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Biochemical Application of New Synthetic Compounds of Pyridine Derivatives Incorporating on Tetrazole Moieties

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ABSTRACT

Introduction: Pyridine has a liquid state, bad odor, pungent taste, toxic effects, and has the ability to mix with alcohol, water and some sperms, and it has many effects in the event of severe exposure such as suffocation. Methods: In this work, a new series of tetrazole derivatives is synthesized by reacting sodium azide with Schiff bases derivatives, which are prepared by condensation reaction between some pyridine derivatives (2-amino-5-chloropyridine, 2-amino-4-methyl pyridine) and some aromatic aldehydes (dimethyl aminobenzaldehyde, p-aminobenzaldehyde, p-chlorobenzaldehyde, p-bromobenzaldehyde, and salicylic aldehyde). Result: All the resulting compounds were characterized by FT-IR and milting points. The study of the biological activity of Schiff base derivatives and tetrazole derivatives against E. coli shows that all derivatives give positive results at different diameters, but the compounds (2,6,10) give a lower inhibition at concentrations of 100 mg/ml, as well as the compounds (2,3,5,7,9) give a lower inhibition at concentrations of 75 mg/ml. The compounds (6,8,10) give lower inhibition at concentration (100 mg/ml) against S. aureus, as well as the compounds (1,3,6,8,10) give lower inhibition at concentration (75 mg/ml). Conclusion: It was shown during the process of preparing the compounds that the difference in the groups substituted for the same compound leads to a difference in the percentages, reaction time, and biological activity of the resulting compounds.

Keywords: Heterocyclic compound, Schiff bases, Pyridine, Anti-bacterial

1 INTRODUCTION

Heterocyclic compound is a term given to any organic ring system that contains besides a carbon atom atoms of other elements such as sulfur, oxygen and nitrogen. Some of these compounds enjoy the stability of aromatic compounds and are called hetero cyclo aromatic compound, such as Pyrolle and Indole, and are similar of benzene in its properties where a Huckles role applies to it, whether it is composed of six atoms orless [1,2]

These compounds are found in nature and in many natural products such as hemoglobin and chlorophyll (Figure.1) and are found in vitamins, amino acids, enzymes and hormones that have an important role in metabolism processes such as Vitamin B, whose composition contain pyridine and vitamin C, which contains Furan, may have a role in metabolism and transmission of nerve information and many processes that take place inside the human body [3,4], which in turn are necessary for life.

Its importance has increased in recent year because of their activity as anti-viral [5], antidepressant [6], antibacterial [7], anti-inflammatory [8], herbicidal activity [9], antimalaria [10].

Pyridine is a heterogeneous hexagonal plane colorless cyclic compound has chemical formula C5H5N [11]. Its resembles benzene with the difference in the presence of an atom that is heterogeneous in its structure, which is nitrogen, which is electrophilic and negatively better than that of the carbon atom [12]. Pyridine has a liquid state, bad odor, pungent taste, toxic effects, and has the ability to

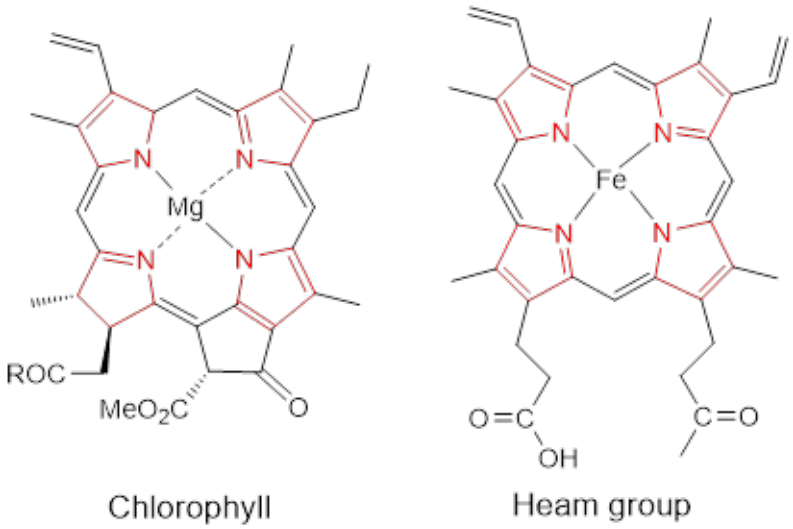

Fig. 1. Show the structure of chlorophyll and heam group.

mix with alcohol, water and some sperms, and it has many effects in the event of severe exposure such as suffocation, liver damage and eye inflammation [13].

