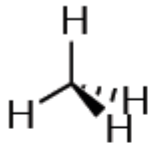
Carbenes and Nitrenes:
Structure, generation and reactivity

Carbenes

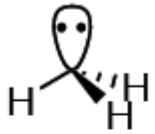
Review of carbon valencies and hybridization



Methane

CH_4

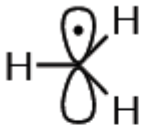
sp^3



Methyl anion

CH_3^-

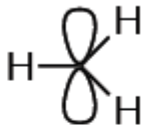
sp^3



Methyl radical

$CH_3^{\bullet}$

sp^2

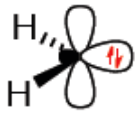
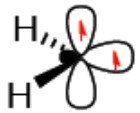
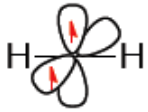


Methyl cation

CH_3^+

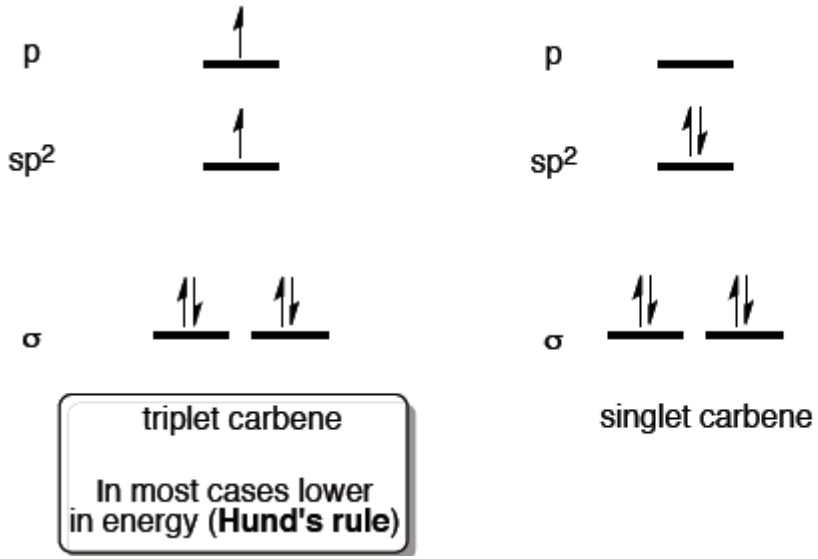
sp^2

"Carbenes are neutral, highly reactive species containing a **divalent carbon atom with an electron sextet**"

Structure			
Hybridization	sp^2	sp^2	sp
Geometry	Bent	Bent	Linear (not observed)
State	Singlet	Triplet	Triplet

Comparison between triplet and singlet carbenes

Spin state



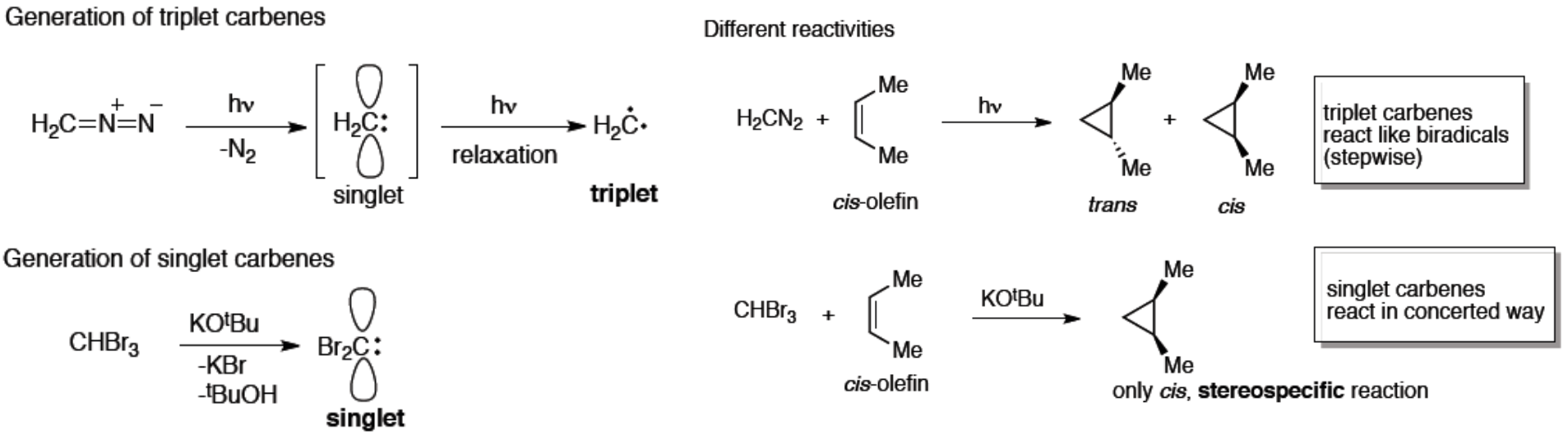
These two spin systems can be distinguished by EPR

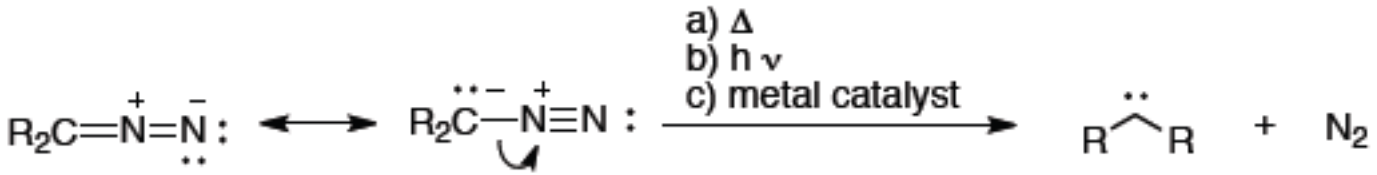
Geometry

From X-ray structures we know that both singlet and triplet states are bent.

	Triplet carbene	Singlet carbene
Bond angle	130-150°	100-110°

Generation and reactivity differences of singlet vs triplet carbenes





Wuth light: Triplet carbene

With gentle warming: singlet cerbene

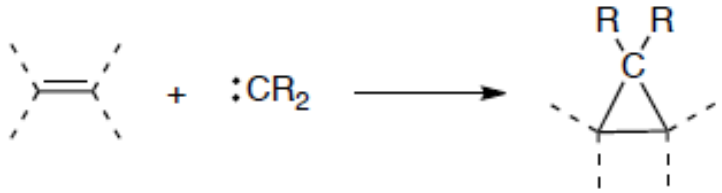
With metals (catalyst) like Rh(II) or Cu(II): Carbenoids (similar to singlet carbene)

Carbenoids: are compounds that react like carbenes but are not true divalent C species

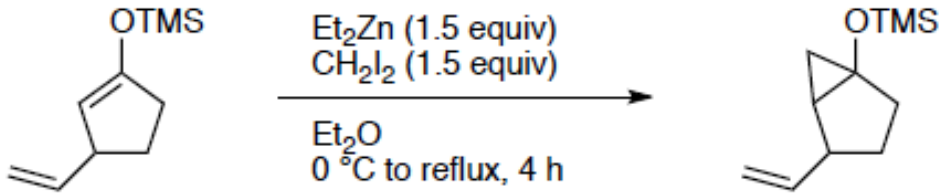
Reactions of Carbenes and Carbenoids

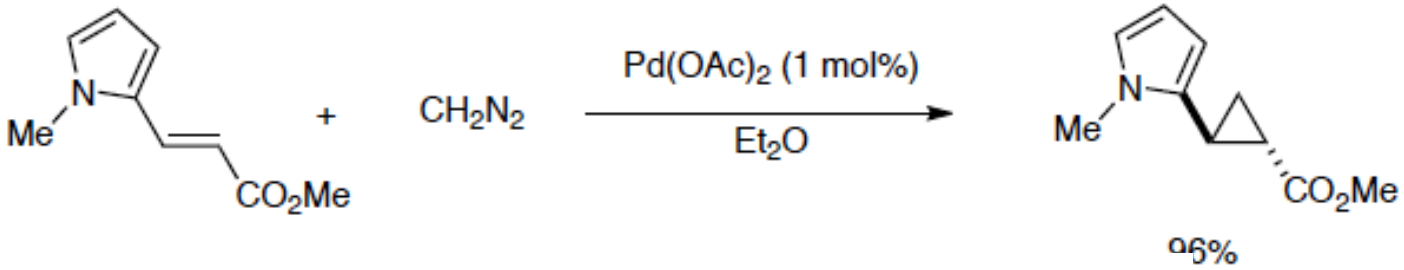
No matter how they are generated, four typical reactions

