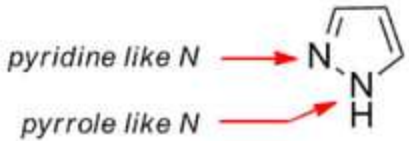
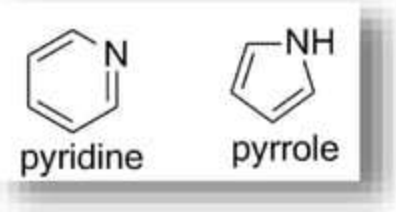
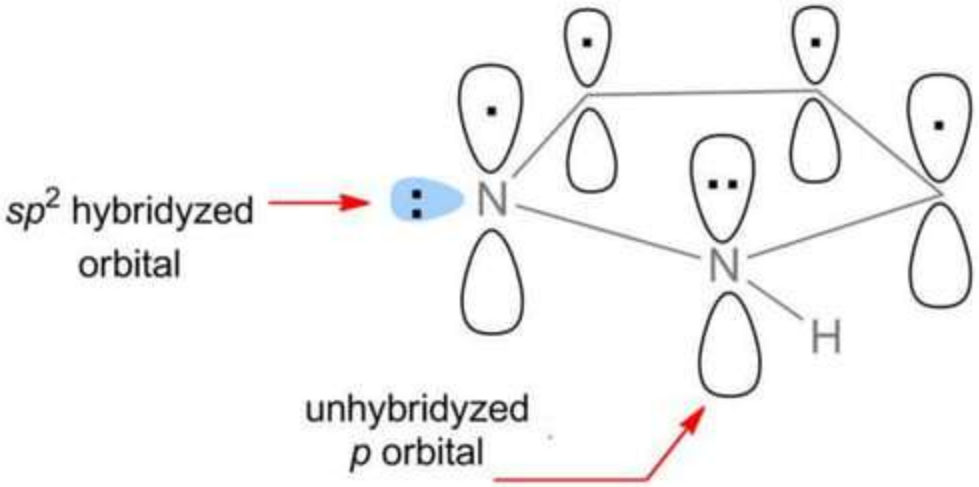
Properties

1. Aromaticity







Properties

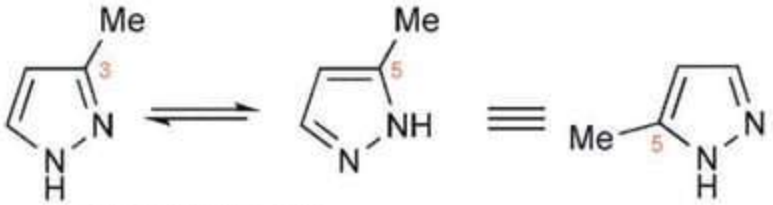
1. Aromaticity

- Pyrazole have 3 C and 2 N , all are sp^2 hybridized
- sp^2 hybridization is planar, it makes a planar pyrazole ring structure.
- Each ring atoms also contains unhybridized p orbital that is perpendicular to the plane of σ bonds (plane of ring).
- Here p orbitals are parallel to each other, so overlapping btwn p orbitals is possible.
- the total nu of non bonding e- are 6 (3 of three C, 1 from one N and 2 of other N)
- The resonance of 6 e- follows the Hückel's rule
- So the pyrazole is aromatic .

Properties

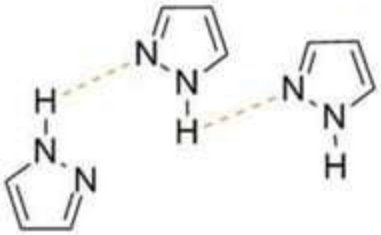
2. Tautomerism

- Rapid migration of hydrogen from one nitrogen to the other.



