OBAFEMI AWOLOWO UNIVERSITY

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITIES OF OXAZOL-5-ONE DERIVATIVES

By

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CERTIFICATION

This is to certify that this research study was carried out by Adebayo John AKINBOYE as part of the requirement for the award of the Degree of Masters of Science (M.Sc.) in Chemistry of the Obafemi Awolowo University, Ile-Ife.

Dr. T. O. Olomola …….. ……**(Supervisor)**
Signature **Date**

Prof. E.A. Oluyemi ……. ……
(Head of Department) **Signature** **Date**

DEDICATION

This work is dedicated to God Almighty, the creator of the earth and the giver of life for seeing me through the course of this academic programme.

ACKNOWLEDGEMENTS

Firstly, I want to say a big thank you to my supervisor, Dr. T. O. Olomola, for his mentorship, guidance, constructive criticism and moral support throughout the period of this study. Thanks for opening my eyes to the field of synthetic chemistry. You are really a source of inspiration to me and how much I cherish you being my supervisor cannot be over-emphasized. I pray the good Lord continue to take you and your family to greater heights. Thank you Sir.

Special thanks go to my parents, my parents, Dn. & Mrs. Akinboye for their never-ending love and constant support morally, financially and spiritually. Thank you for believing in me. I pray that God Almighty will prolong your lives in good health to reap the fruits of your labour.

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I want to specially appreciate my siblings for their encouragement and support. I love you so much and I pray that God will take us all to the top. Also to Dolapo Daramola, thanks for being a treasure I've always hoped you would be to me. I love you so much.

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Finally, to all my friends from Murtala Muhammed Postgraduate Hall, thanks for the love you've always shown to me before, when and after I was your director of sport. I hope to see you all at the top.

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LIST OF ABBREVIATIONS

CDI	-	Carbonyldiimidazole
CIB	-	Clinical Isolate from Blood
DAMN	-	Diaminomaleonitrile
DDQ	-	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DMF	-	Dimethyl formamide
DMSO	-	Dimethyl Sulphoxide
DNA	-	Deoxyribonucleic acid
LIO	-	Locally Isolated Organisms
MBC	-	Minimum Bactericidal Concentration
MIC	-	Minimum Inhibitory Concentration
NCIB	-	National Collection for Industrial Bacteria
NMR	-	Nuclear Magnetic Resonance
RNA	-	Ribonucleic acid
STA	-	Staurosporine
TFA	-	Trifluoroacetic acid
THF	-	Tetrahydrofuran
TMSCl	-	Trimethyl silylchloride

LIST OF SCHEMES

ABSTRACT

This study synthesized some oxazol-5-one derivatives, characterized these compounds and carried out *in vitro* antibacterial and antifungal study. This was with a view to providing more information about the microbial potential of these targeted oxazol-5-one derivatives.

N-Acetylglycine, **141** was prepared by the reaction of glycine with acetyl bromide in the presence of sodium hydroxide, followed by purification *via* recrystallization. Various oxazol-5-one derivatives **142a-f** were obtained by an intramolecular cyclodehydration of *N*-acetylglycine using acetic anhydride, followed by an aldol-condensation with different aromatic aldehydes with anhydrous sodium acetate as catalyst in one pot. The synthesized compounds were characterized using ^{1}H-NMR, ^{13}C-NMR and IR spectroscopy. The synthesized compounds were screened *in vitro* for antimicrobial activity, using ampicillin and streptomycin as clinical references for antibacterial activity and nystatin as reference for antifungal activity.

N-Acetylglycine, **141** was obtained in a yield of about 58% while the oxazolone derivatives, **142a-f** were obtained in yields of up to 39%. Compounds **141, 142a-f** were screened for antimicrobial activity against bacterial and fungal strains. Among the tested compounds, compound **142e** showed a better activity against *Escherichia coli*than ampicillin but a comparable activity with streptomycin. Against *Streptococcus pneumoniae*, compound **142e** showed a better activity than both ampicillin and streptomycin. Compound **142e** also showed the highest bactericidal concentration than other synthesized compounds against *Escherichia*

coli,better than ampicillin, but comparable with streptomycin. None of the synthesized compounds showed any activity against the tested fungal strains.

The study concluded that compound **142e**which showed better activity than ampicillin and a comparable activity to streptomycin against*Escherichia coli* and *Streptococcus pneumoniae* could be explored in the treatment of microbial infections caused by these organisms.

CHAPTER ONE

INTRODUCTION

1.1 Background to the Study

Heterocyclic compounds are class of organic compounds whose molecules contain one or more rings of atoms with at least one atom (the heteroatom) being an element other than carbon, most frequently oxygen, nitrogen, or sulphur. Nitrogen, sulphur and oxygen containing five and six membered heterocyclic compounds have occupied enormous significance in the field of medicinal chemistry (Figure 1.1) (Aaglawe *et al*., 2003).

Many heterocyclic compounds are biosynthesized by plants and animals and some of these compounds are biologically active. A common example is imidazole, which is incorporated into many important biological molecules; the most pervasive is the amino acid histidine, with an imidazole side-chain. Histidine is present in many proteins and enzymes and plays a vital role in the structure and binding functions of hemoglobin (Shargel and Swanson, 2004).

