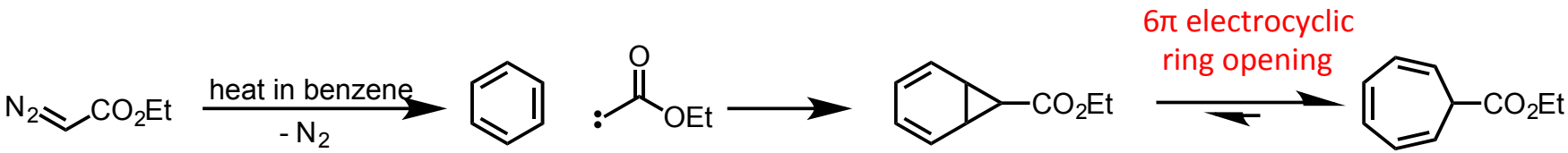
- Reimer – Tieman reaction



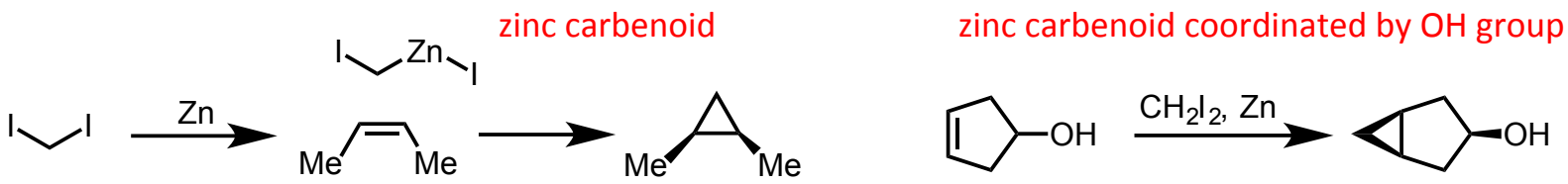
- dichlorocarbene adds to pyrrole followed by rearrangement



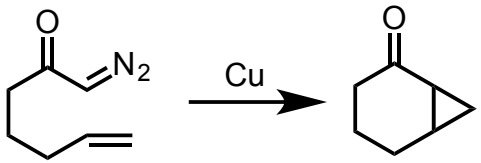
- very electrophilic carbenes will add to benzene