3(5)-methylpyrazole

3. Hydrogen bonding

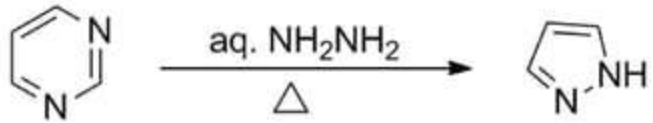


2 Hydrogen bonding within 2 molecules (cyclic dimer)

Synthesis

1. From pyrimidine

- Pyrimidine is very susceptible to nucleophilic addition.
- it reacts with hot hydrazine solution to give pyrazole.



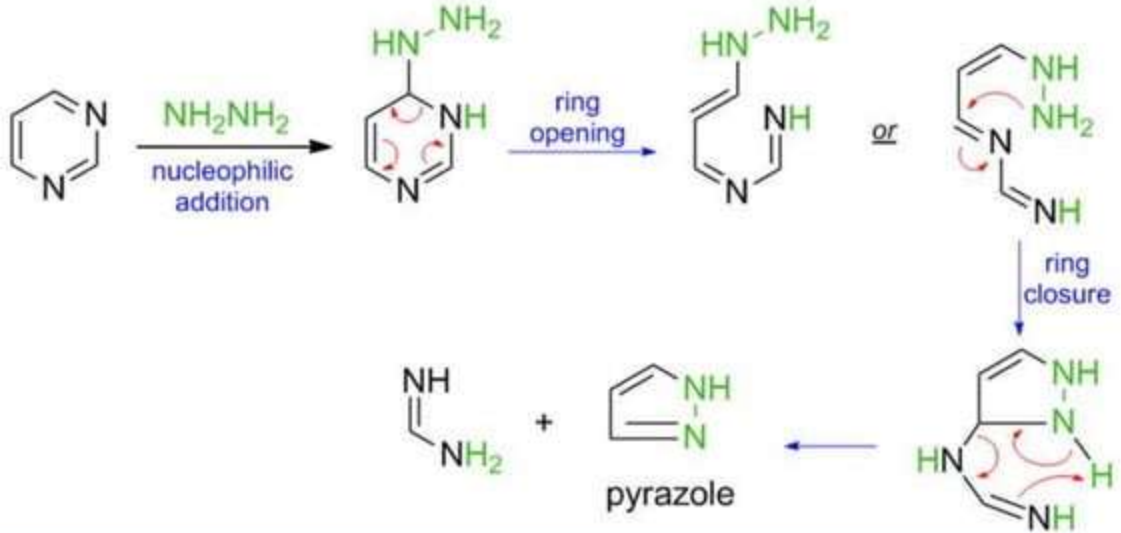
Pyrimidine pyrazole

Synthesis

1. From pyrimidine

mechanism

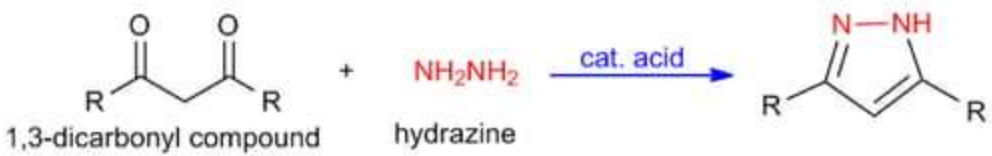
- Mechanism follows Addition of Nucleophile Ring Opening Ring Closure (ANRORC) sequence.