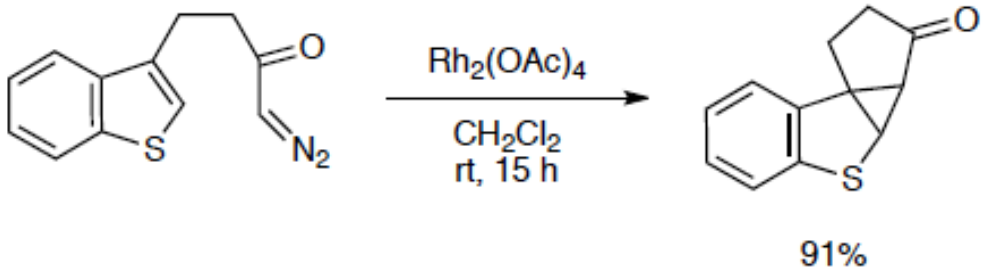
Cyclopropanation



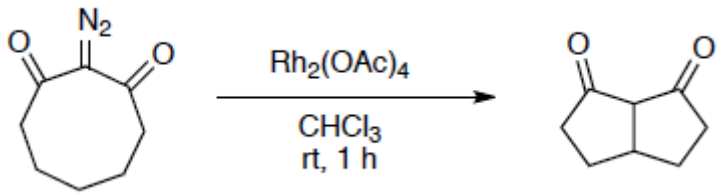
Simmons-Smith



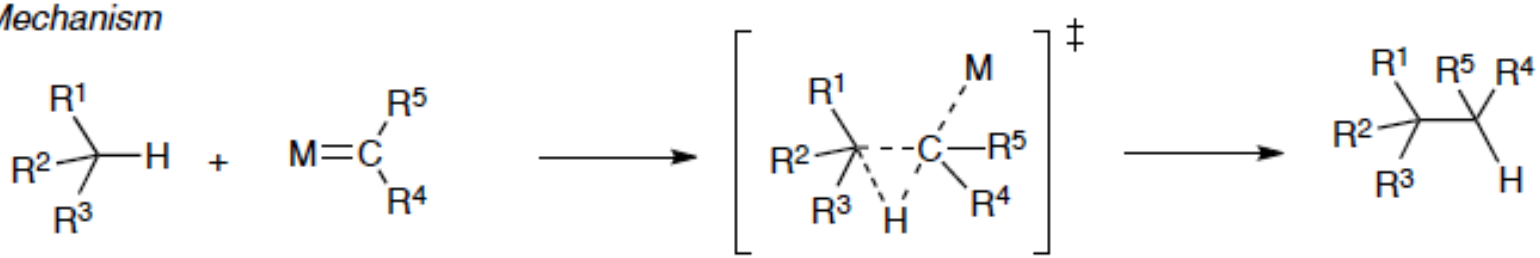




Insertion into a C-H

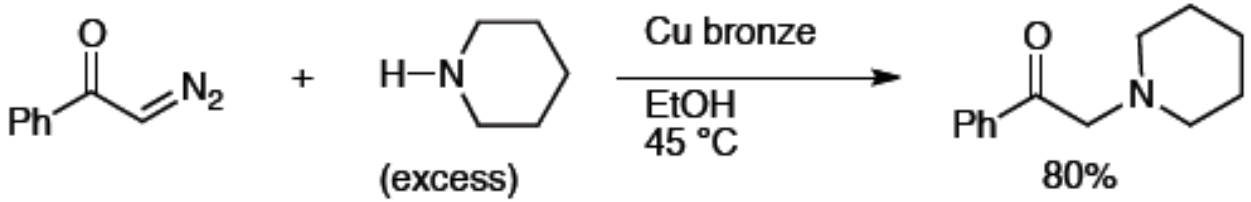


Mechanism

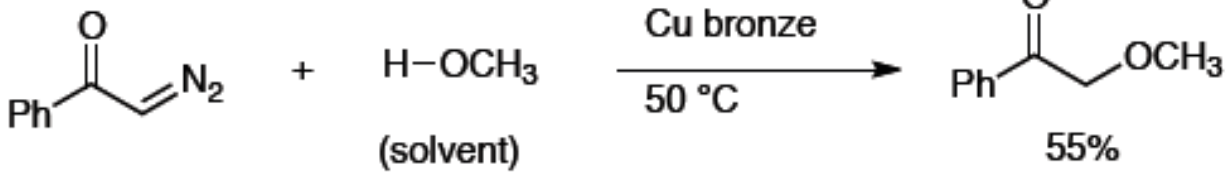


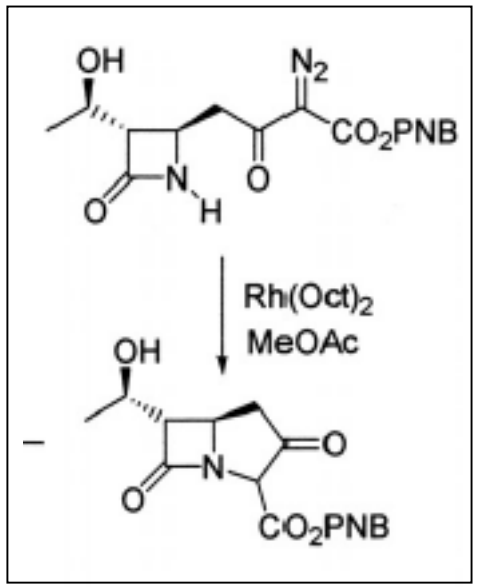
Insertion into a O–H & N-H

N–H insertion

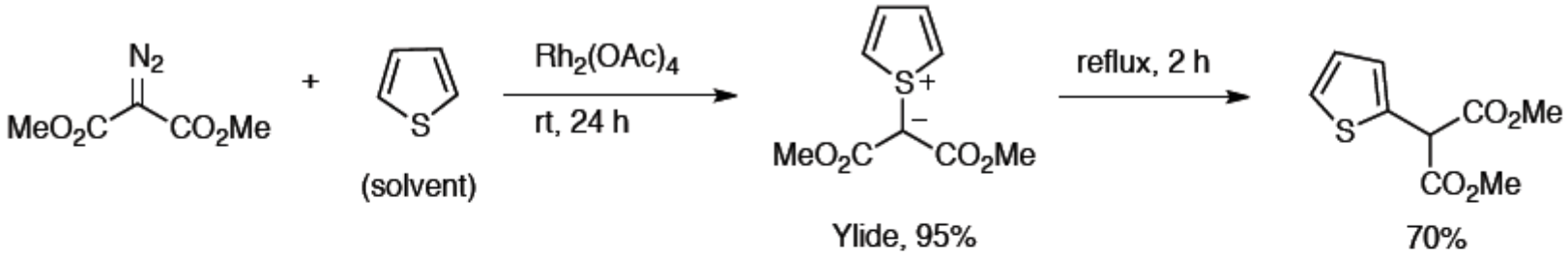


O–H insertion

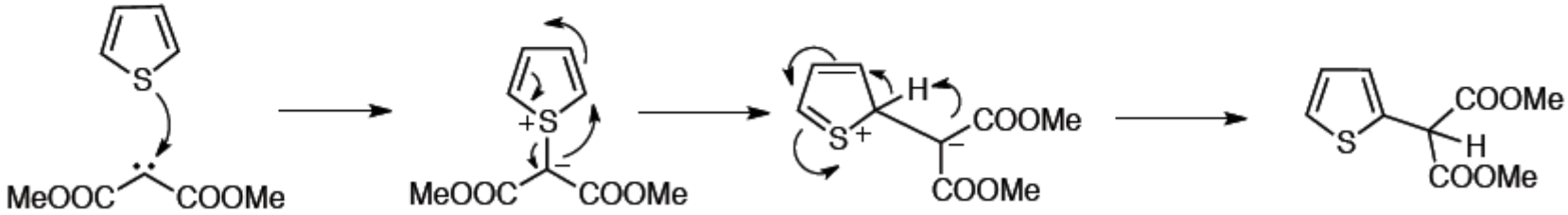


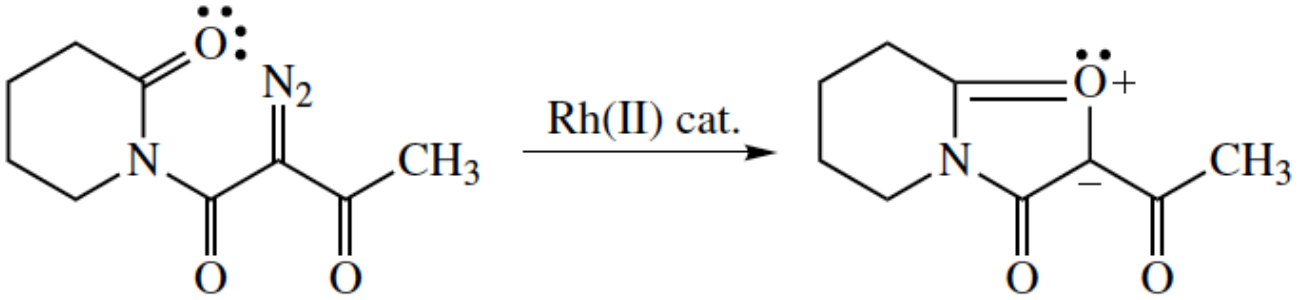


Combination with a nucleophile (that have a reactive lone pairs)



Mechanism



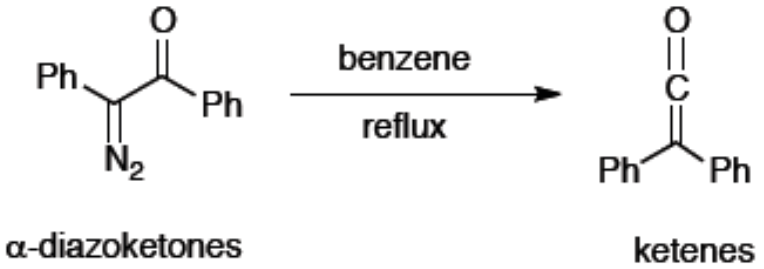


The fourth typical reaction of carbenes is a 1,2-shift (Rearrangements)

A group on the adjacent C migrates to the carbene C with its pair of electrons, giving an alkene.

The 1,2- shift severely limits the usefulness of many substituted carbenes.