It's one of the most important compounds on which it depends to form other important compounds that can be used in industrial fields such as manufacturing Medicines, as a solvent and a chemical reagent, as well as in the manufacture of DNA in the laboratory [14, 15].

pyridine has been laboratory prepared in 1876 by William Ramsay by reacting acetylene with hydrogen cyanide in a furnace and this process was the first laboratory organic industry for a heterogeneous ring procession and after successive attempts a Russian scientist managed to develop Reaction to obtain pyridine by relying on chemical reagents at a low price and this method is still used to prepare it [16]. found in many natural products such as (Diploclidine) and it is found in the roots and leaves of some plants such as the (Atropa Belladonna)and considred the skeleton of alkaloidsnicotine, niacin [17].

Pyridine derivatives can be combined with polymers such pvp (poly vinyl pyridine) and it's also found in many medicines such as Mimosine (anti-tumor), Ciclopirox(anti-fungal), Iproniazid(anti-depressant) [17], so its derivatives have wide range of biological activities such anti-microbial [18], anti-malaria, anesthetic , vasodilator [19], Antiviral [20], anti-cancer, Antitubercular [21].

Schiff bases are Imine compounds first prepared in the year 1864 [22] resulting from the interaction of primary amines with aromatic or aliphatic (ketones ,aldehydes) at certain condition of tempruture , solvent and catalyst [23].

Schiff bases compounds that result from the reaction of condensation of primary amines. With ketones called ketimines ,while which are derived from the interaction of amines with aldehydes, they are called aldimines and the reaction of aldehydes or ketones with acid hydrazides produces the hydrazones [24]. The general formula of Schiff's bases (R1R2C = NR3), where R2 and R1 are either aromatic, aliphatic or hydrogen groups, while R3 attached to the nitrogen atom is either alkyl or Ariel group.

Schiff bases compounds with a solid state (crystalline) or oily with high thermal stability Relatively, they are often colored, and their solubility in water is not possible, but they dissolve in organic solvents. As for their formation reactions, they are reversible, where it is possible that the products giving off raw materials due to the presence of a water molecule resulting from condensation, and this is what I mean with the hydrolysis of Schiff bases [25].

The stability of these compounds related to the aromatic and aliphatic properties of the raw materials required for its preparation, where the compounds resulting from the reaction of aliphatic amines are mostly liquids, while the derivatives resulting from condensation aromatic amine with aromatic aldehyde are more stable [26] The Schiff's bases compounds are among the important mediators in the preparation of compoundsand it possess interesting biological activity where they used as anti-tumor materials,Angiotension-II(AII) Receptor [27], anti-microbial- anti-fungal [28], anti-oxidant [29], anti-bacterial [30] and antiviral [31], also as sedatives ,anticancer -anti-TB activity [32], cytotoxic activity [33], anti-anxiety,as they were distinguished by their anti-tuberculosis [34].

It is used in the manufacture of printer ink and many dyes, as it was used in Diels-Alder reactions and in the reactions of organic synthesis and as insecticides because they contain active group such as chlorine and azo.