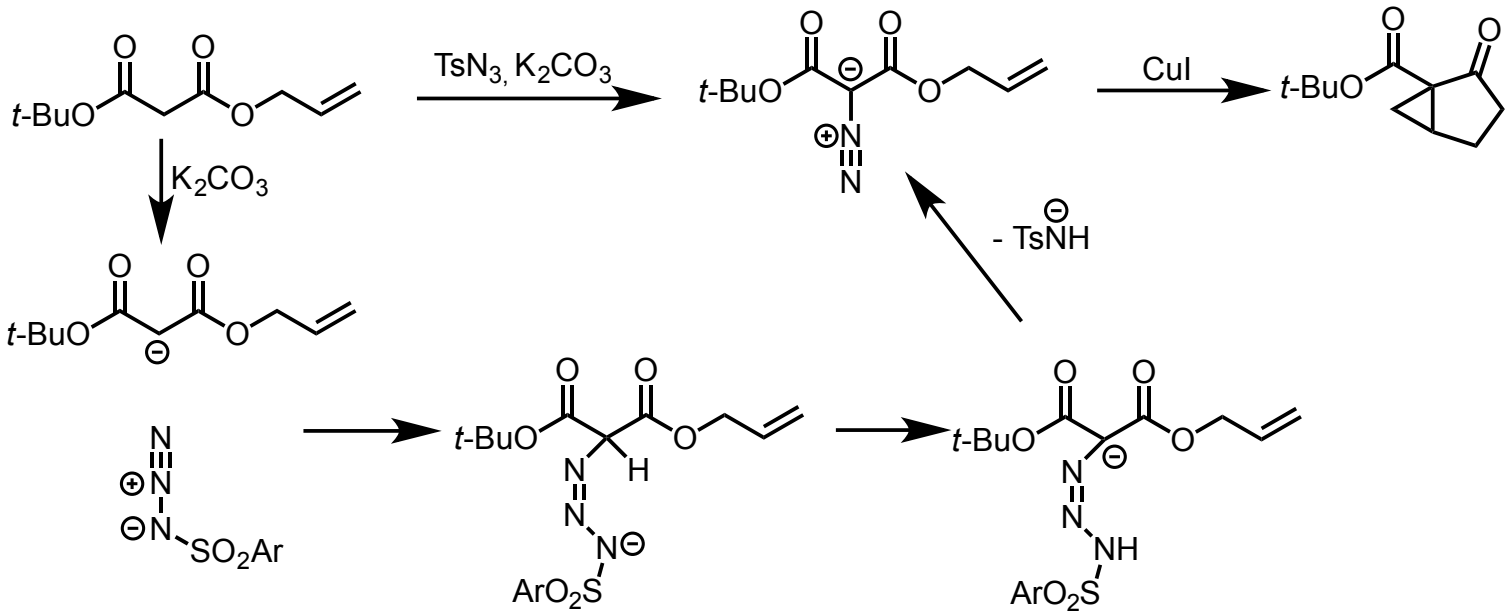


- Simmons Smith cyclopropanation

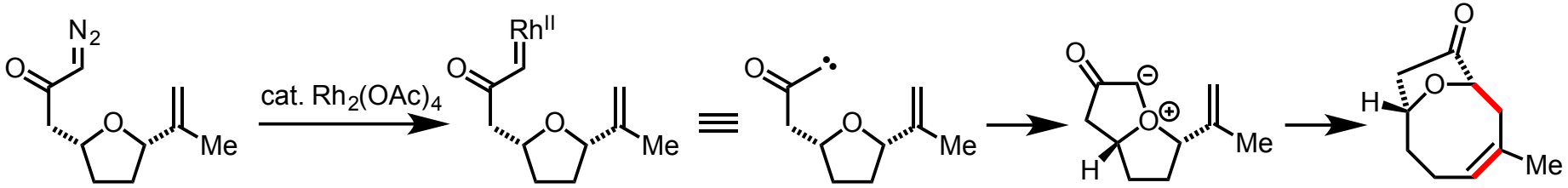


- metal catalysed addition reactions of diazocompounds - common catalysts include: Cu, CuI, $Rh_2(OAc)_4$, $Cu(OAc)_2$