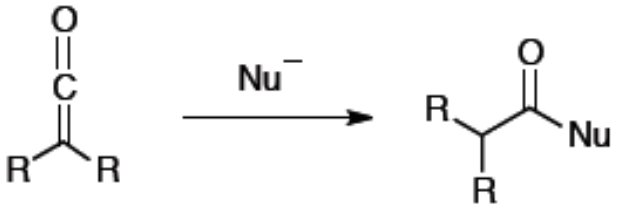
Wolff Rearrangement



α-diazoketones

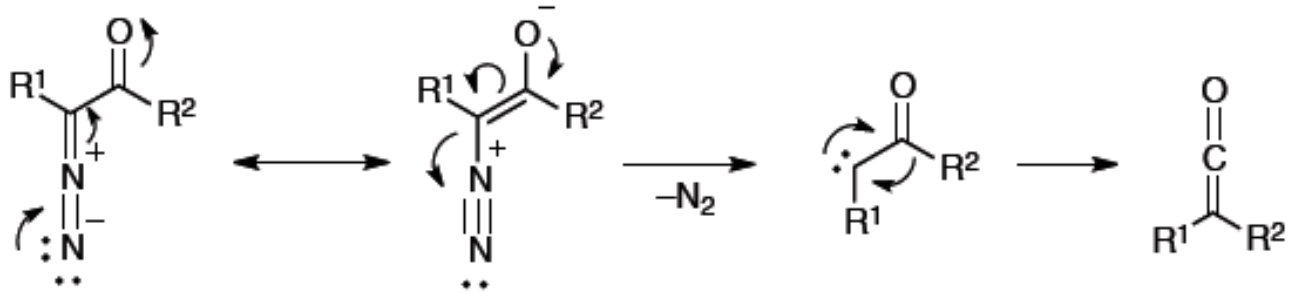
ketenes

Reminder:

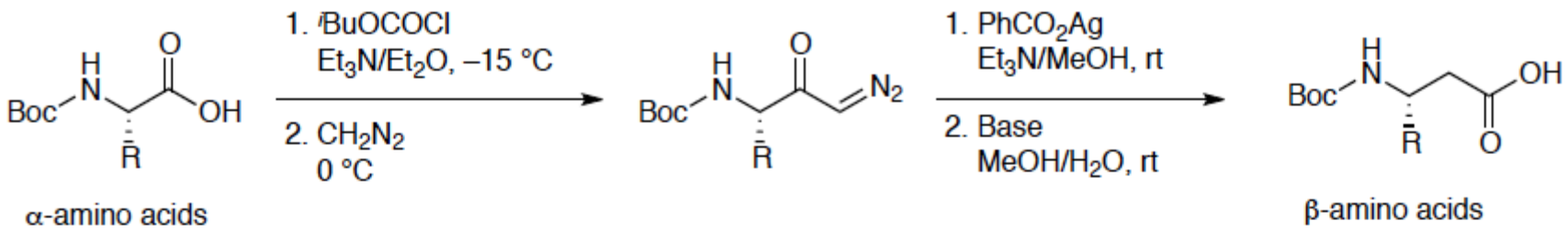


Nucleophiles: amines, alcohols...