Synthesis

2. Knorr pyrazole synthesis

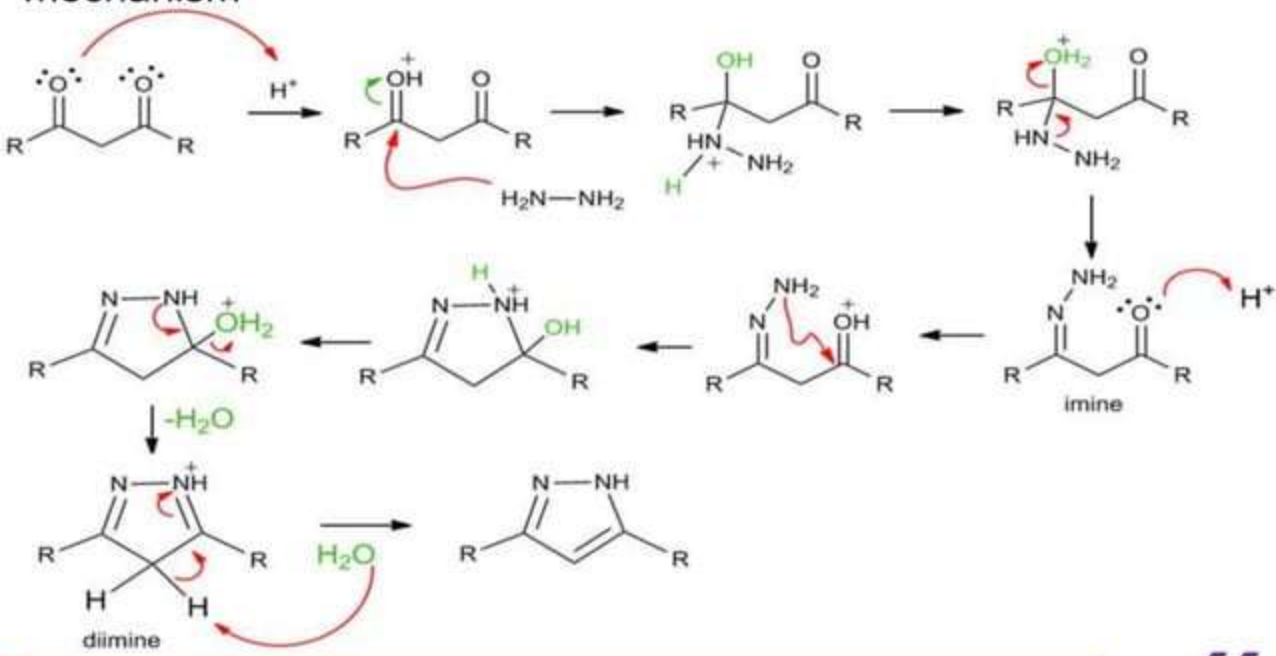
- Rxn convert a hydrazine or its derivatives and a 1,3-dicarbonyl compound to a pyrazole using an acid catalyst.



Synthesis

2. Knorr pyrazole synthesis

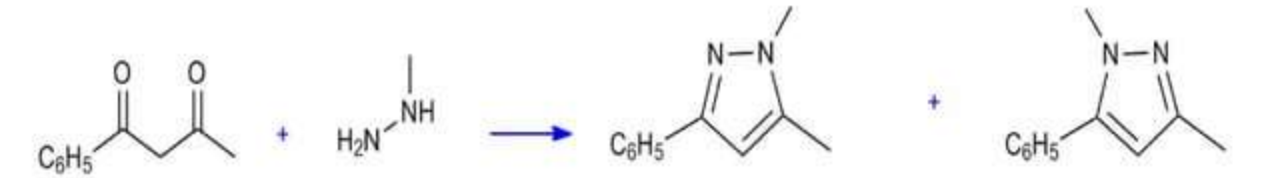
mechanism



Synthesis

2. Knorr pyrazole synthesis

Examples



1-phenylbutane-1,3-dione + methylhydrazine → 1,5-dimethyl-3-phenylpyrazole + 1,3-dimethyl-5-phenylpyrazole

unsymmetrical dicarbonyl compound

isomeric mixture

Synthesis

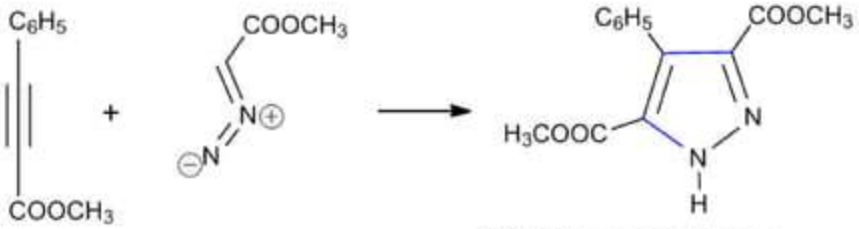
3. From Nitrile Imines

- Pyrazoles are produced by the <u>dipolar cycloaddition</u> btwn alkynes with nitrile imines.

