

Review on Types of Three Components Reactions

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Abstract: This review described the three-component chemical reactions, their types, how they got there, and their importance in preparing compounds that have biological and pharmaceutical significance and in other magazines of chemistry. Among them are the enammin-mannich reactions, the formazane reactions, the sulfazane, and some annular closure reactions. Three-component interaction is included in the preparation of the pharmaceutical compounds, as they need the shortest steps and the fastest results, so such interactions are used in the preparation of many drugs and the simplest examples are tramadol and some anesthetics used in surgical processes.

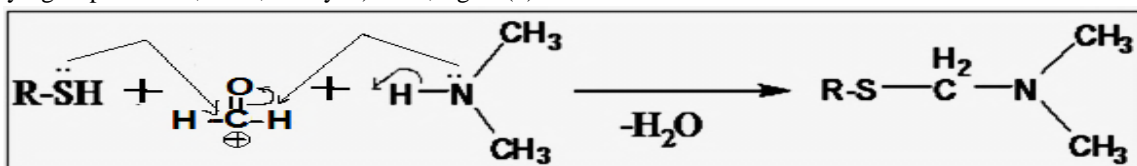
Keywords: mannich reaction, formazane reaction, sulfazane reaction, three components reaction.

I. Introduction

The formula of three components reactions can be inferred using collision theory. Sometimes the initial double reaction velocity equation is called the law of mass activity. The Mass effect was drafted from the chemical scientists⁽¹⁻⁴⁾(Goldberg and Waggie) in 1864. One of these interactions is the interaction of the addition of rings. Based on that theory, it assumes that a triple reaction takes place as three substances interact at one time and in a "one step", but the possibility of collision⁽⁵⁻⁹⁾ of three molecules from the three substances at the same moment is very weak, and in particular it is necessary at the same time that these shocking molecules It has enough energy to complete the reaction⁽¹⁰⁻¹⁵⁾. Therefore, we find that it is unlikely that a triple reaction will take place in the first reaction method⁽¹⁶⁻²⁵⁾ that is, in one step. Elsewhere, we will see that the interaction of three substances takes place in several steps⁽²⁶⁻³⁵⁾, not in one step.

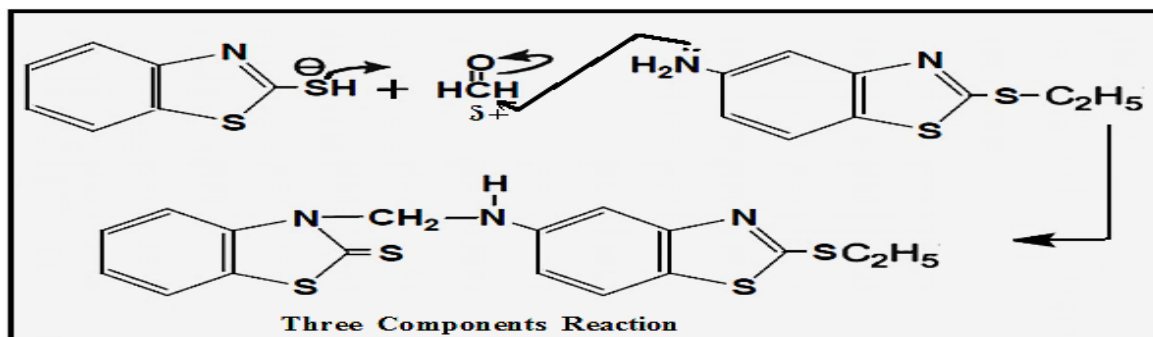
II. Types of Three Components Reactions⁽¹⁴⁻¹⁶⁾:

Mechanism of three components reactions⁽¹⁴⁻¹⁶⁾ involve the reaction between three compounds (two amine groups in same compound {NH₂}, amine and carbanion{CH₂⁻} of any alkyl or ketone, amine {NH} and Thiol{SH} in same compound, di- thiol group {SH}, di amine groups, hydroxyl {OH} and amine group {NH},) with carbonyl of (carboxyl group in acid, ester, aldehyde)⁽¹⁴⁻¹⁶⁾, figure(1).