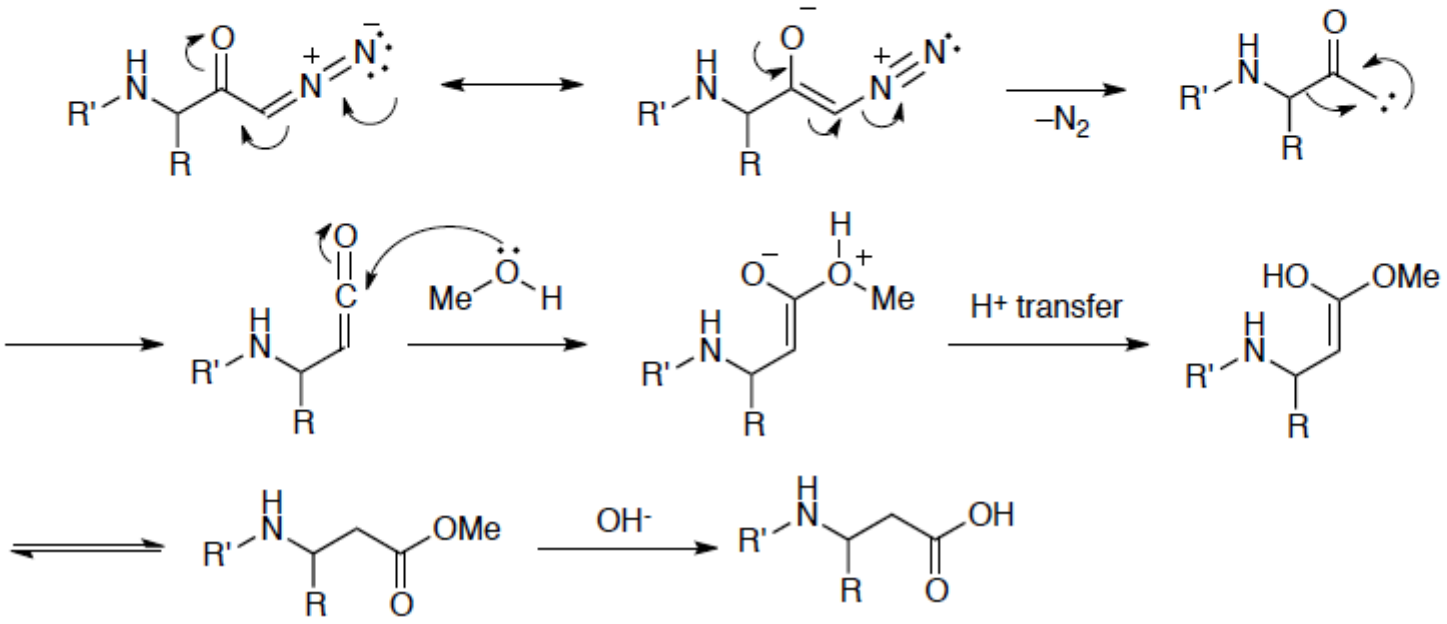
Mechanism



Arndt-Eistert β-amino acid synthesis

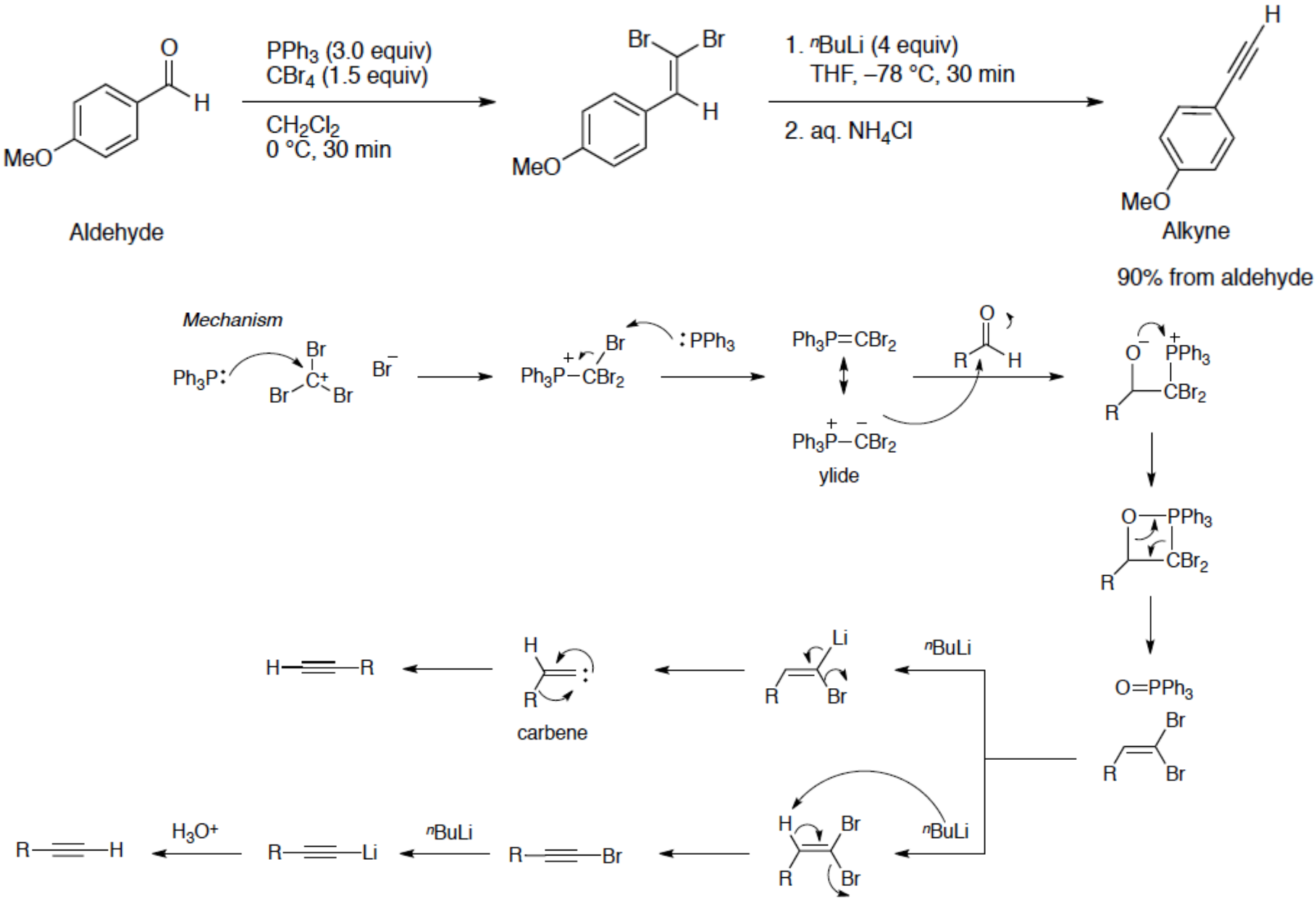


Mechanism

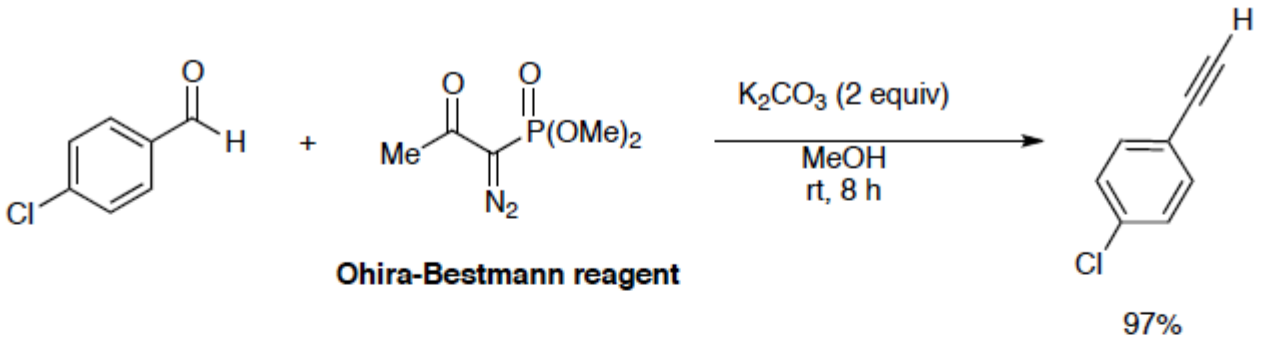


Alkyne synthesis

Corey-Fuchs reaction

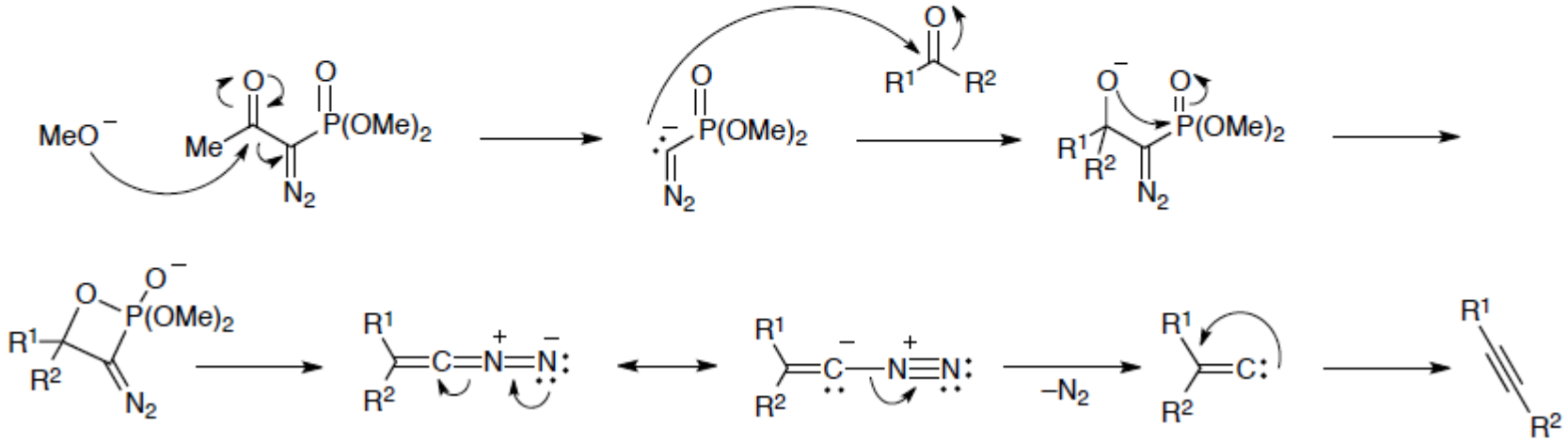


Seyferth-Gilbert Homologation



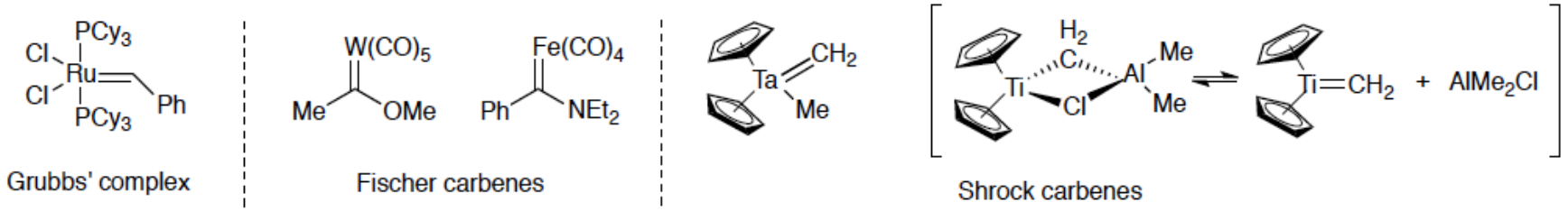
Ohira-Bestmann reagent

Mechanism



Carbenoids (metal stabilized carbenes) described often as $M=CR_2$

A transition metal carbene complex is an organometallic compound featuring a divalent organic ligand.



Reflecting the growth of the area, carbene complexes are now known with a broad range of different reactivities and diverse substituents..

The Fischer carbenes named after Ernst Otto Fischer feature strong π-acceptors at the metal and being electrophilic at the carbene carbon atom.
Schrock carbenes, named after Richard R. Schrock, are characterized by more nucleophilic carbene carbon centers, these species typically feature higher valent metals.

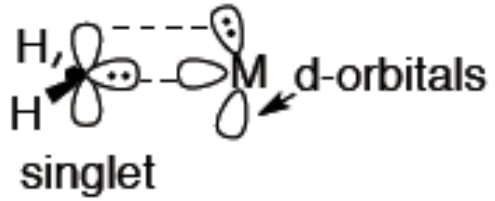
Often it is not possible to classify a carbene complex with regards to its electrophilicity or nucleophilicity

Properties

Improved thermodynamic and kinetic stability with respect to the non-stabilized carbenes.

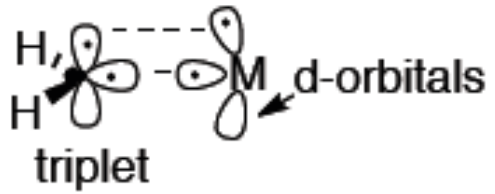
Fischer carbenes

- low oxidation state metals;
- middle and late transition metals Fe(0), Mo(0), Cr(0), W(0);
- π-acceptor metal ligands;
- π-donor substituents on methylene group (-OR or -NR_2).



Shrock carbenes

- high oxidation states metals;
- early transition metals Ti(IV), Ta(V);
- non π-acceptor ligands non π-donor substituents.

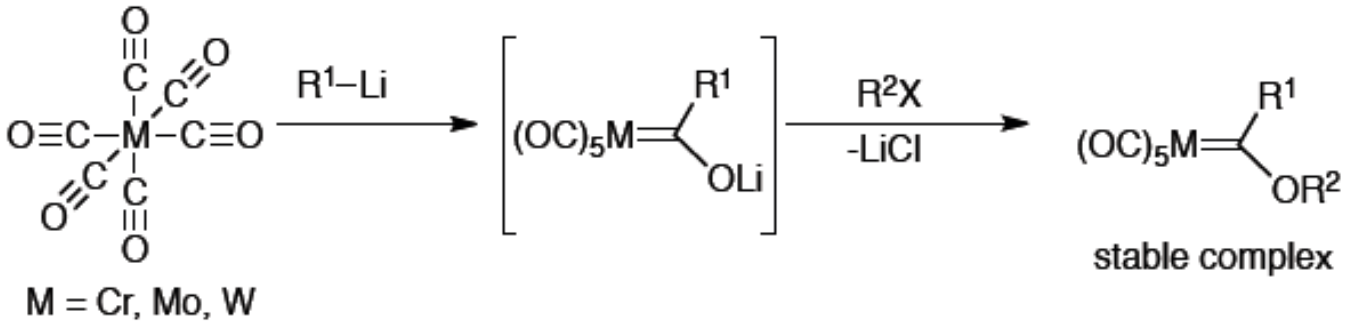


Fischer carbenes can be likened to ketones, with the carbene carbon being electrophilic, much like the carbonyl carbon of a ketone.
Infact, Fischer carbene species can undergo Aldol-like reactions, the hydrogen atoms attached to the carbon α to the carbene carbon are acidic, and can be deprotonated by a base such as n-butyllithium, to give a nucleophile which can undergo further reaction.

