

## SCHIFF BASES

It was first reported by Hugo Schiff at (1864). *Under specific conditions when any primary amine reacts with an aldehyde or a ketone, imine is formed, which **structurally** is a nitrogen analog of an aldehyde or ketone in which an imine group (C=N) has replaced the carbonyl group (C=O).*

*Schiff base is imine contains at least one aromatic moiety and is stable in comparison to imine due to conjugation.*

*Hydrazone is imine or schiff base in which the amine part is hydrazine.*

*Acyl hydrazone is schiff base in which the amine part is hydrazide.*

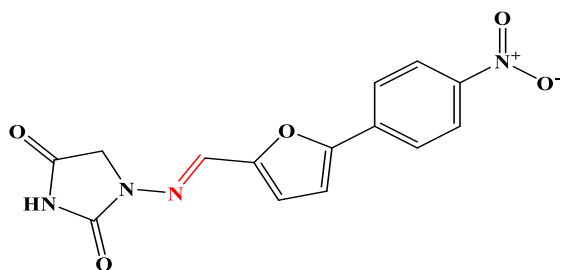
## Biological Activities

*Schiff bases derivatives may act as:*

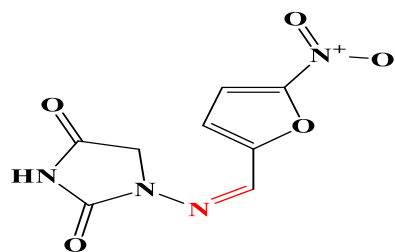
- Antibacterial
- Antifungal
- Antitubercular
- Antiviral
- Anticancer
- Anti-inflammatory
- Analgesic