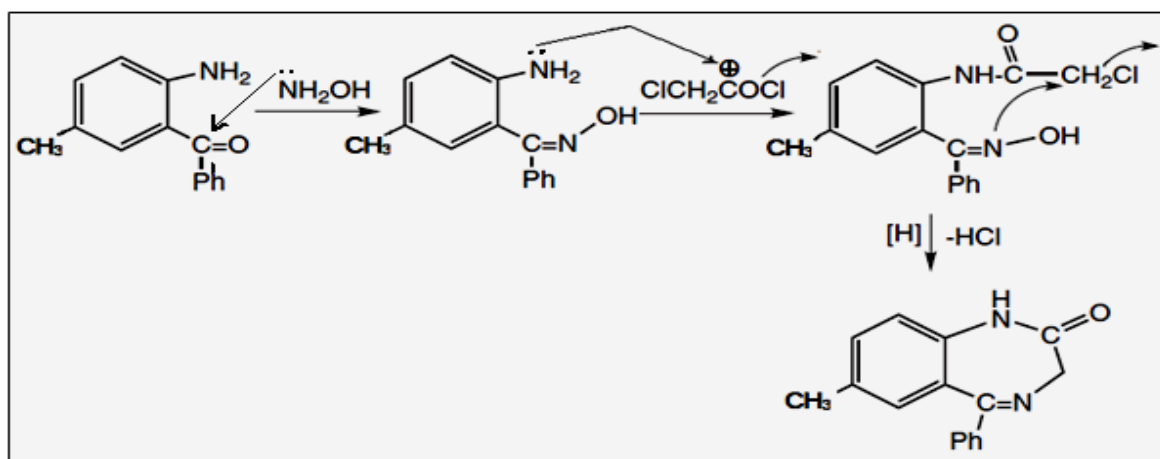
Fig(1): Three components reaction via formaldehyde, secondary amine and thiol group

Also It occurs via the reaction between (Thiol SH ,formaldehyde $\text{H}_2\text{C}=\text{O}$, amine NH–aliphatic or aromatic) ,figure(2) .



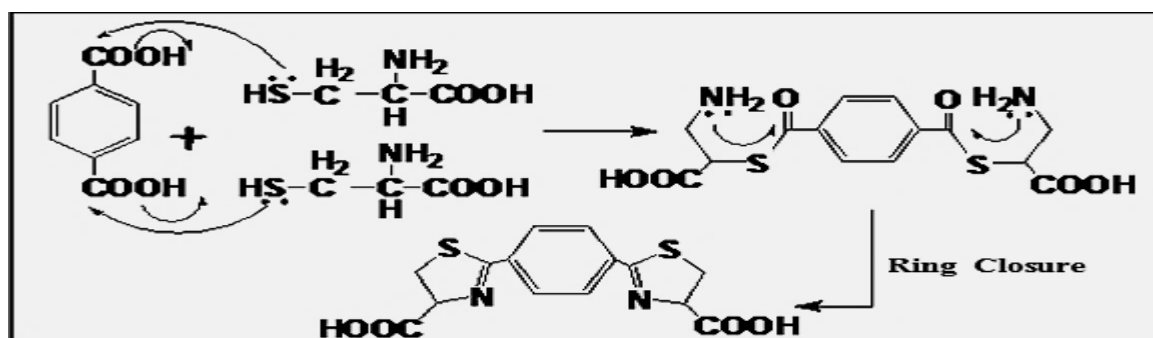
Fig(2): Three components reaction via thiol and amine groups with Formaldehyde

Also three components reaction occurs by departing of leaving group ,then imine group –Schiff base will react with $-\text{CH}_2\text{-Cl}$ to formation cycle⁽³⁶⁻⁴⁵⁾ (seven membered ring), figure(3)