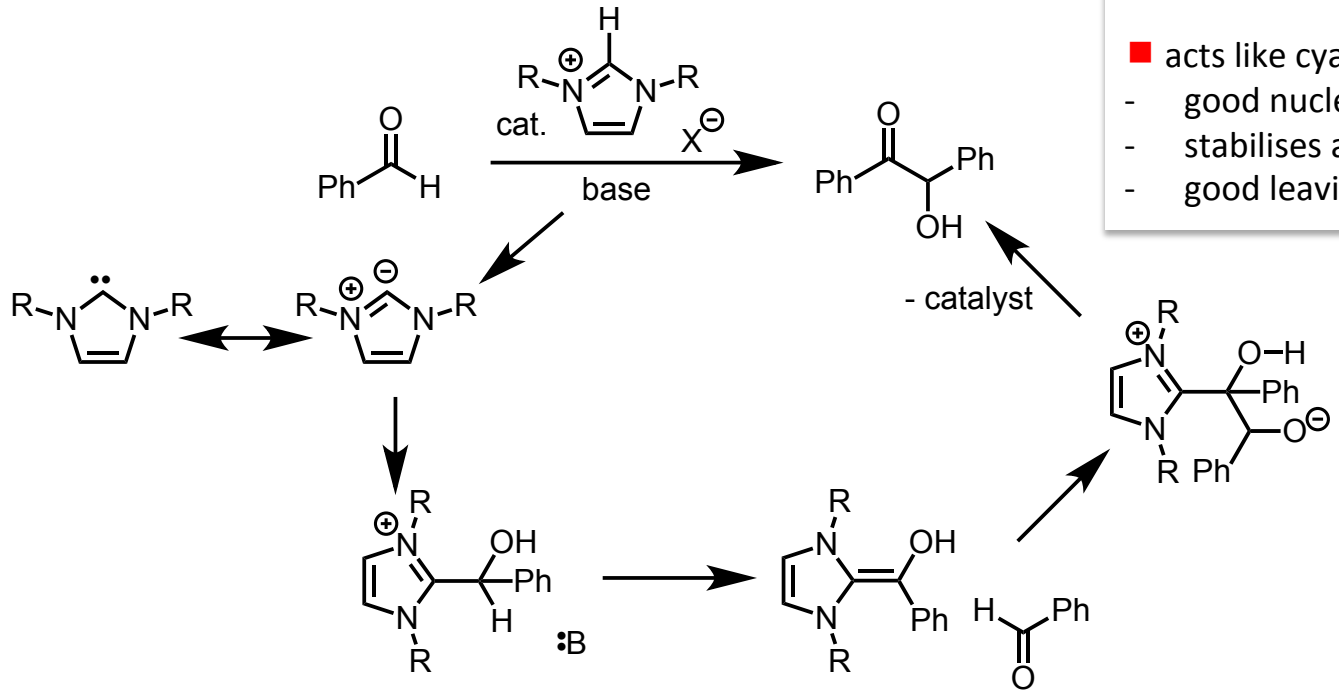




- carbenes readily react with nucleophiles



- nucleophilic carbenes are useful catalysts

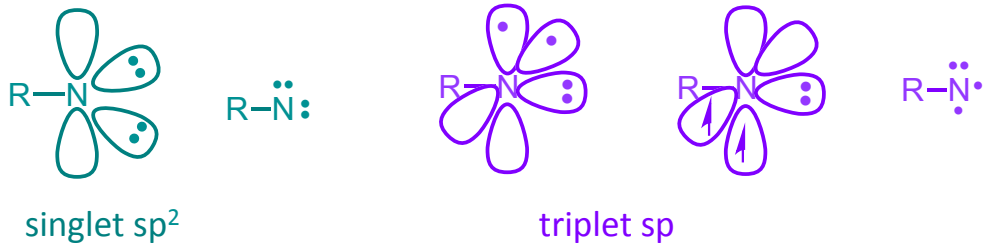


- *N*-heterocyclic carbene catalyses the benzoin reaction

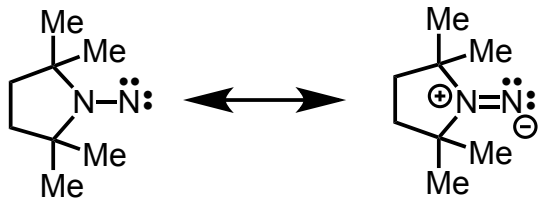
- acts like cyanide:
  - good nucleophile
  - stabilises adjacent negative charge
  - good leaving group

Nitrenes

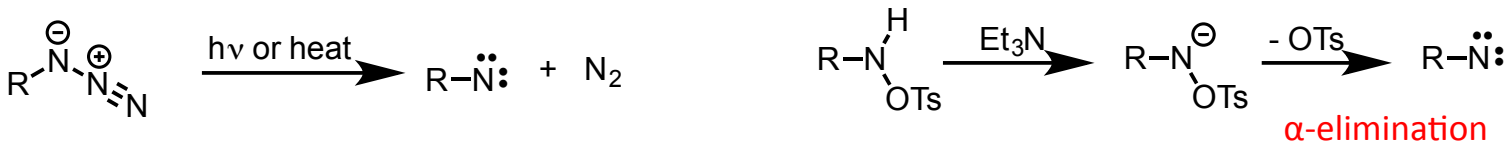
- neutral monovalent nitrogen species – 6 electrons around nitrogen atom, isoelectronic with carbenes
- similar chemistry to carbenes, some differences and nitrenes are generally more reactive



- nitrenes are by definition linear, as with carbenes they have singlet and triplet states
- nitrenes have a larger energy separation between the triplet and singlet states – triplet is usual ground state
- as with carbenes, good π donor substituents can give singlet ground sates

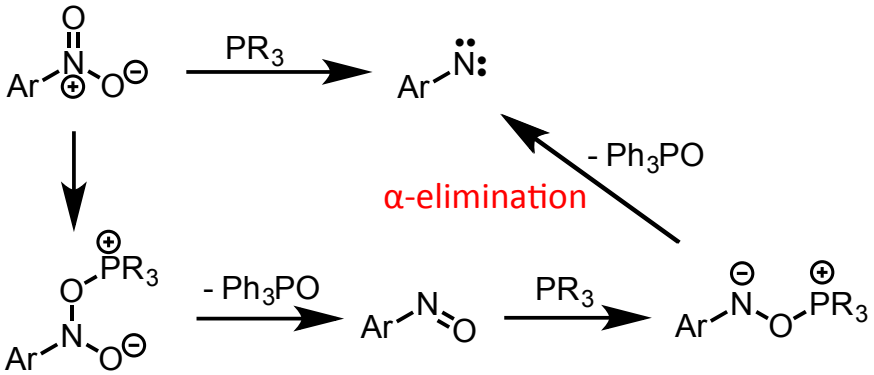


- most common method for generation is thermolysis or photolysis of azides

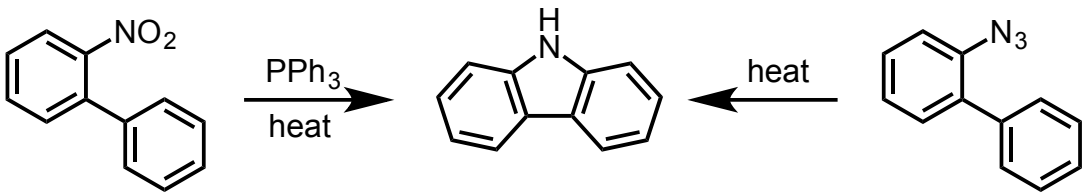


- a number of methods for nitrene generation, analogous to the methods for carbene generation, are known
- free nitrenes are not always formed under these conditions

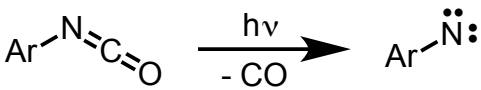
- generation by reduction of nitro compounds