Tetrazole is a type of heterogeneous solid cyclic compounds whose ring structure consists of four nitrogen atoms and one carbon atom with two hydrogen atoms .Its color white to yellow with weak characteristic odour as well as it has high acidity due to the presence of four

nitrogen atoms and is classified into 1H -5-substituted Tetrazole, 2H -5-substituted Tetrazole , 3H-5- substituted Tetrazole [35]. The tetrazol ring is classified within aromatic rings as it contains 6 π - electrons, two of these electrons are provided by the electronic duplex located on one of the nitrogen atoms, while the other electrons are provided by the remaining nitrogen atoms [36], and its solubility is high in polar solvents such as DMSO, alcohols and water [37]. The World Health Organization has declared the Tetrazole ring an important drug in the design of pharmaceutical compounds due to its ability to act as bioisoester to carboxylicacid [38], it therefore used to prepare drugs of anti-bacterial [39], anti-fungal, anti-convulsant, anti-microbal [40], analgesic [41], anti-hypertensives, anti-inflammatory [42], Anti-candidal [43], anti-cancer [44], anti- tumor and anti-viral agents, as well as anti-histamine agents as it affects the formation of DNA.

In addition to its importance in other applications such as photography and information recording systems [45],crop protection [46], as these compounds rich with nitrogen atoms are used as herbicides and in the manufacture of Explosive industry and as fuel for transportation [47].

2 EXPERMINTAL PART

2.1 *Synthesis of Schiff bases*

We put a certain amount of the amino pyridine derivatives with a certain balanced amount of aldehyde compounds and dissolving each separately with an appropriate amount ofethanol after the complete dissolution in the ethanol the two compounds were mixed and the addition of drops of glacial acetic acid and the escalation process for the prepared mixture and after completing the escalation process the mixture was left to cool and during the process the reaction was monitored by TLC technique using (methanol and dry benzene) by (1:4) as an eluent [48].

2.2 *Synthesis of tetrazole*

Tetrazoles derivatives prepare by dissolving a (0.001)mole of schiff base in 20 ml of 1,4-dioxane in a circular flask equipped with a magnatic stirrer and reacting it with (0.002) mole of sodium azide , the reaction was escalated for 50 hours at 56 °C, the prepared mixture and after completing the escalation process the mixture was left to cool and during the process the reaction was monitored by TLC technique using (methanol and dry benzene) by (1:4) as an eluent

3 RESULTS

FT-IR spectrum data for compounds show bands at:

4 DISCUSSION

In FT-IR spectrum data for (1,2,3,4,5) compounds its clearly the disappearance of NH2 peak at (3433-3300 cm^{-1}) and appearance azomethen group (1610-1666 cm^{-1}) mean formation of Schiff base derivatives . At (6,7,8,9,10) compounds its clearly the appearance of (N=N) at (1448-1475) cm^{-1} and (N-H) at (3346-3456)cm^{-1} mean the formation

