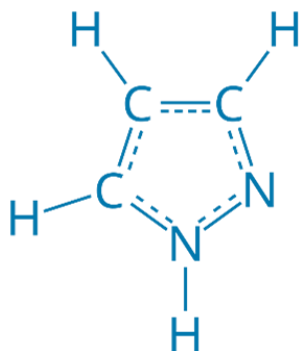


Pyrazole

Chemical Formula:

- $C_3H_4N_2$



Physical Properties:

Property	Value
Appearance	White crystalline solid
Melting Point	~66 °C
Boiling Point	~186 °C
Solubility	Soluble in water, alcohol, ether
Basicity	Weakly basic

Medicinal Uses:

- Found in **analgesic**, **anti-inflammatory**, **antipyretic**, and **antidepressant** drugs.
- Examples:
 - Phenylbutazone**: Anti-inflammatory
 - Celecoxib**: COX-2 inhibitor (pyrazole ring)
 - Sildenafil (Viagra)**: Pyrazole moiety contributes to activity

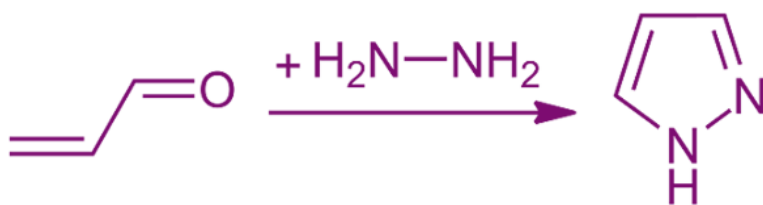
Synthesis of Pyrazole

Condensation of 1,3-Dicarbonyl Compounds with Hydrazine (*most common method*)

Reactants:

- **1,3-diketones** (e.g., acetylacetone)
- **Hydrazine** (NH_2NH_2) or substituted hydrazines

Reaction:



Mechanism:

1. Formation of hydrazone at one carbonyl
2. Intramolecular cyclization
3. Elimination of water → Pyrazole ring

Advantages:

- Simple, high-yielding, allows substitution at 3 and 5 positions

Knorr Pyrazole Synthesis

- **Reactants:** α-hydrazino ketones + β-ketoesters
- **Use:** For substituted pyrazoles with varying groups at C-3 and C-5

From α,β-unsaturated ketones and hydrazines

- Hydrazine adds to the double bond and then cyclizes.

Reactions of Pyrazole

A. Tautomerism:

- Pyrazole exhibits **prototropic tautomerism** between N-1 and N-2.



- This affects reactivity at the nitrogen atoms and the electron density distribution on the ring.

B. Electrophilic Substitution Reactions (EAS):

- Due to the electron-rich ring, **EAS is favored at position-4 (C-4).**

1. Nitration:

- Reagents: $\text{HNO}_3 + \text{H}_2\text{SO}_4$
- Major product: 4-nitropyrazole

2. Halogenation:

- $\text{Br}_2/\text{FeBr}_3 \rightarrow 4\text{-bromopyrazole}$

3. Sulfonation:

- Rare, only under harsh conditions.

C. Nucleophilic Substitution Reactions (NAS):

- Less common due to electron-rich ring.
- Possible if electron-withdrawing groups (e.g., NO₂) are at C-3 or C-5.

D. Metal Complex Formation:

- Pyrazole can coordinate metals through **N-2**.
- Often used in ligands like **tris(pyrazolyl)borates** for transition metal complexes.

E. Ring Functionalization:

- Lithiation at C-4 or C-5 followed by electrophile quench (e.g., CO₂, RCHO).
- C-alkylation possible via deprotonation with strong base (LDA).

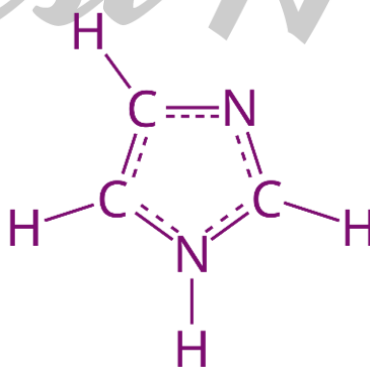
F. Oxidation & Reduction:

- Not easily reduced due to aromaticity.
- Oxidation at N possible under strong conditions → N-oxides.

Imidazole

Chemical Formula:

- C₃H₄N₂



Physical Properties:

Property	Value
Appearance	White crystalline solid
Melting Point	~90–91 °C
Boiling Point	~257 °C
Solubility	Very soluble in water and polar solvents
Basicity	More basic than pyrazole

Medicinal Uses:

- Present in biological molecules and many drugs.



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