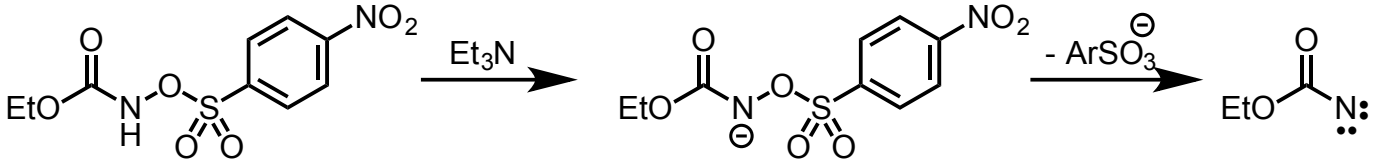
- carbazole synthesis

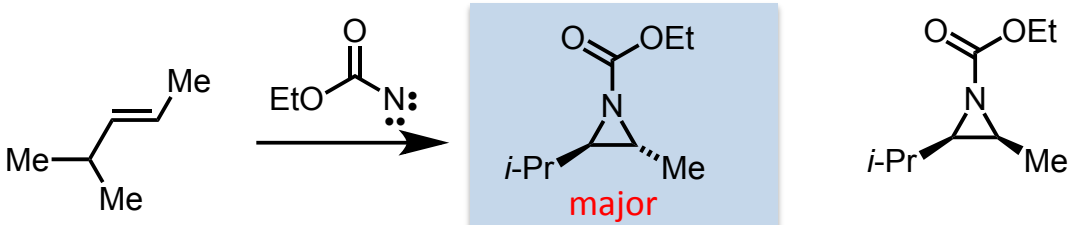


- generation from isocyanates



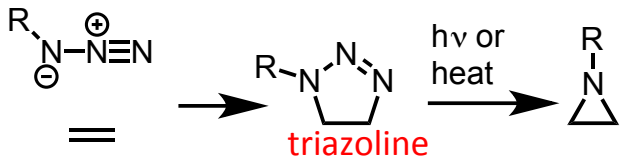
- addition to C=C bonds
- as with carbenes, addition of nitrenes to alkenes is stereospecific with singlet nitrenes, and non-stereospecific with triplet nitrenes

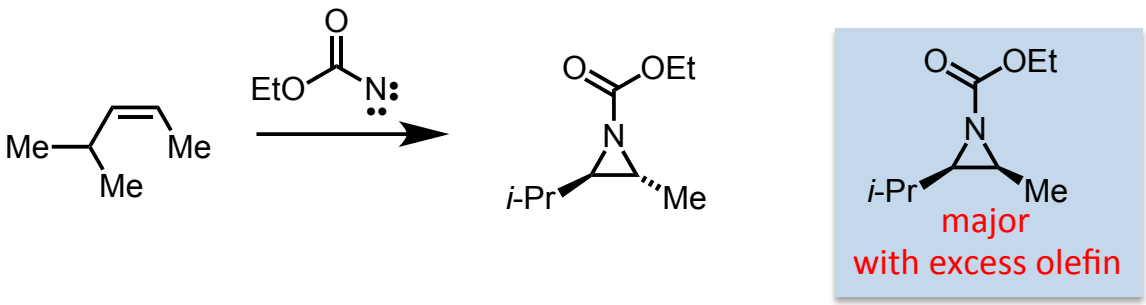




mixture of cis and trans aziridines
with 1 equivalent olefin

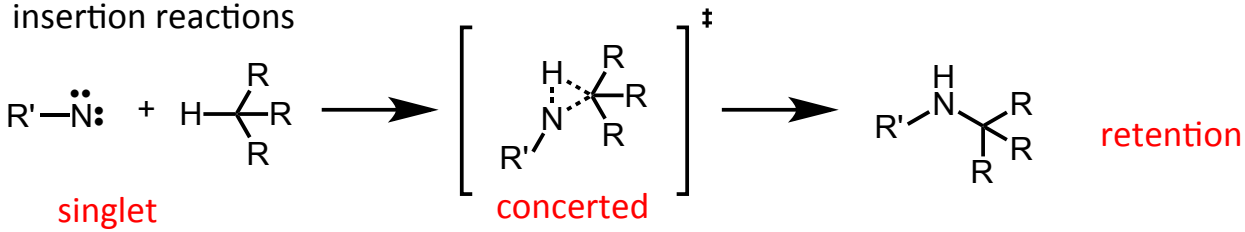
- competing reaction – 1,3-dipolar cycloaddition