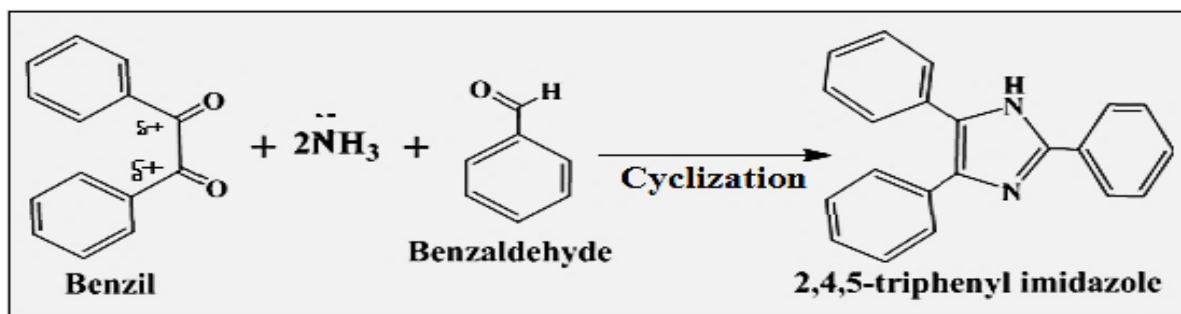
Fig(3): Three components reaction via Imine group

While in other reaction from type of three components reaction ,noted that the reaction occurs between (di- thiol group SH and amine NH group) in same compound with carbonyl of (carboxyl group) via ring closure reaction in acid medium, figure(4).



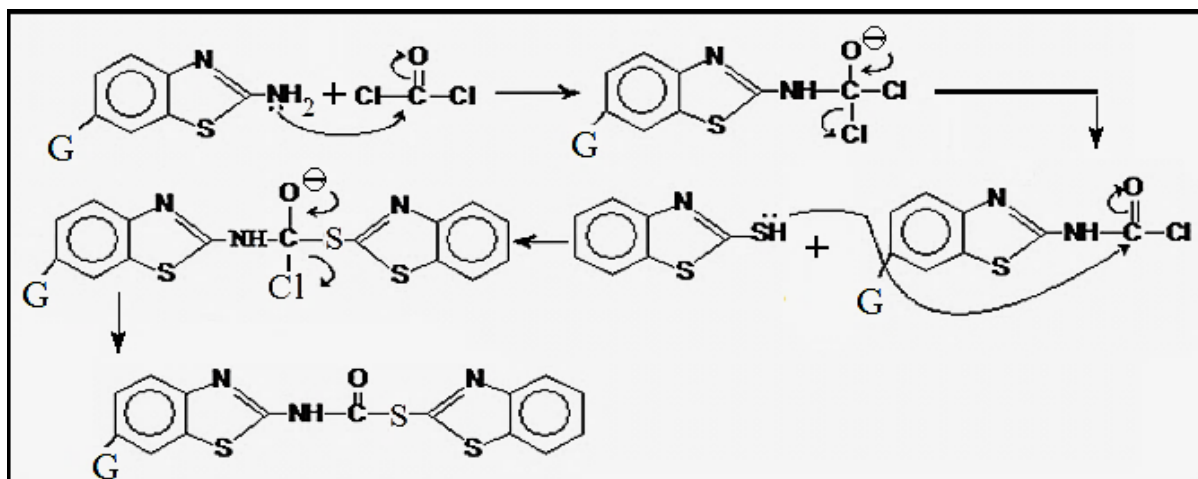
Fig(4): Three components reaction via thiol and amine groups through Ring Closure

Also three components reaction occurs via reaction between (Ketone, Aldehyde like benzaldehyde ,Amine compound), that acts⁽⁴⁶⁻⁵¹⁾ (Nucleophilic- Electrophilic) reaction, figure(5).



Fig(5): Three components reaction via carbonyl with amine through Ring Closure

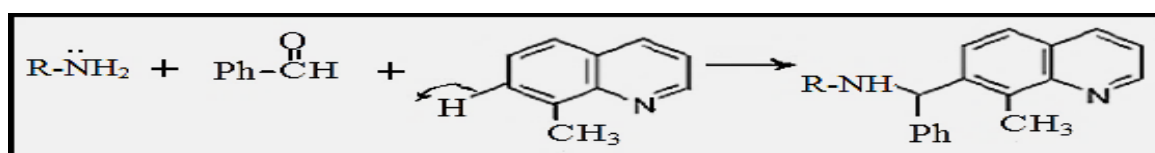
Besides that ,this type of reaction occurs through the reaction between amine group (R-NH) with carbonyl group (-C=O) of (COCl₂), figure (6).