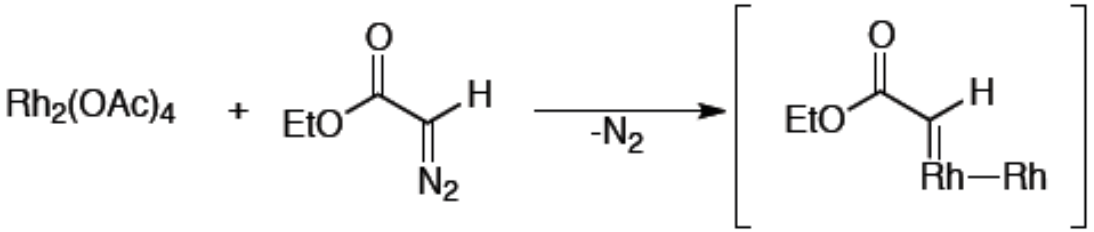
Shrock carbenes the bonds are polarized towards carbon and therefore the carbene atom is a nucleophile, much like organometallic cmp-

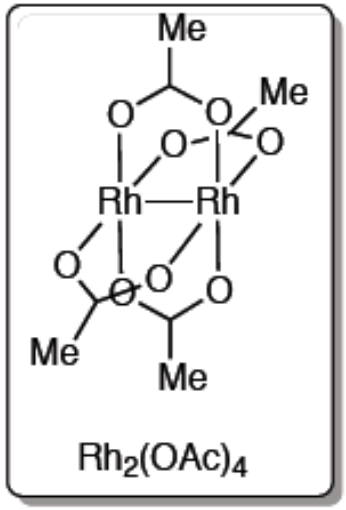
Generation

Fischer route



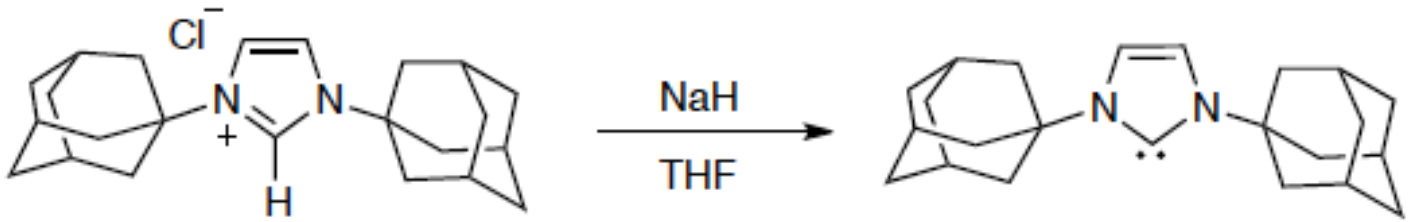
From diazocompounds





Then, **N-heterocyclic carbenes (NHCs)** already seen.

The first applications of thiazolydenes in umpolung organocatalysis were reported as early as 1943 (J. Pharm. Soc. Jpn. **1943**, *63*, 296) and metal complexes of NHCs were already reported in the late 60's. However, it is only in the last two decades (milestone: 1991, Arduengo, first X-ray structure of a carbene) that NHCs have become ubiquitous both as **ligands** in organometallic chemistry and as **organocatalysts**.

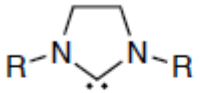


stable carbene
(Arduengo 1991)

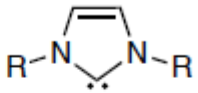
NHCs are singlet carbenes

For NHCs the singlet state is lower in energy than the triplet state, the reason being π-donation into the porbitalof carbon from the heteroatoms adjacent to the carbene.

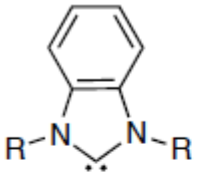
Examples of the most frequent NHCs and their nomenclature



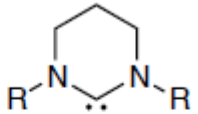
Imidazolynidene



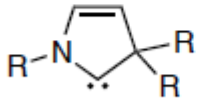
Imidazolydene



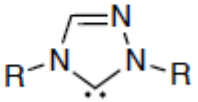
Benzimidazolydene



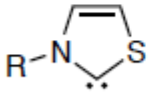
Tetrahydropyrimidiylidene



Pyrrolidinylidene



Triazolydene

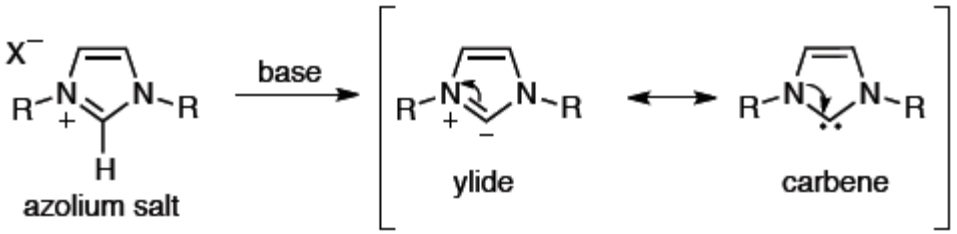


Thiazolidene

R can be modified to fine-tune the chemical behavior of the NHC (R = alkyl or aryl).

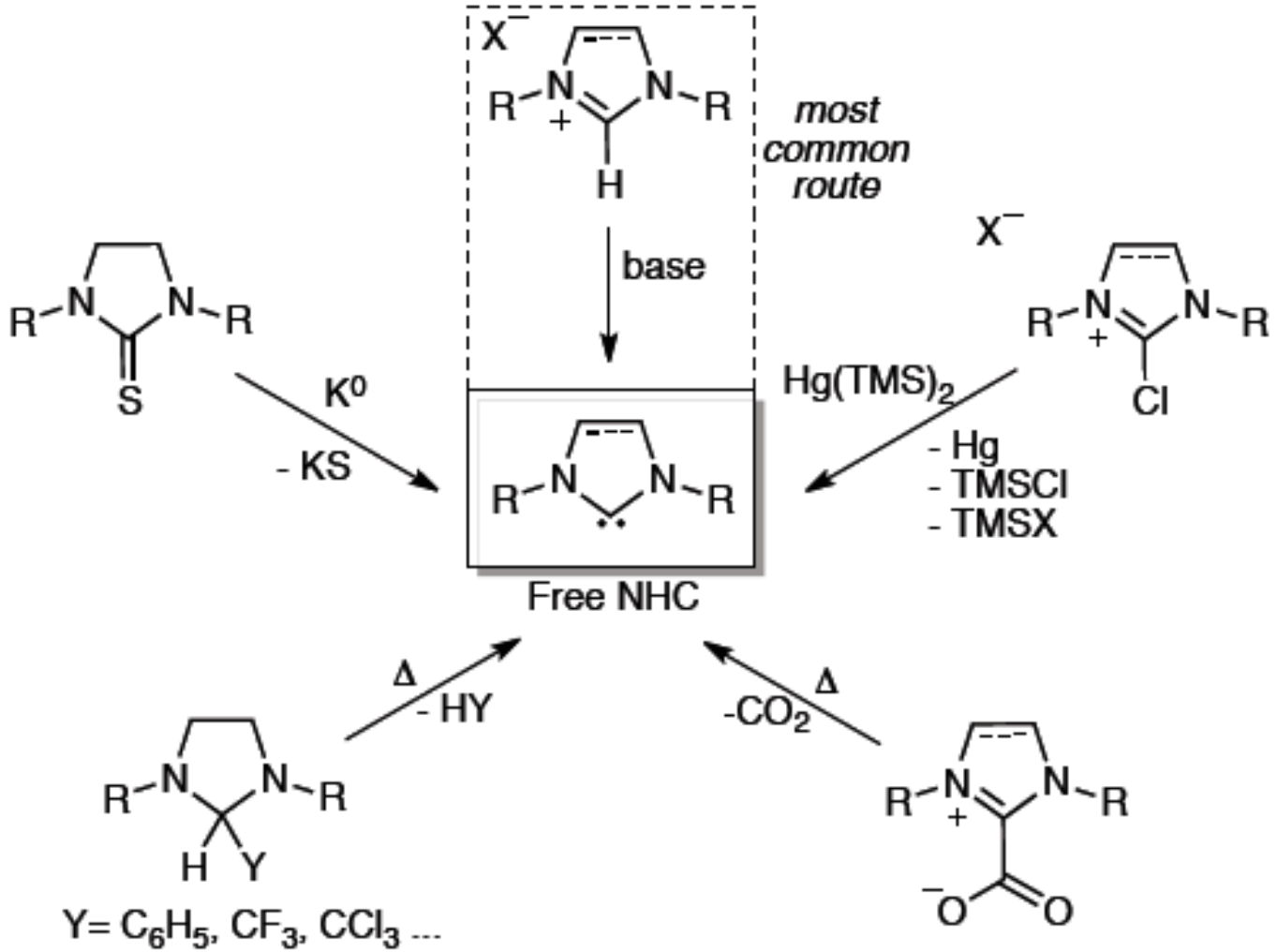
Properties

NHC are electron rich and particularly stable carbenes. The stability arises both from:
-**shielding effect** by sterically demanding substituents (minor effect);
- **electronic stabilization** (mesomeric interaction of the lone pairs of electrons on the nitrogen atoms
with the empty p orbital of the sp2 hybridized carbene).



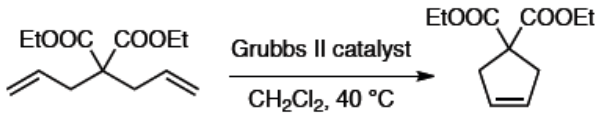
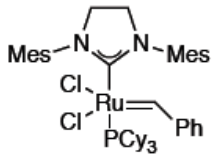
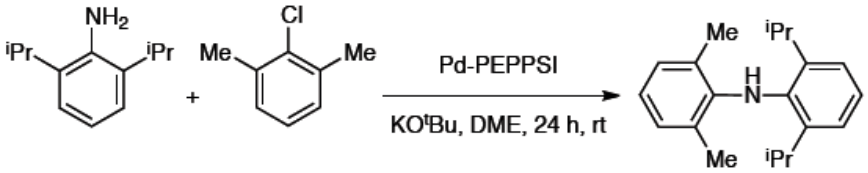
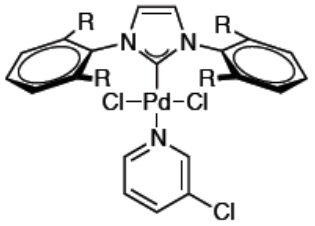
Acidic proton: the pKa value of the 2-position of imidazolium salts ranges from 16 to 23 (in DMSO).