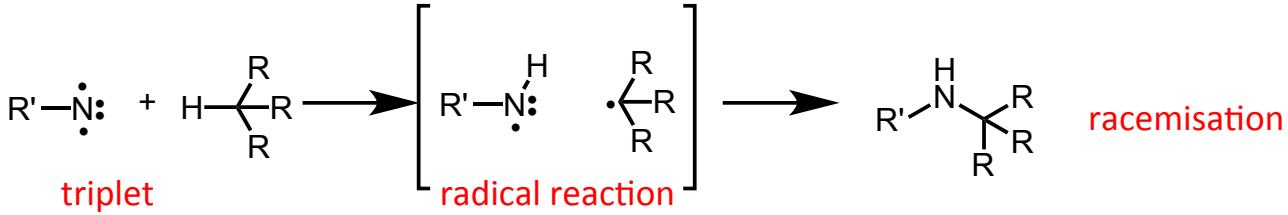


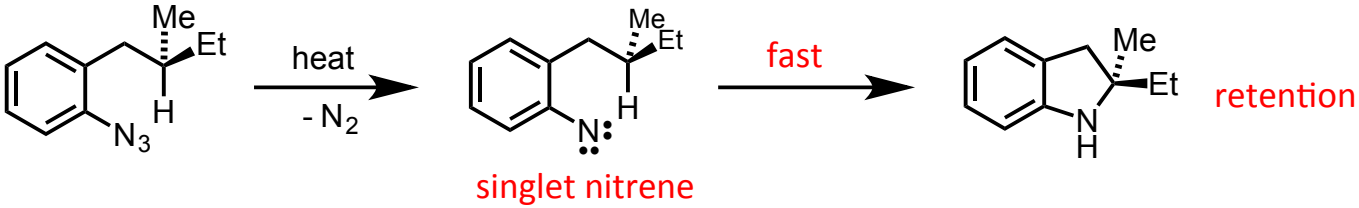


- with high concentration of olefin singlet nitrene reacts stereospecifically to give aziridine products – trans-olefin gives trans-aziridine; cis-olefin gives cis-aziridine
- with low concentraion of olefin singlet nitrene undergoes intersystem crossing to ground state triplet and reacts non-stereospecifically with each alkenes (diradical mechanism) to give mixtures of aziridine products
- photochemical generation of nitrene gives analogous results

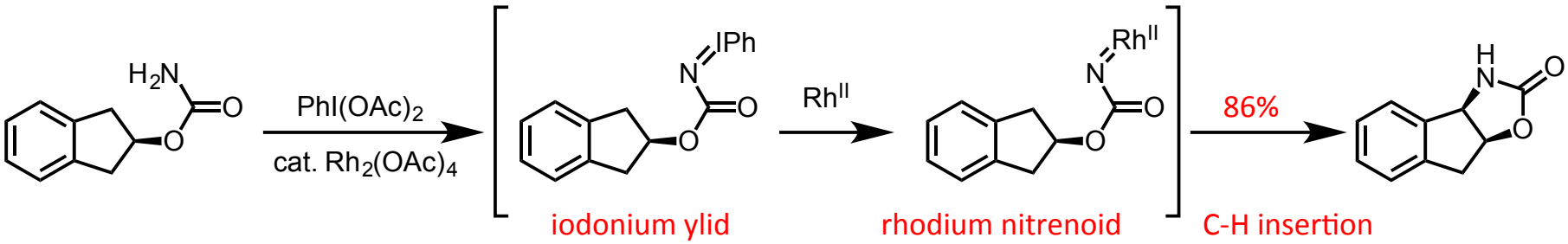
- insertion reactions





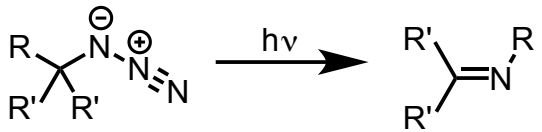


- nitrenoids frequently give better yields of C-H insertion reactions under milder conditions



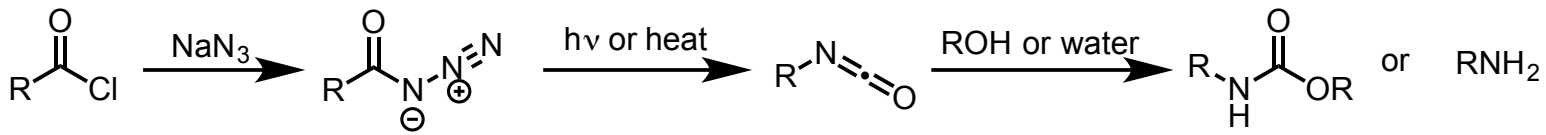
- in a similar manner transition metal nitrenoids react with alkenes to give good yields of aziridines

- rearrangement of nitrenes
- photolysis of alkyl azides yields imines – nitrenes are most likely not intermediates in such reactions