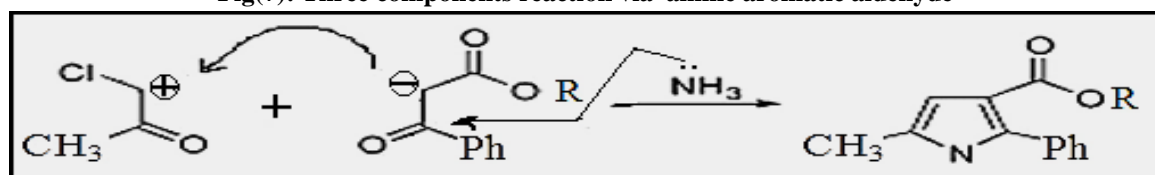
Fig(6): Three components reaction via amine group with thiol and carbonyl in (COCl₂)

III. Other Types of Three Components Reactions

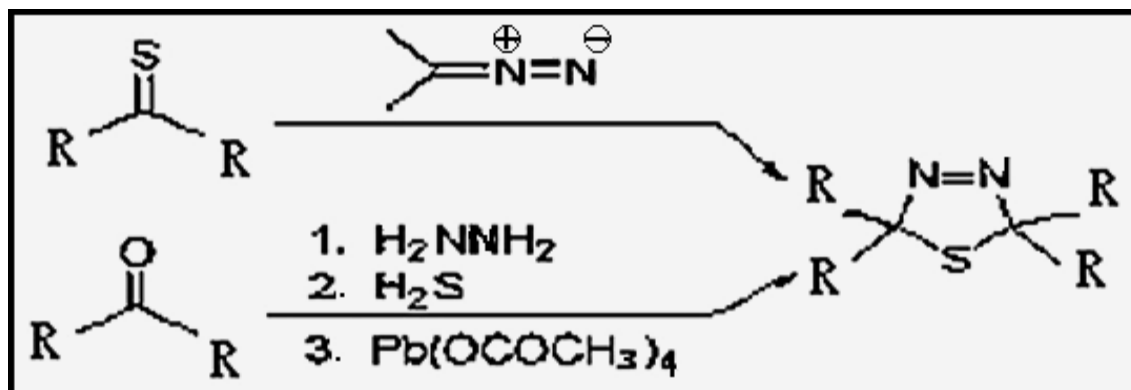
Other types of three components reaction produce from reaction between aromatic aldehyde and primary amine⁽⁵²⁻⁶⁰⁾ with aromatic compounds in substitution reaction, figure (7) ,also it occurs via reaction of carbanion and amine compound with carbonium ion , figure(8), or via hydrazo with thion and carbonyl⁽⁶¹⁻⁶⁷⁾ groups, figure (9).