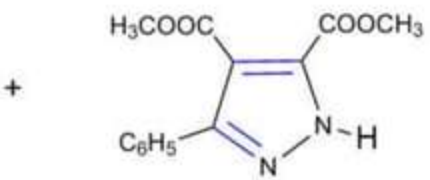
Synthesis

4. From diazo compound

- Diazo compound adds to an acetylenic derivative gives pyrazole



3,5-Dicarbomethoxy
-4-phenylpyrazole



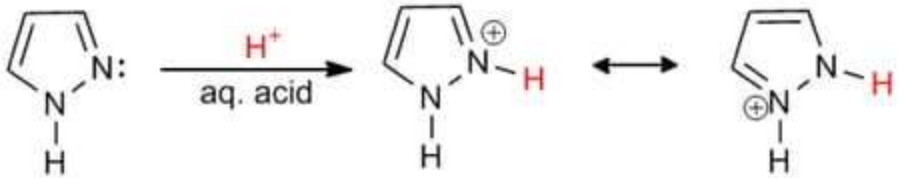
4,5-Dicarbomethoxy
-3-phenylpyrazole

Reactions

1. Electrophilic addition to N

a. Protonation (basic property)

- Pyrazole accept proton, act as base.

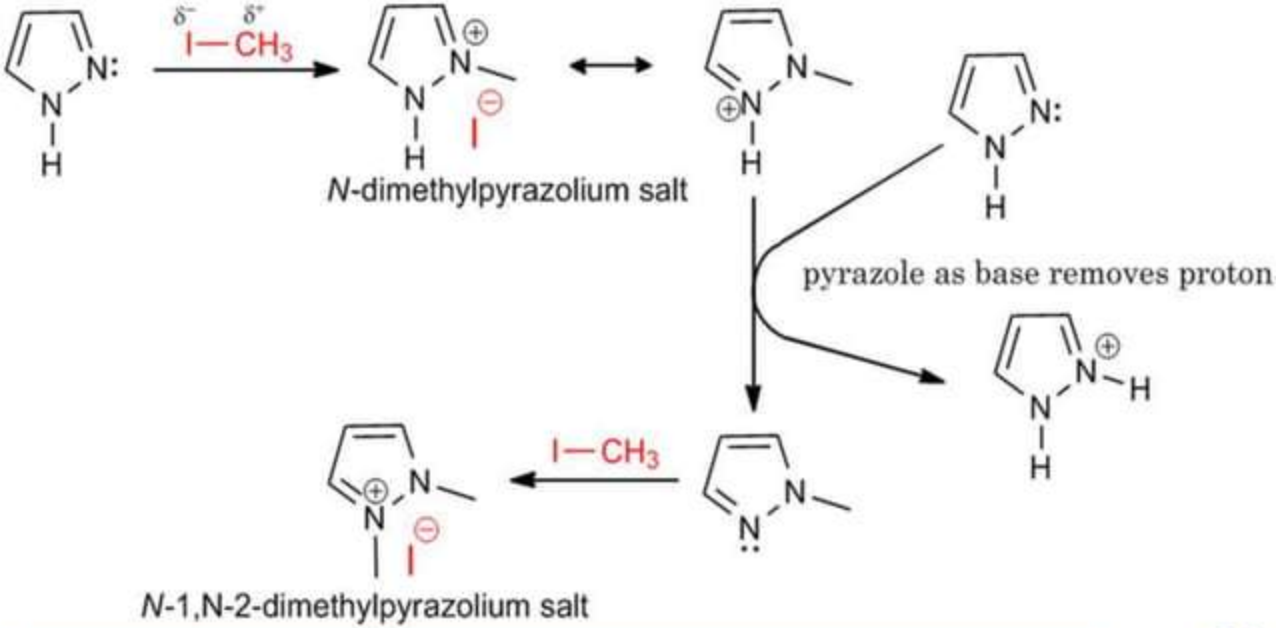


pyrazolium cation

Reactions

1. Electrophilic addition to N

b. *N*-alkylation



Reactions

1. Electrophilic addition to N

b. *N*-alkylation

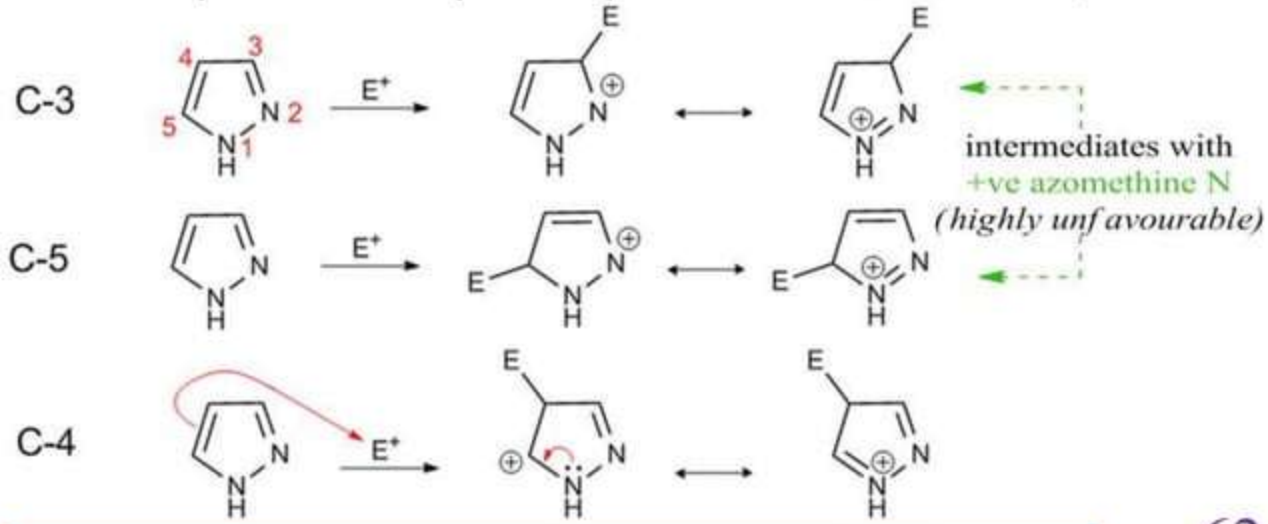
- Pyrazole reacts with alkyl halide and first gives *N*-alkyl pyrazolium salt.
- This salt can lose an *N*-proton in an equilibrium with unreacted pyrazole, generating *N*-alkyl pyrazole.
- *N*-alkyl pyrazole reacts with alkyl halide and gives *N*-1,*N*-2-dialkylpyrazolium salt.

Reactions

2. Electrophilic substitution to C

Pyrazole undergoes electrophilic substitution reaction at 4th position.

- Electrophilic attack at possible positions with intermediates.



Reactions

2. Electrophilic substitution to C

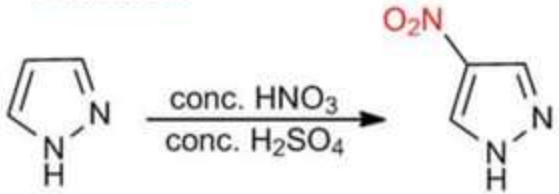
- Electrophilic attack at C-3 & C-5 generates highly unstable +vely charged azomethine intermediate.
- Electrophilic attack at C-4 completes without any such highly unstable intermediate.
- Thus Ts is much higher for C-3 & C-5 attack than C-4.
- So…

- Electrophilic attack takes place readily at neutral *or* alkaline media as pyrazole protonated pyrazole is more resistant to electrophilic attack than pyrazole.