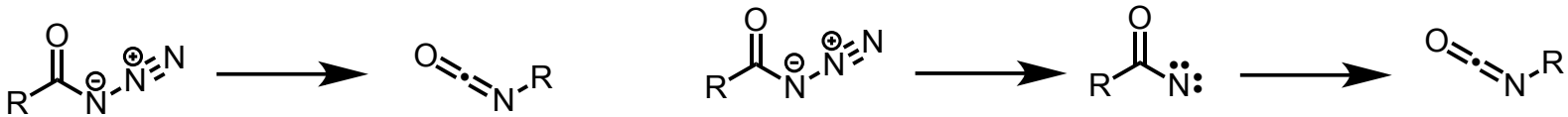


concerted 1,2 shift

- Curtius rearrangement or acyl azides



- there are two plausible mechanisms



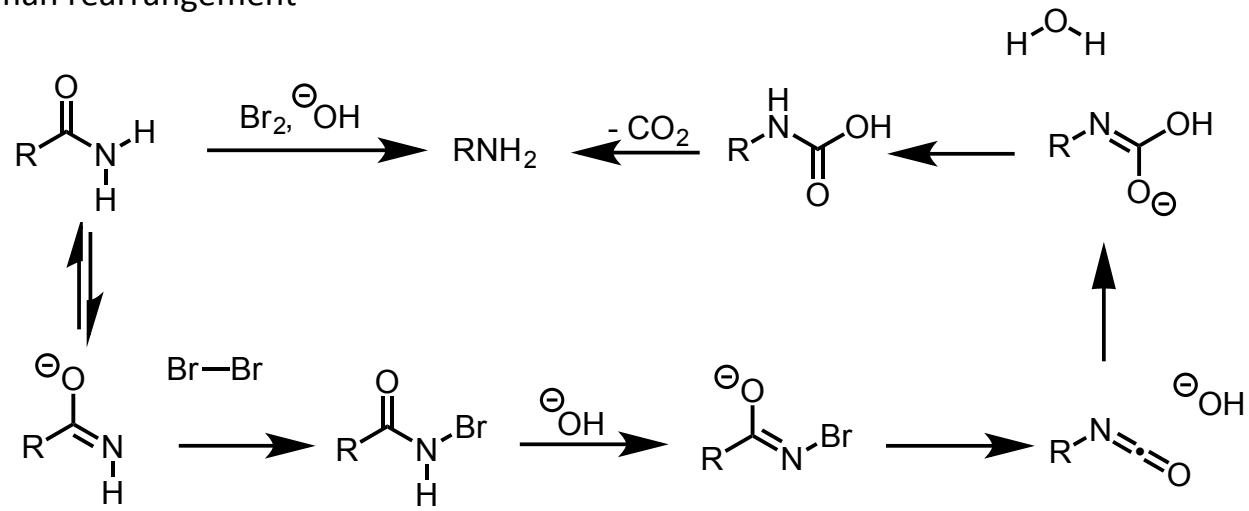
concerted

stepwise via nitrene

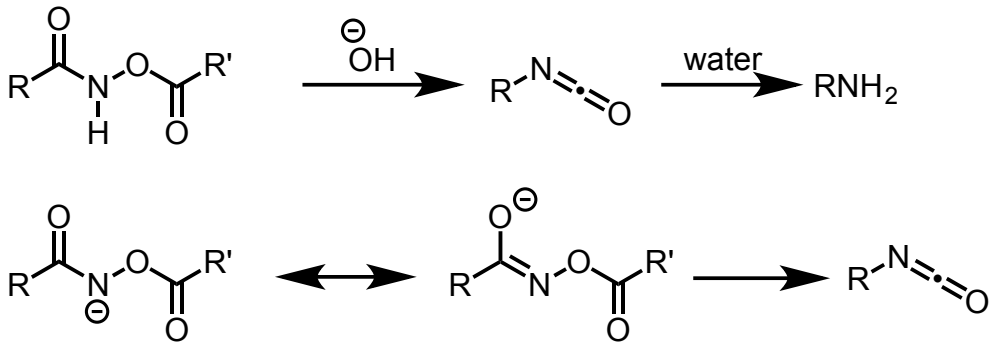
- the thermal reaction is concerted; the photochemical reaction may proceed *via* a nitrene, but may be concerted

- the Curtius rearrangement proceeds with retention of configuration in the migrating group

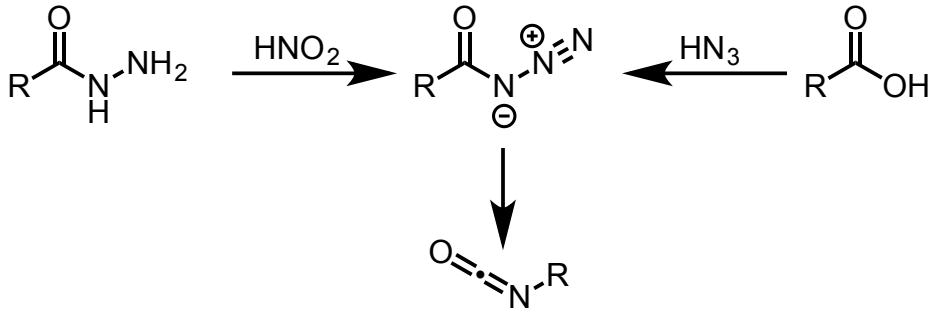
- other rearrangements to electron deficient nitrogen – these rearrangements are unlikely to involve nitrenes
- Hoffman rearrangement