Fig(7): Three components reaction via amine aromatic aldehyde

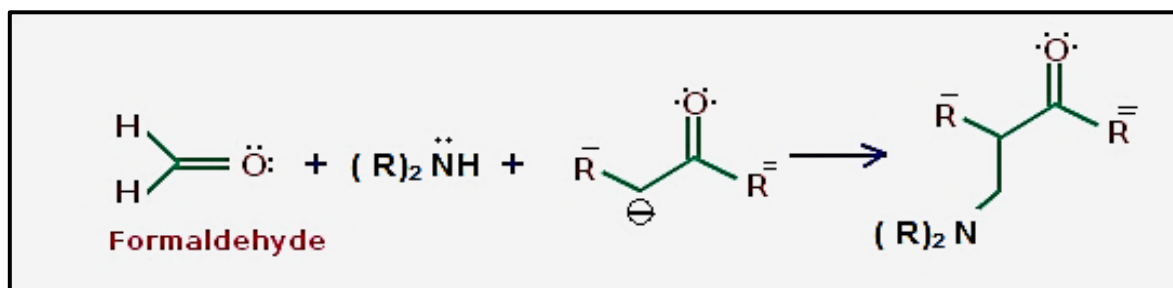


Fig(8): Three components reaction via amine and carbanion with carbonium ion

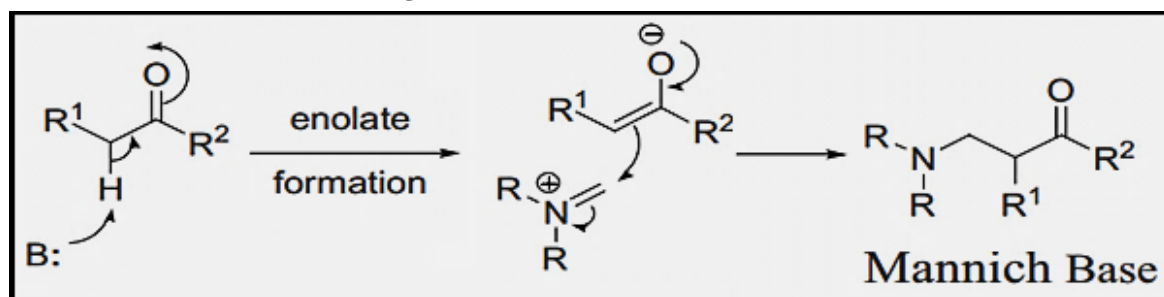


Fig(9): Three components reaction via Hydrazo with Thion and carbonyl groups

Mannich Reaction-Inamine: Mannich Reaction (Inamine) is a type of three components reaction that involves reaction of secondary amine with carbonyl compounds (aldehyde) and carbanion of (ketone) which include (alpha-hydrogen atom) in their structure⁽⁶⁸⁻⁷⁰⁾, figure (10) and keto-enol form of inamine compounds.

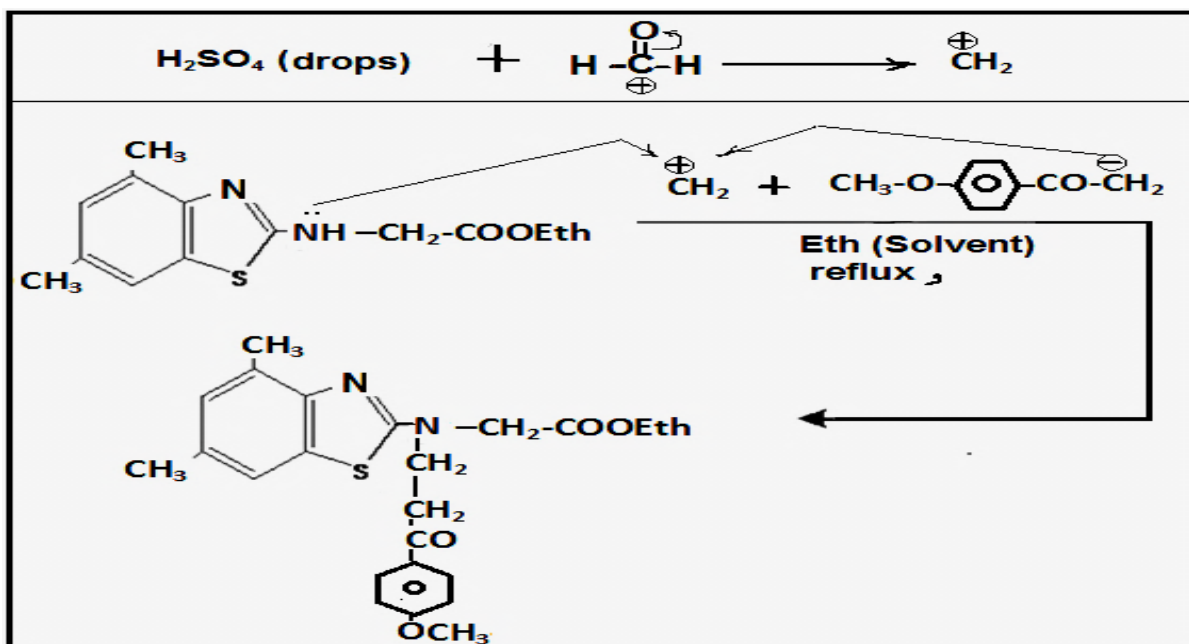


Fig(10):Mannich Reaction (Inamine)