## Role Of Schiff Base Compounds In Organic Pharmaceutical Chemistry

### DRUGS



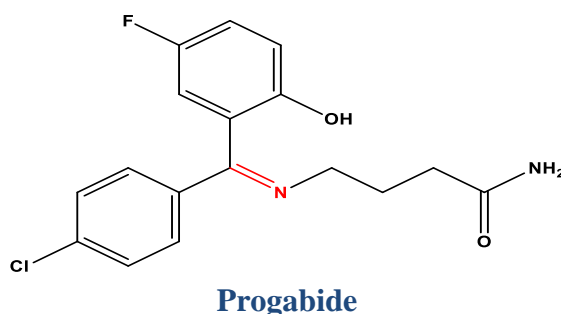
**Dantrolene**



**Nitrofurantoin**

**Q// Are these structures imines? Schiff bases? Hydrazones? Azomethines?**

## PRODRUGS

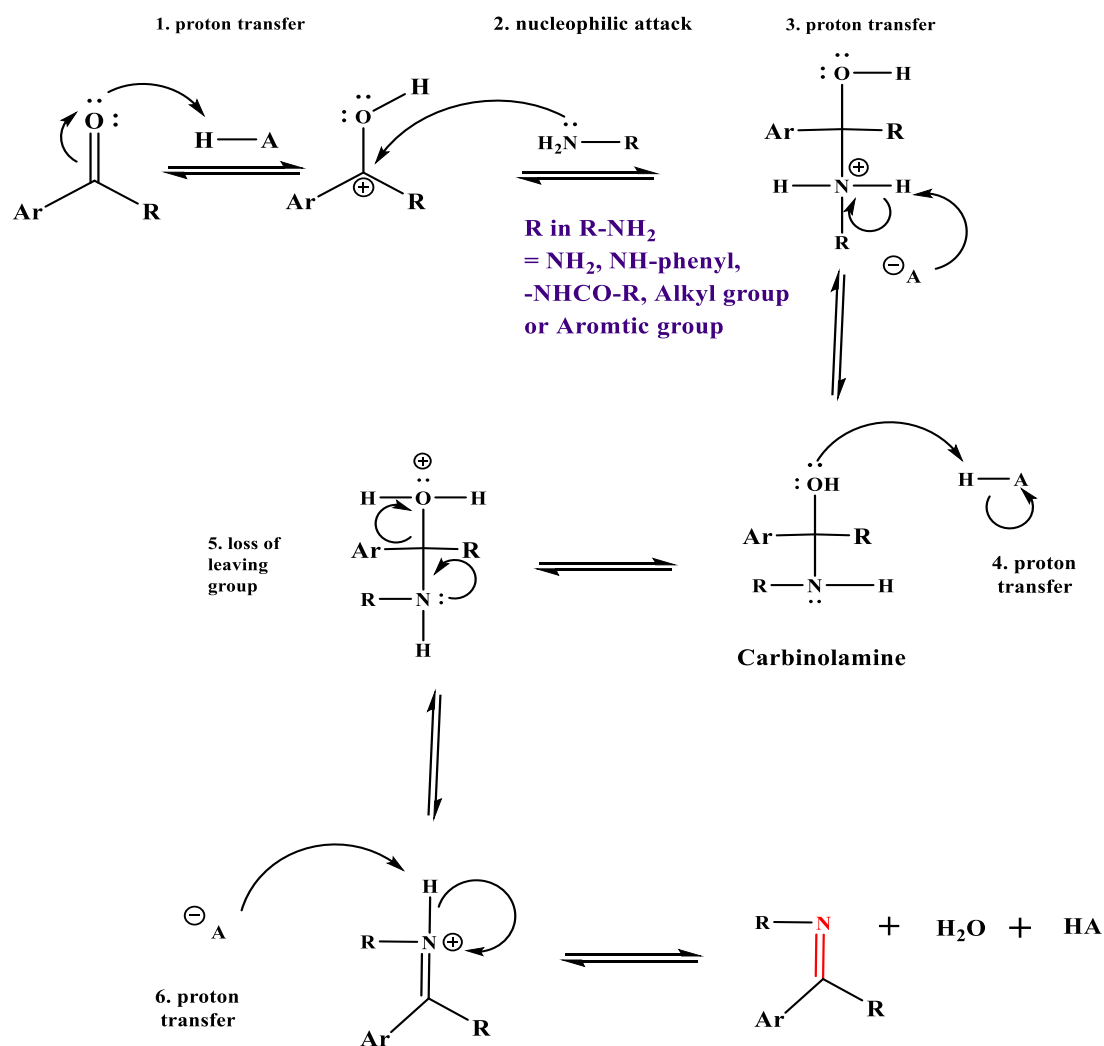


### Chemistry Of Schiff Base

*Aldehydes or ketones will react with a primary amines to form imines in mildly acidic conditions.* A six-step mechanism for imine formation (scheme 4.1) is best to be divided into two parts:

- The first three steps produce an intermediate called a carbinolamine and
- The last three steps convert the carbinolamine into an imine

*When the pH is around 4.5, greatest rate of reaction will be obtained. As the acidity decreases above pH 4.5, the rate decreases because less and less of the carbinolamine is present in the reactive protonated form. As the acidity increases below pH 4.5, the rate of the reaction decreases because more and more of the amine becomes protonated. As a result, less and less of the amine is present in the nucleophilic nonprotonated form; so optimal pH to be required.*



Scheme (4.1): Mechanism of Schiff base formation.

### Procedure

- Place 0.3g of 4-chlorobenzaldehyde in round-bottomed flask and add 2.5ml of absolute methanol to it; stir the mixture until clear solution is obtained (solution 1).
- Add 3 drops of glacial acetic acid to the solution 1 with stirring for 10 minutes (solution 2).
- Weigh 0.28g of INH and add it to the solution 2; continue stirring for additional 15 minutes and observe the changes.
- Collect the product by filtration and dry it by oven.
- Crystallization from boiling methanol (approximately 15-20ml) and check the TLC using Toluene: Ethyl acetate: Ethanol (2:2:0.5) as eluent. Finally calculate the % of yield.