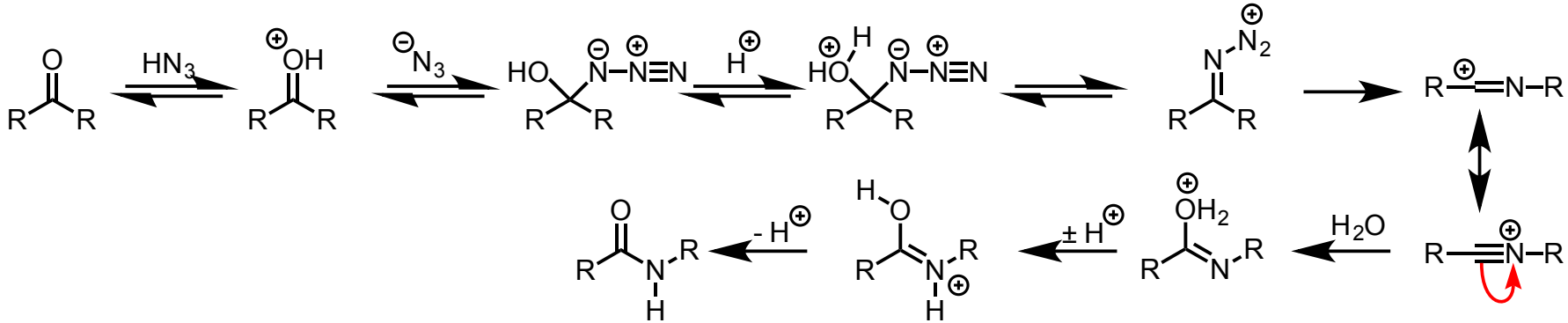
- Lossen rearrangement



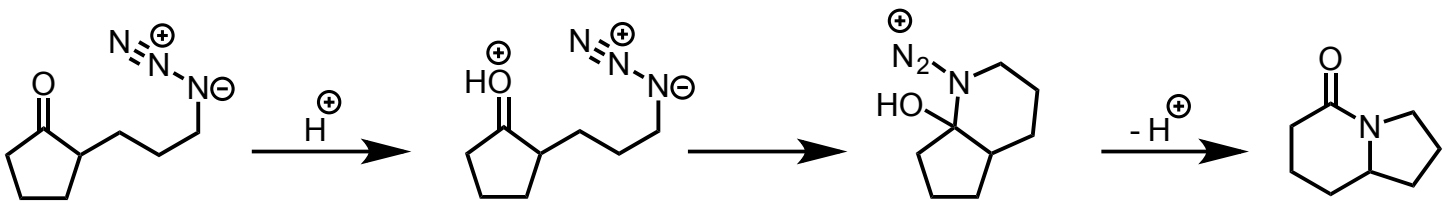
- Schmidt rearrangement



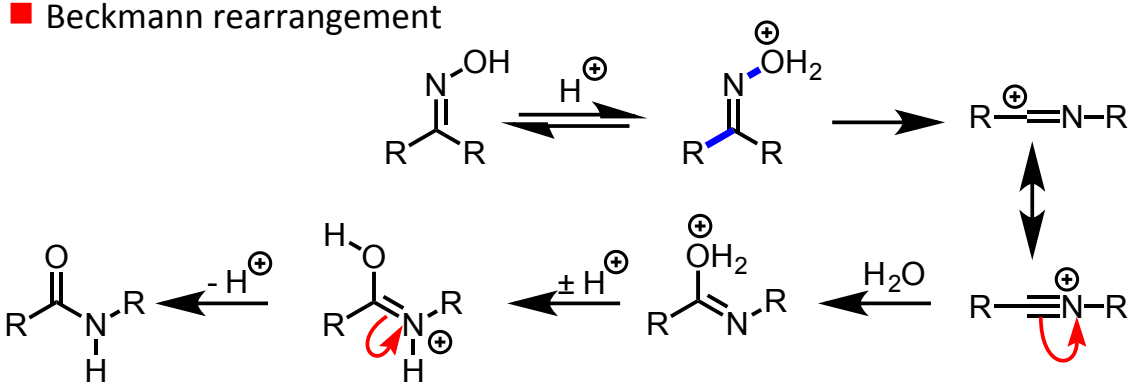
- Schmidt rearrangement with ketones (aldehydes give nitriles)



- Intramolecular Schmidt rearrangement with alkyl azides

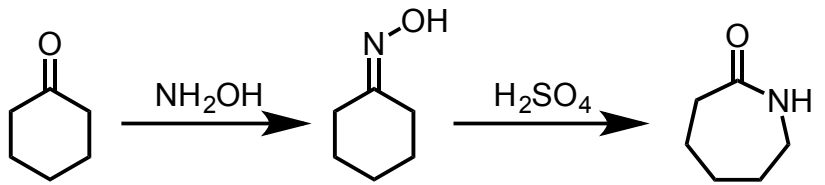


- Beckmann rearrangement

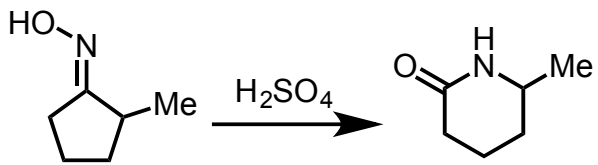


- the group anti to the leaving group migrates (σ_{C-C} to σ^*_{N-O})
- oximes can undergo *E*/*Z* isomerisation under the acidic reactions conditions
- migration with retention of configuration