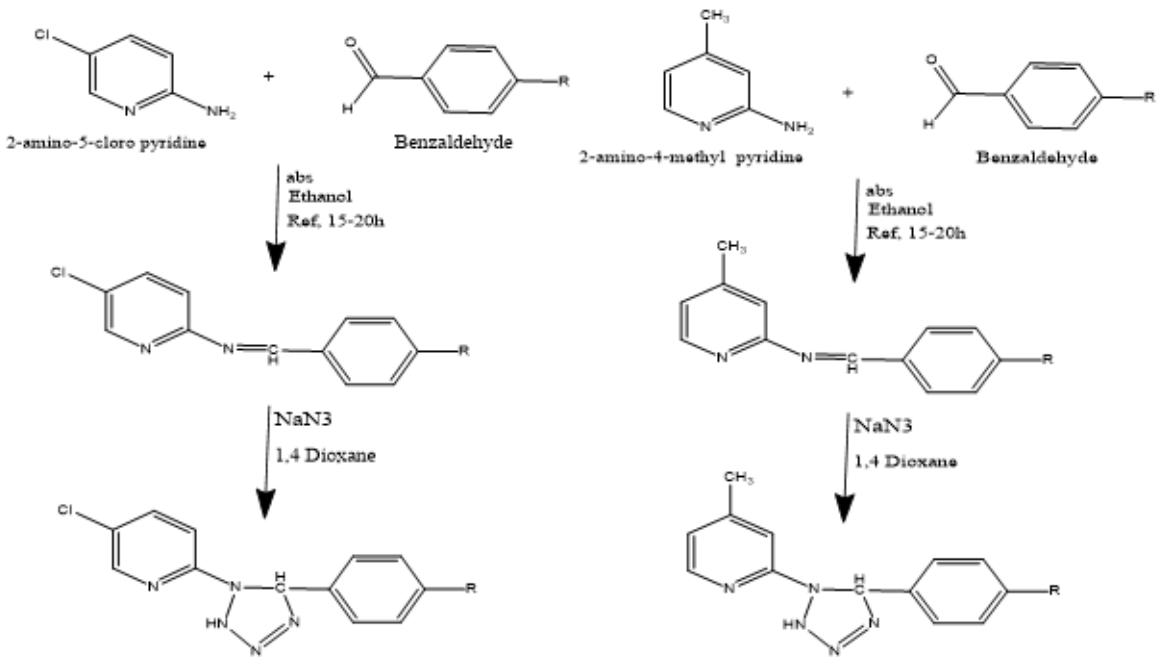

Fig. 2. Synthesis of tetrazole.

Table 1. FT-IR spectrum data.

compounds	C=N (cm^{-1})	C=C (cm^{-1})	C-H (aromatic) (cm^{-1})	C-N (cm^{-1})	Others
1	1622	1570	3080	1109	840 cm^{-1} for C-Cl
2	1620	1571	3080	1107	840 cm^{-1} for C-Cl , 817cm^{-1} for C-Br
3	1662	1597	2910	1165	3300 cm^{-1} for N-H
4	1666	1597	3045	1165	
5	1610	1570	3076	1184	1278 cm^{-1} for C-O

Table 2. FT-IR spectrum data.

compounds	N-H cm^{-1}	C=C	C-H (aromatic) cm^{-1}	N=N cm^{-1}	OTHERS cm^{-1}
6	3456	1566	3022	1448	1105 for(C-N), 821 for(C-Cl)
7	3435	1595	3086	1448	1114 for(C-N) , 839 for(C-Cl), 815 for(C- Br)
8	3346	1598	3022	1438	1165 for(C-N)
9	3358	1598	3051	1475	1165 for(C-N)
10	3354	1570	3049	1458	3453 for (OH), 1346 for(C-O), 1130 for(C-N)

Table 3. E.coli and S.aureus results.

Compounds	E. Coli		S. Aureus	
	Concentration 100 mg/ml	Concentration 75 mg/ml	Concentration 100 mg/ml	Concentration 75 mg/ml
1	+++	+++	+++	++
2	++	++	+++	+++
3	+++	++	+++	++
4	+++	+++	+++	+++
5	+++	++	+++	+++
6	++	+++	++	++
7	+++	++	+++	+++
8	+++	+++	++	++
9	+++	++	+++	+++
10	++	+++	++	++

(++)= (1.1.5 cm) of inhibition diameter; (+++)=(3-3.5 cm) of inhibition diameter

of tetrazole derivative .

5 CONCLUSION

It was shown during the process of preparing the compounds that the difference in the groups substituted on the same compound leads to a difference in the percentages, reaction time and biological activity of the resulting compounds.

The study of biological activity of Schiff base derivatives and tetrazole derivatives against E. Coli show that all derivatives give a positive results at different diameter but the compounds (2,6,10) give a lower inhibition at concentration 100 mg/ml as well as the compounds (2,3,5,7,9) give a lower inhibition at concentration 75mg /ml.

The compounds (6,8,10) give lower inhibition at concentration (100 mg/ml) against S. Aureus as well as the compounds (1,3,6,8,10) give lower inhibition at concentration (75 mg/ml). In FT-IR spectrum data for (1,2,3,4,5) compounds its clearly the disappearance of NH2 peak at (3433-3300 cm^{-1}) and appearance azomethen group (1610-1666 cm^{-1}) mean formation of Schiff base derivatives. At (6,7,8,9,10) compounds its clearly the appearance of (N=N) at (1448-1475) cm^{-1} and (N-H) at (3346-3456)cm^{-1} mean the formation of tetrazole derivative.

Conflict of Interest: The authors declare no conflict of interest.
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Ethical consideration: The study was approved by University of Al-Qadisiyah, Al-Qadisiyah, Iraq.

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