Some heterocycles are fundamental to life such as haeme derivatives in blood and the chlorophylls essential for photosynthesis (Figure 1.2). Similarly, the paired bases in ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) are heterocycles, as are the sugars that in combination with phosphates provide the backbones and determine the topology of these nucleic acids.

Heterocycles are also found in plants. Examples include indigo blue, used to dye jeans. A poison of detective novel fame is strychnine, obtained from the seeds of *Strychnos nux-vomica* (Figure

1.3). The biological properties of heterocycles in general make them one of the prime interests of the pharmaceutical and biotechnology industries. Some examples of biologically active pyridine or piperidine derivatives are shown in Figure 1.4.

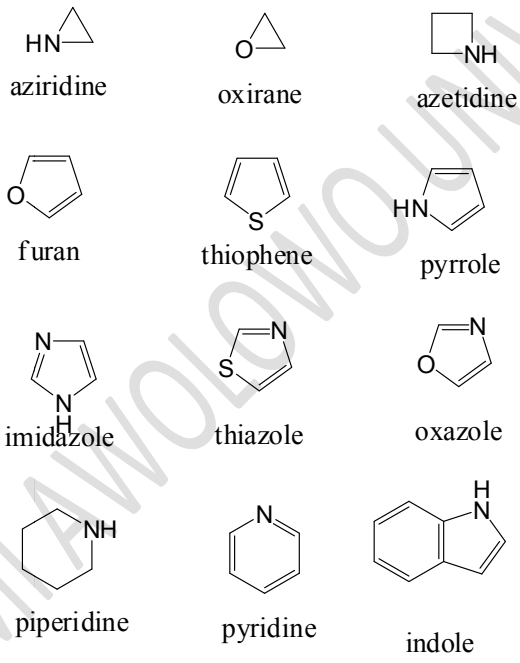


Figure 1.1: Some Common Examples of Heterocyclic Compounds

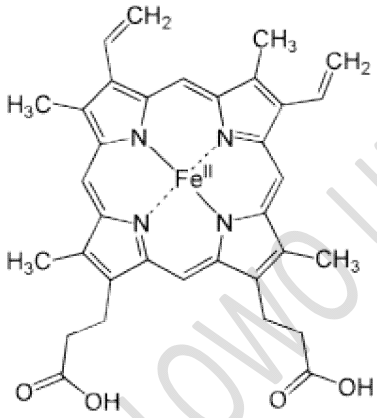
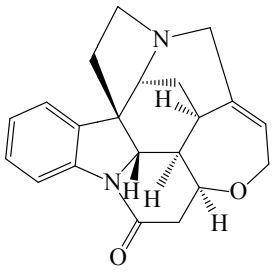
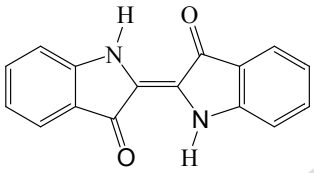


Figure 1.2: Haeme Derivative found in Blood



Strychnine



Indigo

Figure 1.3: Structures of Strychnine and Indigo

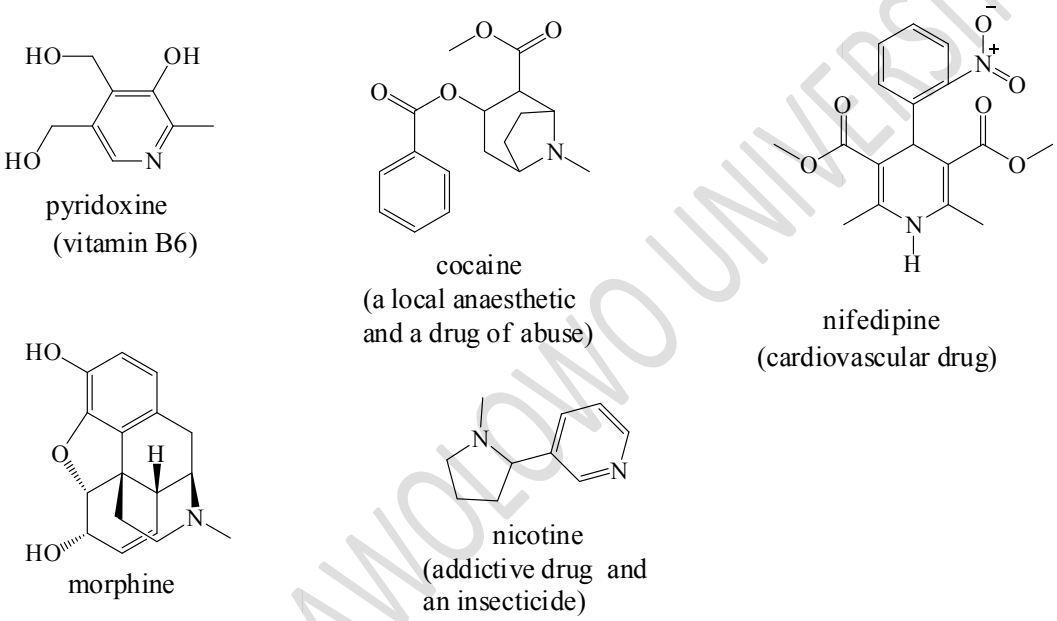


Figure 1.4: Some Biologically Active Pyridine and Piperidine Derivatives