- Beckmann rearrangement – synthesis of caprolactam, precursor to nylon 6

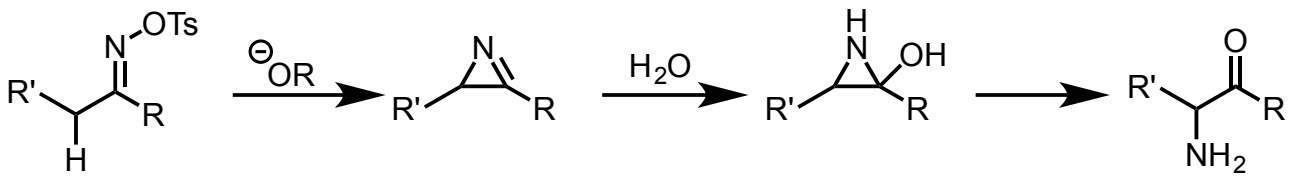


carpolactam

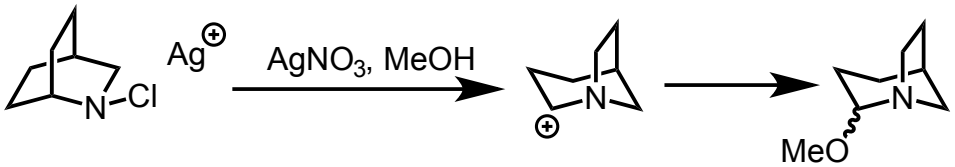


most stable oxime with bulky groups trans

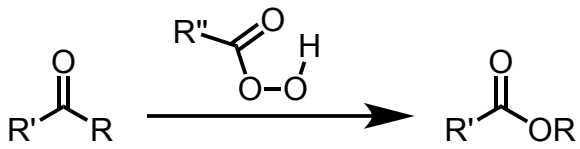
- Neber rearrangement – substituent possessing most acidic hydrogen migrates



- Stieglitz rearrangement

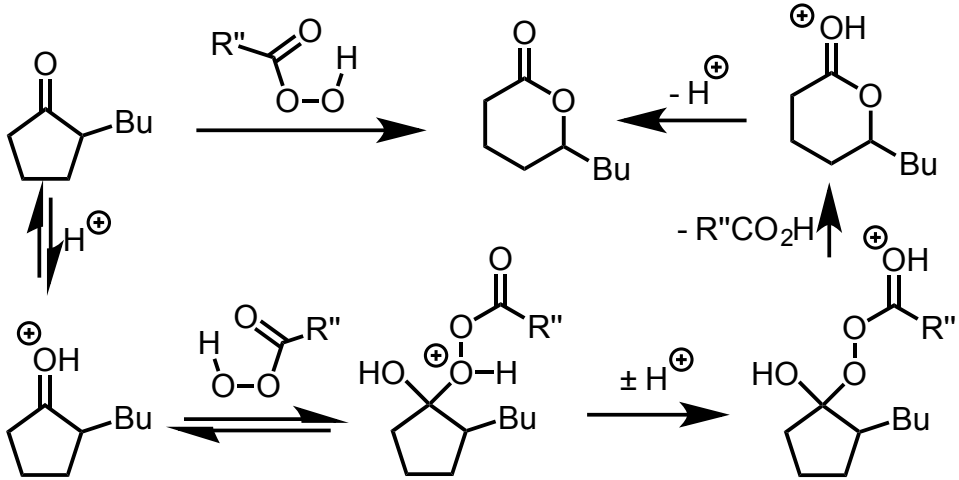


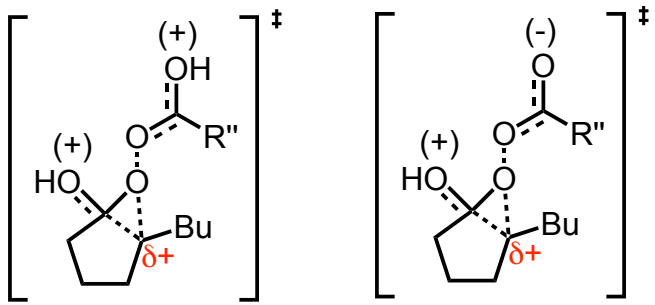
- Baeyer-Villiger



conversion of a ketone into an ester by oxygen insertion

- order of migration A.K.A migratory aptitude
3° alkyl > 2° alkyl > aryl > 1° alkyl > methyl
i.e. the group which best supports a positive charge migrates
- with aromatic groups, electron donating groups increase migratory aptitude
- migration occurs with retention of configuration in the migrating group
- with aldehydes migration of "H" usually occurs to give carboxylic acids



- transition state is electron deficient (electron withdrawing group on oxygen)

- electron releasing groups stabilise the transition state giving the order of migratory aptitude above