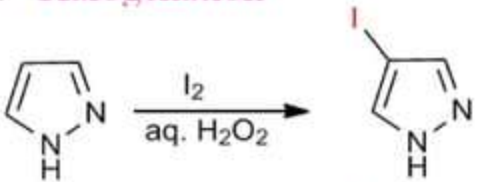
Reactions

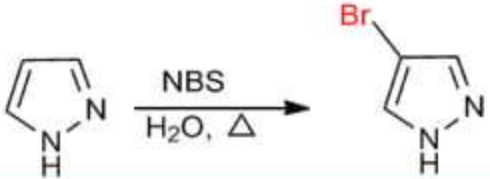
2. Electrophilic substitution to C

a. Nitration



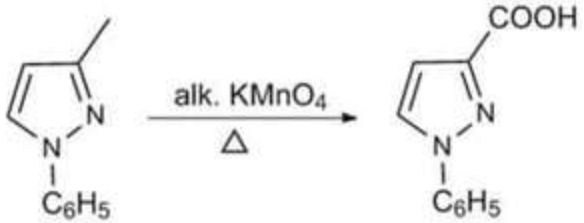
b. Halogenation



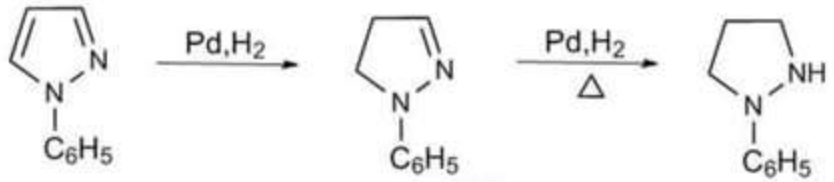


Reactions

3. Oxidation



4. Reduction



1-phenylpyrazole

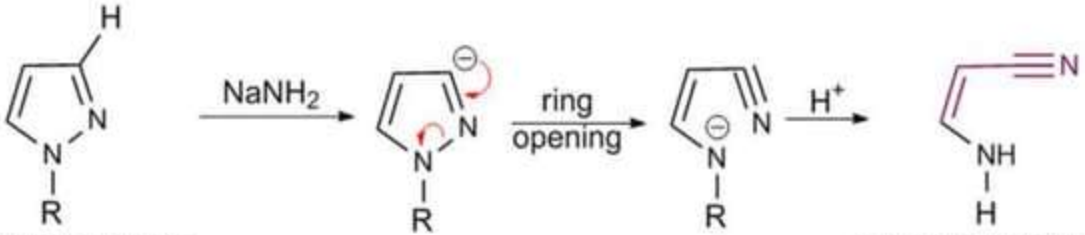
1-phenyl-4,5-dihydropyrazole

1-phenylpyrazolidine

Reactions

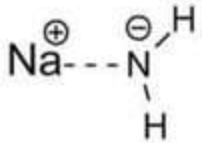
5. Ring opening

- *N*-substituted pyrazole reacted with strong base (sodamide) cause ring opening



N-substitutedpyrazole

acrylonitrile derivative

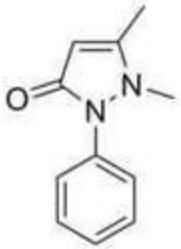


Medicinal Use

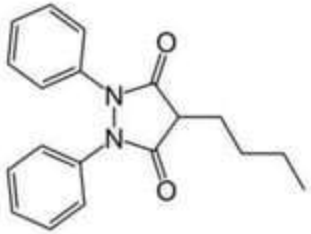
- Many synthetic pyrazole compounds are of importance as dyes and medicines.

E.g.

Antipyrine - used as an antipyretic ,analgesic
Tartrazine - as a yellow dye for food
Phenylbutazone - an anti-inflammatory drug



antipyrine



phenylbutazone