Synthesis (generation)



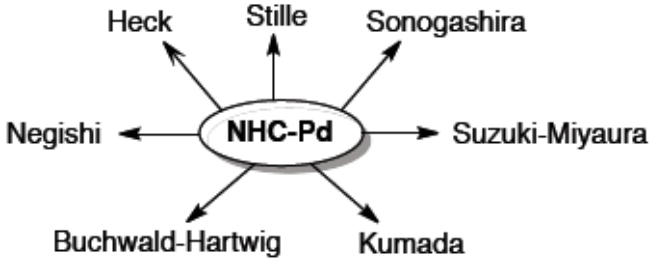
Use as ligands

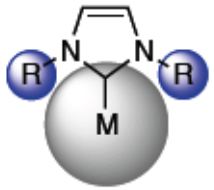
NHC-complexes are known for almost every transition metal, but the most important for organic chemist are:

Metal	Class	Example	Catalyst
Ru	Metathesis reactions		 Grubbs II
Pd	Cross-coupling reactions	Buchwald-Hartwig coupling with hindered substrates  90 %	 Pd-PEPPSI

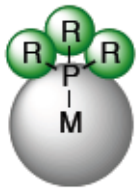
NHC behave like phosphines when they are coordinated to metals (electron donating properties) but they have more influence on the coordination sphere of the metal (sterics).

Cross-coupling reactions





R groups pointing at the metal "coordination sphere"

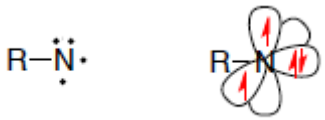


R groups pointing away from the "coordination sphere"

Nitrenes

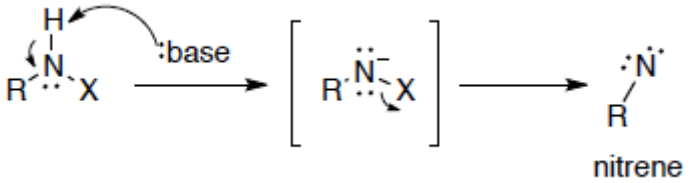
Structure & hybridization

Nitrenes are nitrogen analogues of carbenes. The nitrogen atom possesses only six valence electrons; in nitrenes the triplet state is lower in energy than the singlet state.