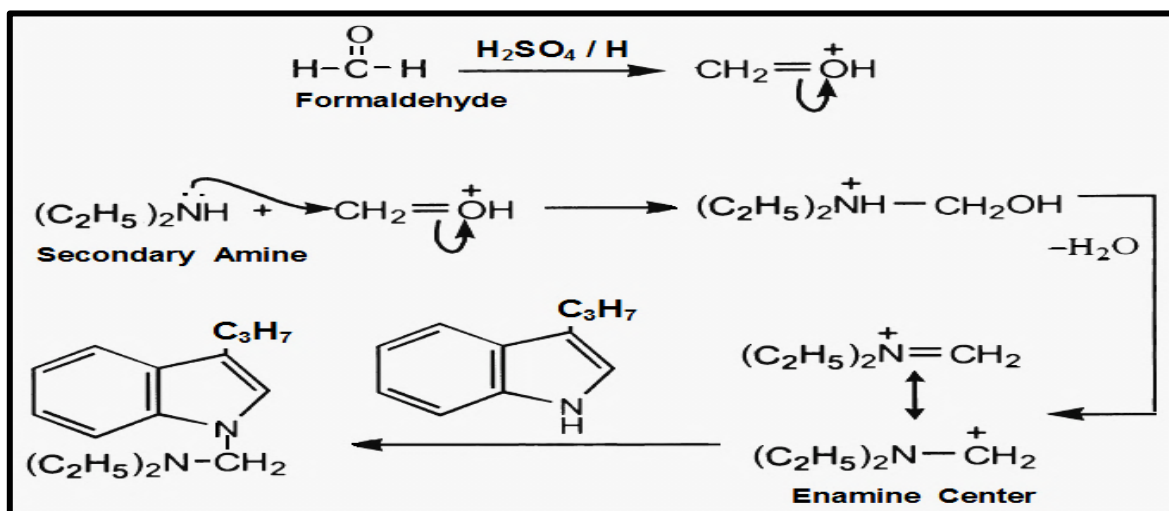
Fig(11): Keto-Enol form of Inamine

Mechanism of Mannich reaction (Enamine): Sulfuric acid is used in the Mannich reaction to protonate the aldehyde and thus the formation of the carbonium ion, which represents the first component of the Mannich reaction, then pulled a proton from the ketone from the (alpha site- H) to form the carbanion which represents the second component of the Mannich reaction and is followed by the third component of the Mannich reaction which is the secondary amine, figure(12).

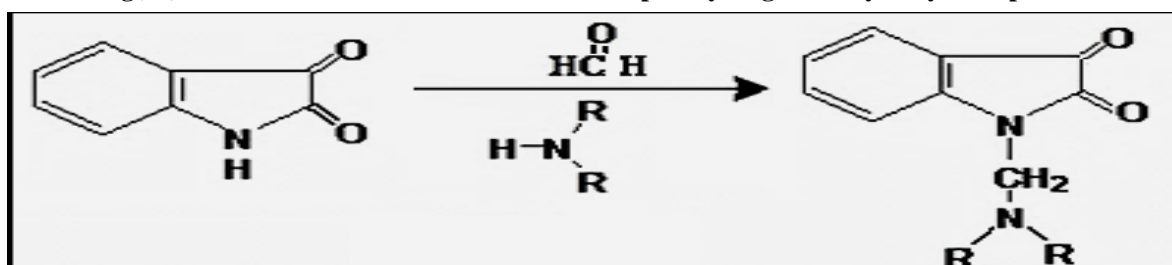


Fig(12): Mechanism of Mannich Reaction

Other types of mannich base occur via reaction of carbonyl of aldehyde and amine with carbanion from alpha-hydrogen of any alkyl compounds not restricted on ketone like figure(13), or from reaction between formaldehyde with di amine compounds, figure (14).