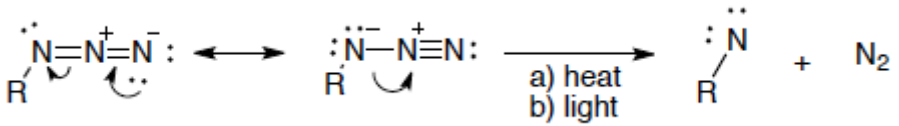


Generation

From 1,1-elemination



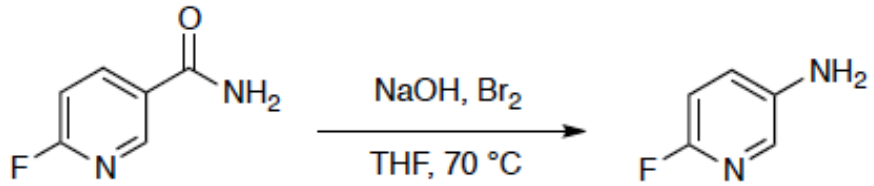
From azides



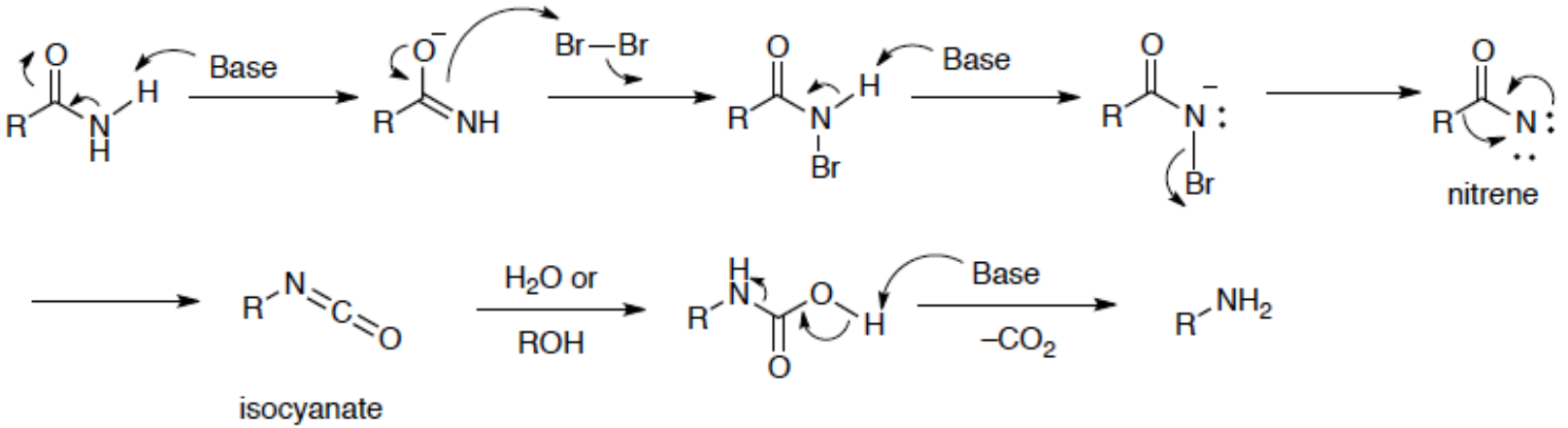
Main reactions: rearrangements

Rearrangements

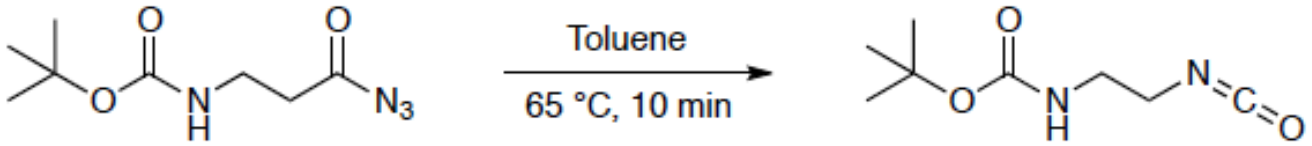
Hoffman rearrangement



Mechanism



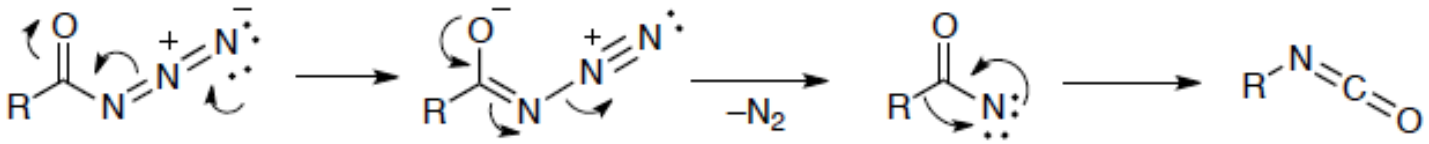
Curtius rearrangement



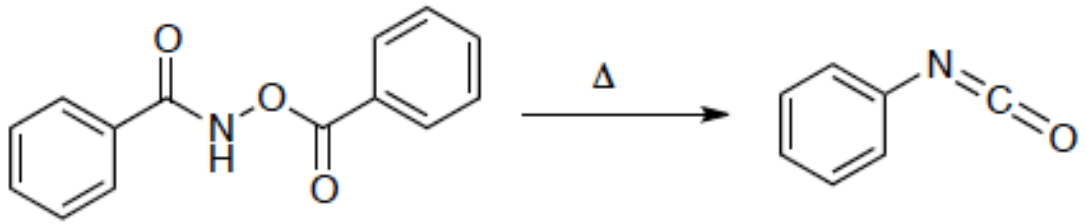
Acyl azide

Isocyanate

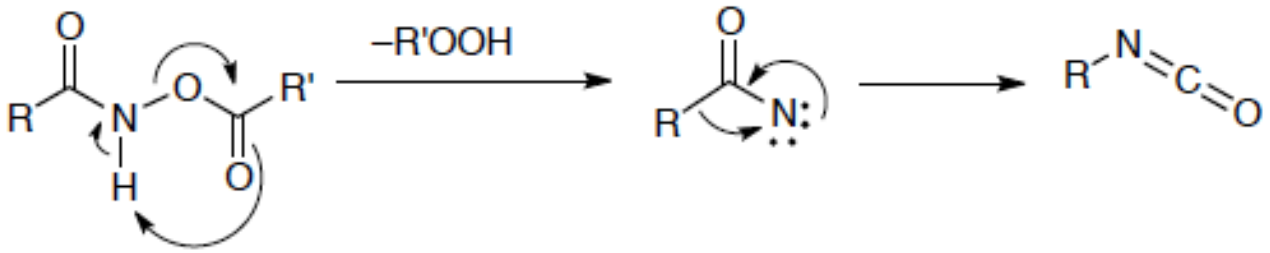
Mechanism



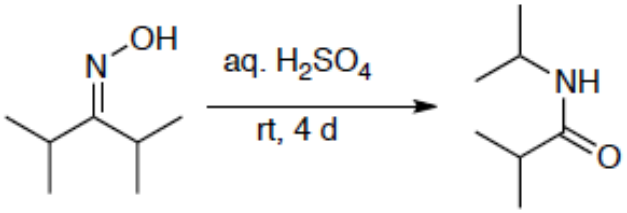
Lossen rearrangement



Mechanism

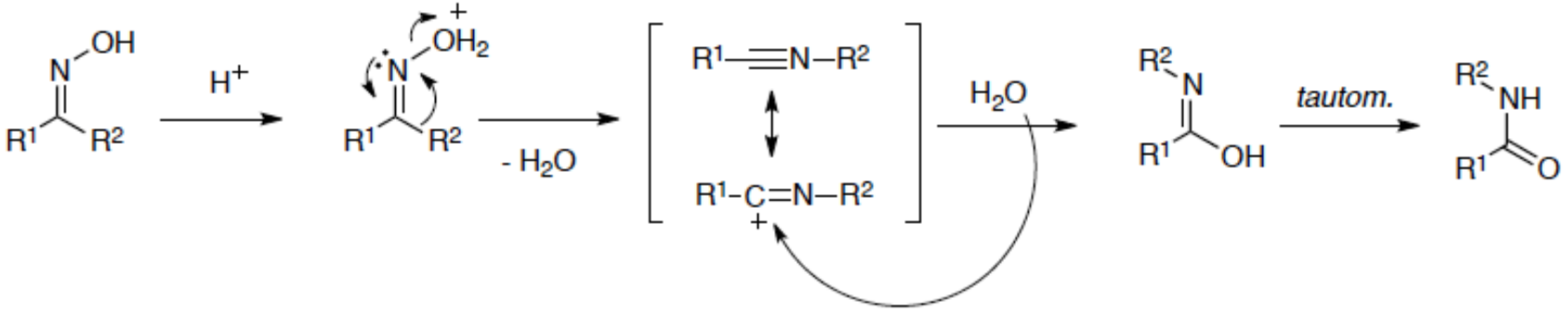


Beckmann rearrangement

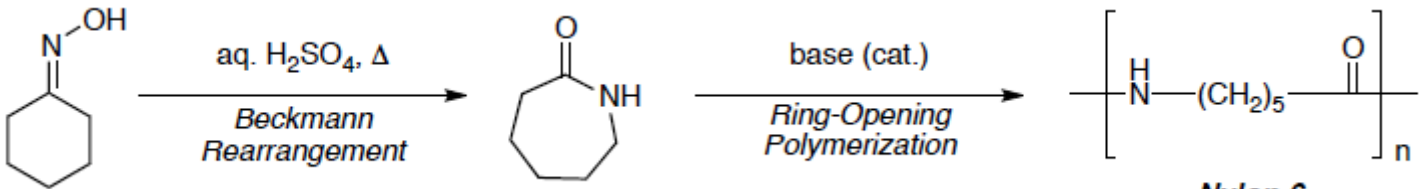


63%

Mechanism

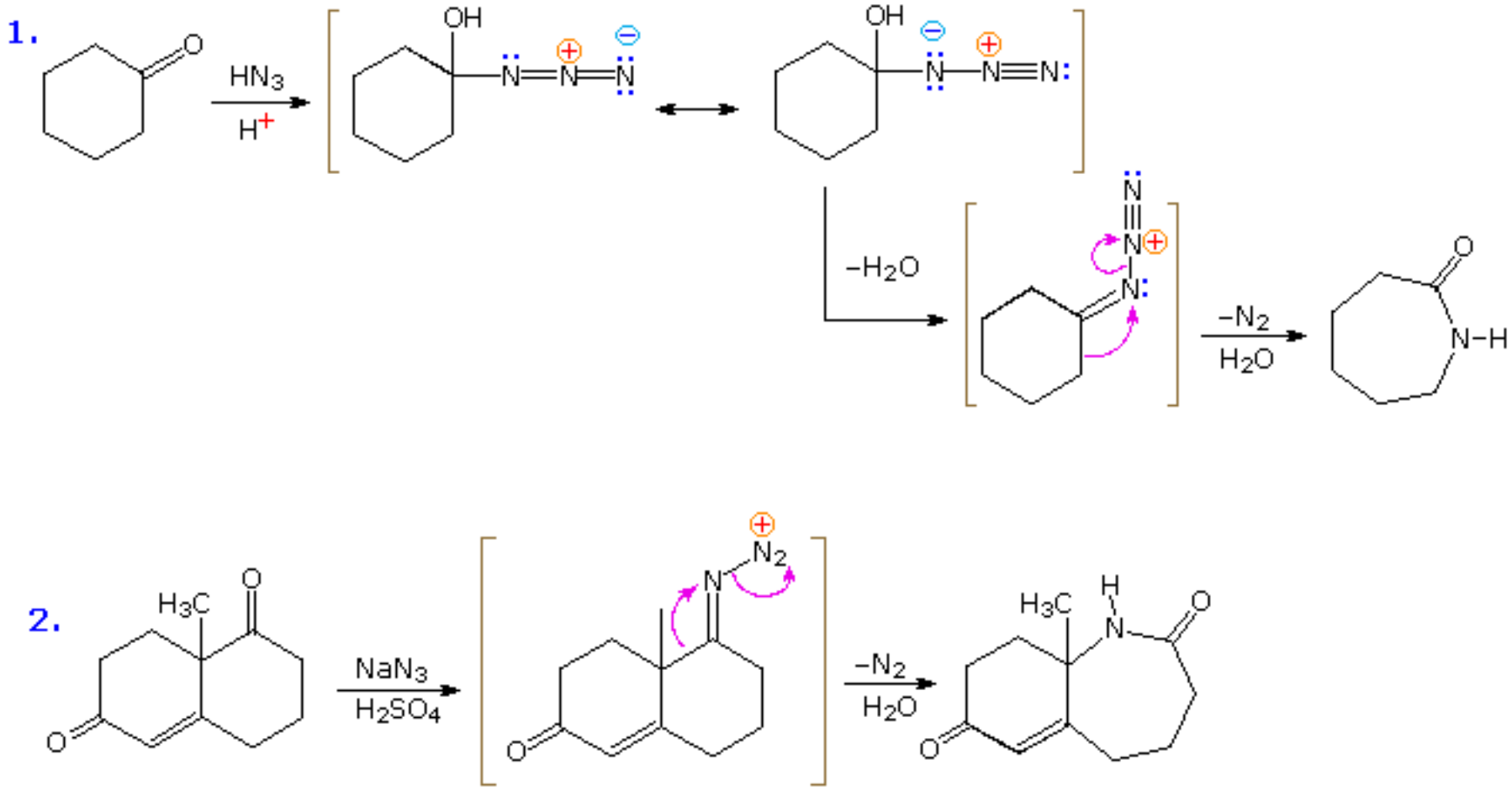


Industrial nylon synthesis

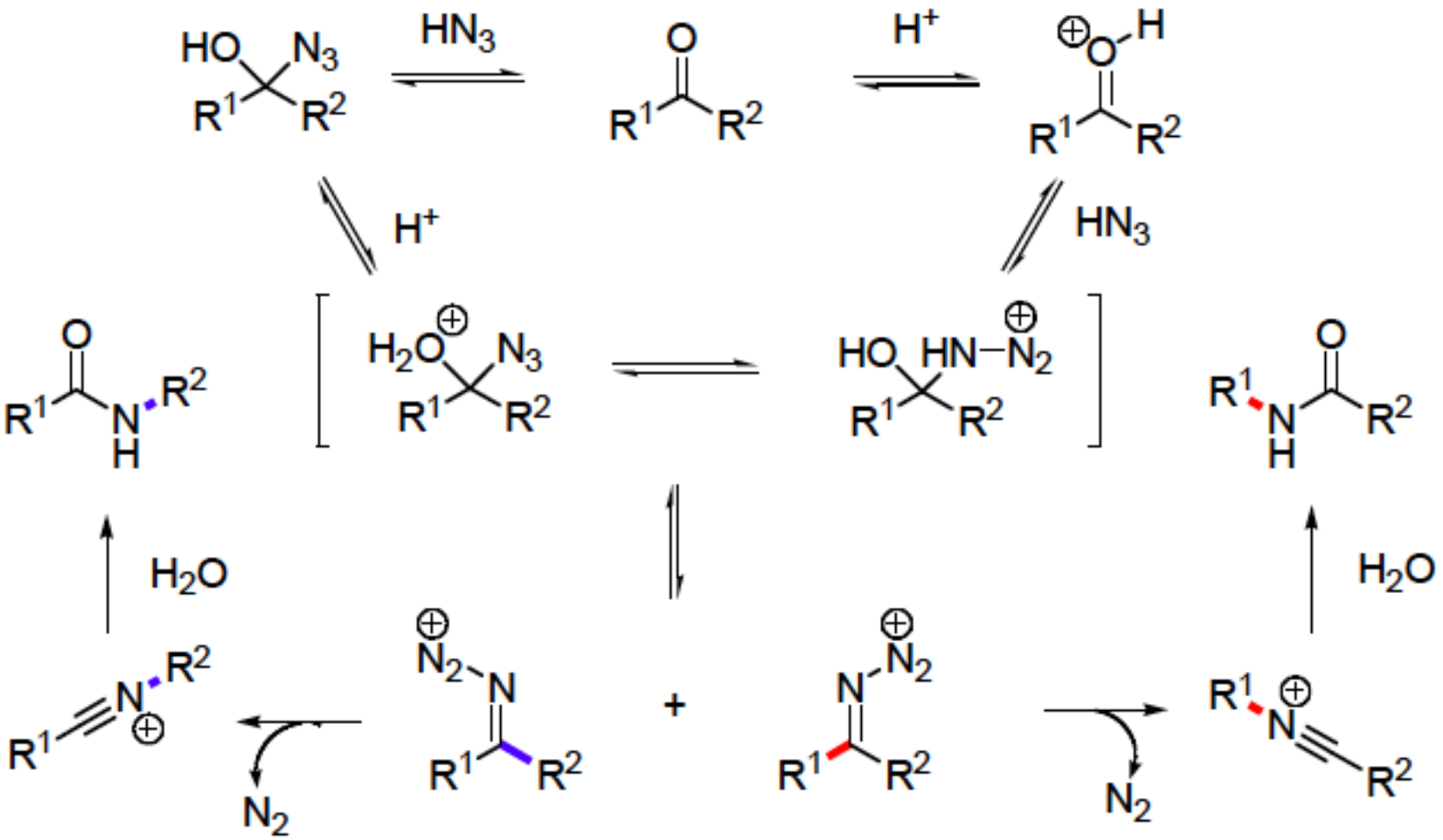


Nylon 6