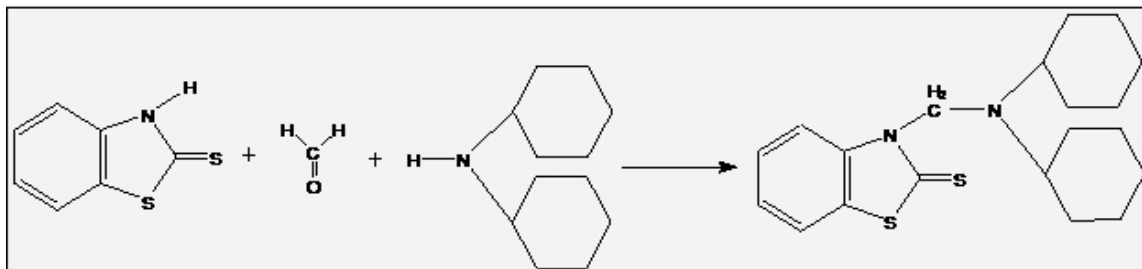


Fig(13): From reaction with carbanion from alpha-hydrogen of any alkyl compounds



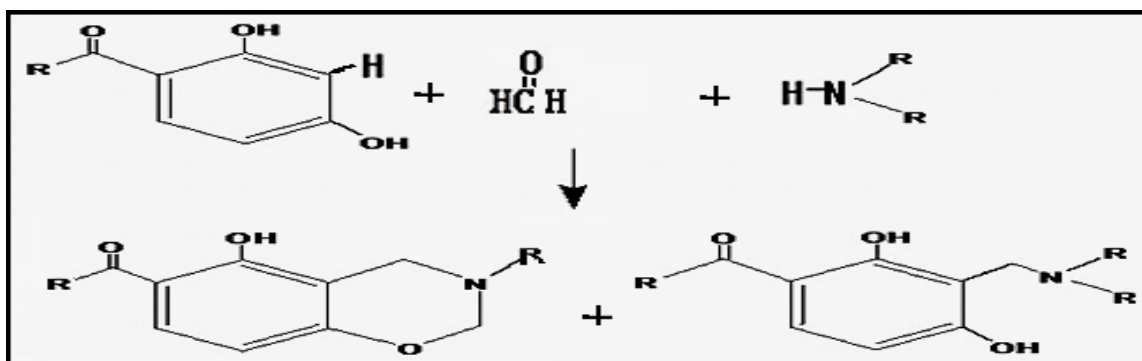
Fig(14): From reaction of formaldehyde with di amine compounds

While there is other type of three components reaction occurs between di-cyclic amine with formaldehyde, it give antibacterial compound against many types of bacteria like E-coli⁽⁷⁶⁻⁷⁰⁾, figure(15)

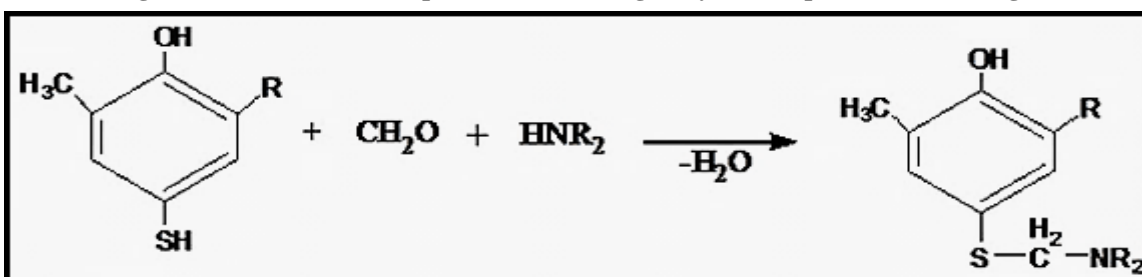


Fig(15): From di-cyclic amine with formaldehyde

The interaction of the secondary amine with aldehyde or ketone is the intermediate compound (carbinolamine) which does not lose hydrogen and thus does not turn into an amine compound. In any case, the compound (carbinolamine) is derived from the secondary amine where it loses its water molecule to be a double sphincter (C = C) and the resulting compound is called (inamine), and the enamine compounds are distinguished by their anti-fungal properties figure(16), especially those that contain sulfur within their composition and some are anti-malaria⁽⁷⁹⁾ like figure (17).



Fig(16): Some of three components reactions give cyclic compounds as antifungal



Fig(17): Product of three components reactions as anti-malaria agent

IV. Conclusion

Three-component chemical reactions include the interaction of three raw materials (nucleophile and electrophile) to form a single compound that changes the arrangement of atoms in chemical molecules, and in such a reaction we see the union of some molecules in other ways to form a form of a larger or more complex compound, or the dissociation of compounds to form smaller molecules, Or rearrange the atoms in the compound. Chemical reactions usually involve

breaking or forming chemical bonds. Chemical reactions play a large role in the metabolism of living organisms and in photosynthesis of plants that provide us with food and oxygen

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