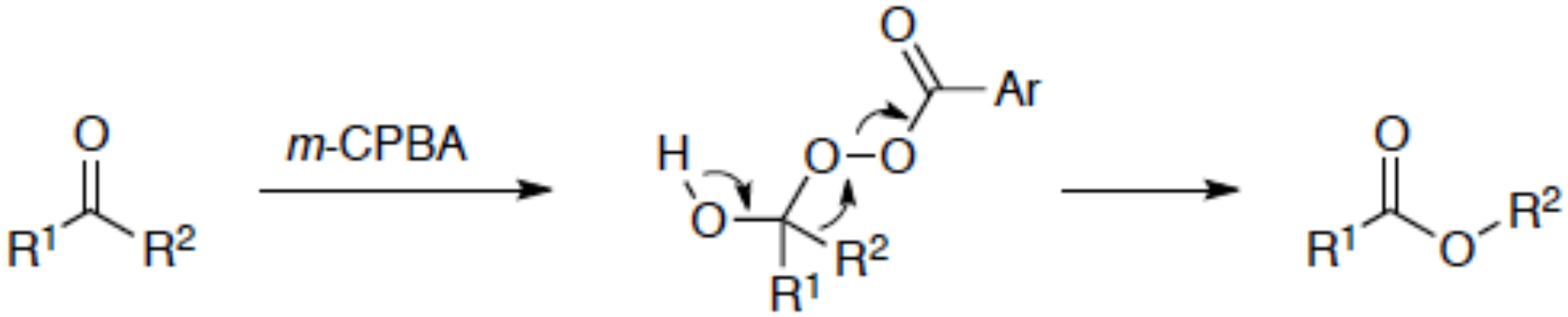
Schmidt Rearrangement of Ketones



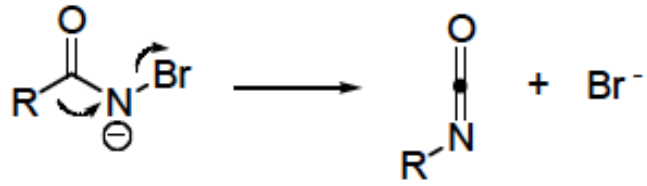
Schmidt Reaction



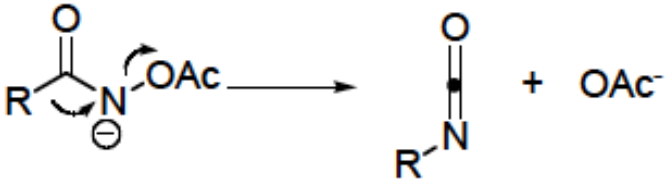
Mechanistic analogy to Baeyer-Villiger reaction



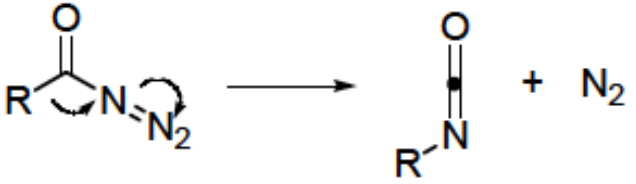
Migration of Carbon to an Electron Deficient Heteroatom



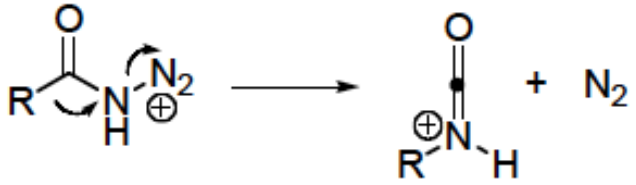
Hofmann



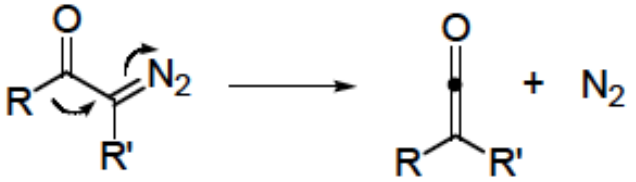
Lossen



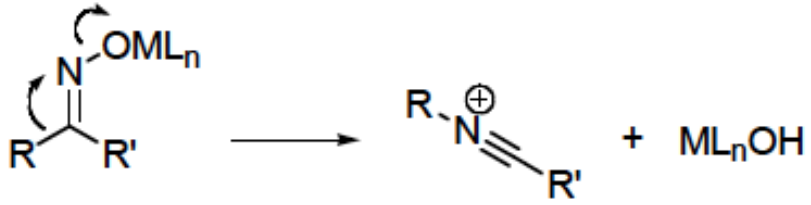
Curtius



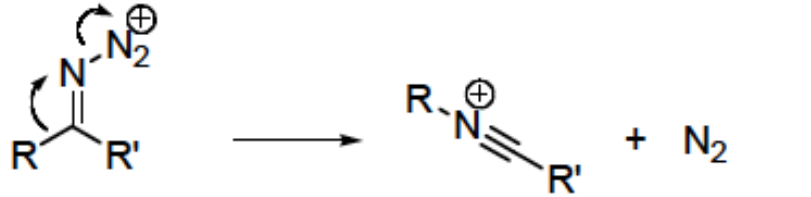
Schmidt



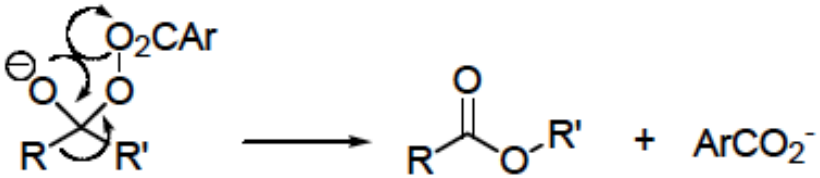
Wolff



Beckmann

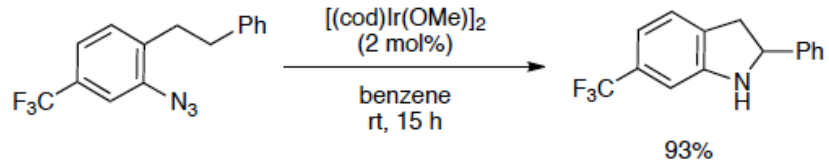


Schmidt

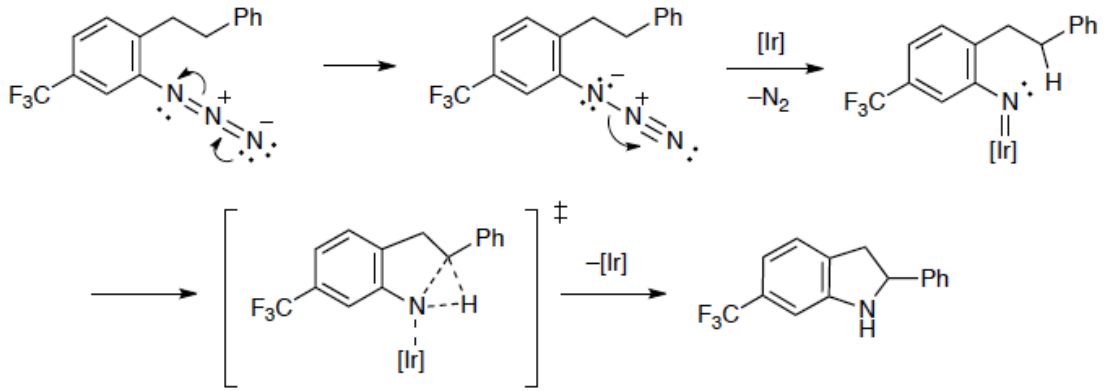


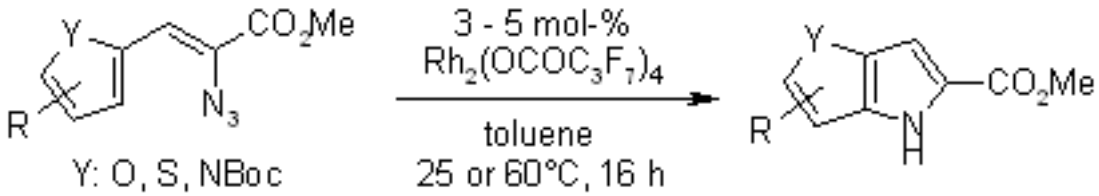
Baeyer-Villager

Metal catalyzed C–H insertion



Mechanism





Azidinitation???