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# SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF 5-(4-HYDROXY-3-METHOXYBENZYLIDENE)-2-IMINO-3-(4-METHOXYPHENYL) OXAZOLIDIN-4-ONE

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## ABSTRACT

2-imino-3-(4-methoxyphenyl) oxazolidin-4-one undergo reaction with vanillin in the presence of anhydrous sodium acetate in ethanol to yield 5-(4-hydroxy-3-methoxybenzylidene)-2 imino-3-(4-methoxyphenyl) oxazolidin-4-one Structure of the synthesized compounds was elucidated by using different spectroscopic techniques such as IR, $^{1}$H NMR, $^{13}$C NMR and elemental analyses. The purity of the intermediate and the product were checked by TLC plates. The product was assayed in vitro by paper disc diffusion method for their antibacterial activities against Staphylococcus aureus bacteria and E.coil bacteria, the compound exhibit promising activity against tested microorganisims.

**KEY WORDS**: Oxazolidinones, NMR, IR, Antibacterial and Synthesis.

## INTRODUCTION

Oxazolidinones were discovered by E. L Du Pont Pharmaceuticals in the late 1980s, [1] but the early lead analogues (DuP 105 and DuP 721) proved unsuitable for pharmaceutical development and the programmer was dropped. Investigation was re-initiated by the then Upjohn Corporation in the early 1990s [2]. Oxazolidinone moiety with oxygen and nitrogen electron donors could easily enter in coordination with metal ions to form metal complex but surprisingly complexometeric properties of these heterocyclics have rare mention in literature, in the field of coordination chemistry of oxazolidinones a report on synthesis and characterization of 2- imino-5-phenayl-4-oxazolidinone, 2-imino-5, 5-diphenyl-4-

oxazolidinone and 2-imino-5-p-biphenyl-4 oxazocomplexes with Cu(II), Ni(II), Mg(II) and Fe(III) are worth reporting.

There are several routes for synthesis of oxazolidinones involving diverse reactants; a few of them are briefed below. Synthesis of oxazolidin-2-ones derivatives was carried out starting from urea and ethanol amine reagents using microwave irradiation in a chemical paste medium in which a catalytic amount of nitro methane absorbed the microwaves and generated hot spots [3,12]. Primary amines reacted with carbonate salts ($Na_2CO_3$, $K_2CO_3$, $Cs_2CO_3$, and $Ag_2CO_3$) and halomethyloxiranes in the presence of a base such as DBU to give oxazolidinones in high yields. The use of $K_2CO_3$ among these carbonate gave the best yield in this synthesis. A reaction mechanism was proposed that the oxazolidinone was obtained from an oxazinanone intermediate via a bicycle intermediate. The present reaction can be widely applied to convenient synthesis of useful N-substituted oxazolidinones and chiral oxazolidinones [4]. Rreaction of oxiranes with carbon dioxide and aliphatic amines [5]. Cyclocondensetion of α-halogenated acetanilide [6].

Literature review on synthesis, structure and physico-chemical and biological properties of oxazolidinones highlighting their multifarious roles in various fields of development, viz. medical science, 2-imino-3-(4-methoxyphenyl) oxazolidin-4-one condensation with vanillin, elucidation of structures by routine physico-chemical techniques, viz. elemental analysis, spectroscopy etc.

## MATERIALS AND METHODS

2-imino-3-(4-methoxyphenyl) oxazolidin-4-one, vanillin, ethanol and anhydrous sodium acetate were used in synthetic work. All solvents used in synthetic work were BDH, CDH (India) Fisher (UK) Products. Melting points of compounds were determined in open glass capillaries using a digital melting point apparatus (Bibby Starling LTD, ST150SA model, U.K) are uncorrected. IR spectra were recorded on FTIR-12 spectrophotometer in KBr disc. Homogeneity or purity of products was monitored on silica gel G coated TLC Plates. Brukner Avance spectrometer operating at 400 MHz was used to record $^1H$ NMR and $^{13}C$ NMR spectra in $CDCl_3$/DMSO solvent using TMS as an internal standard. Laboratory work such as synthesis of compounds, TLC analysis, Melting point were done in Adigrat University organic chemistry laboratory, Ethiopia, NMR analyses were done at Addis Ababa University, Ethiopia,

**Synthetic Procedure**

Title compounds, were synthesized by following the reported procedure [6] in one steps as below.

**Synthesis of 5-(4-hydroxy-3-methoxybenzylidene)-2-imino-3-(4-methoxyphenyl) oxazolidin-4-one**

For the synthesis of these compounds (0.02 mole) 2-imino-3-(4-methoxyphenyl) oxazolidin-4-one [7] and (0.02 mole) vanillin were mixed in dry ethanol and 6 g anhydrous sodium acetate was added and reaction mixtures were refluxed for 4 h. Products obtained was recrysallized in ethanol and dried.

**Antimicrobial Activities**

5-(4-hydroxy-3-methoxybenzylidene)-2-imino-3-(4-methoxyphenyl) oxazolidin-4-one was being tested *in vitro* for their antibacterial activities by using the paper disc diffusion technique [7]. Antibacterial activities of 5-(4-hydroxy-3-methoxybenzylidene)-2-imino-3-(4-methoxyphenyl) oxazolidin-4-one was tested against a few important bacteria like *Escherichia coli and Staphylococcus aureus* using nutrient agar medium. Known antibiotics such as Ampicilin, was used as standard drug as reference in bactericidal.

**RESULT AND DISCUSSION**

Chemical and physical data of 5-(4-hydroxy-3-methoxybenzylidene)-2-imino-3-(4-methoxyphenyl) oxazolidin-4-one was noted in table 1. Theoretical (calculated) elemental analyses are in fair agreement with experimental values of the products.

**Table1. Physical and Elemental Analyses Data of the synthesized compound.**

| S.N. | Molecular formula | Colour | Melting point | Yield % | Elemental Analyses (%) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | C | | H | | N | |
| | | | | | calculated | found | calculated | found | calculated | found |
| 1 | $C_{18}H_{16}N_2O_5$ | Slate blue | 105-107 | 76 | 63.52 | 62.95 | 4.70 | 4.92 | 8.23 | 8.34 |

**Characterization of synthesized Compound**

Synthesis of condensation products of 2-imino-3-(4-methoxyphenyl) oxazolidin-4-one with vanillin in the presence of anhydrous sodium acetate leads to the formation of C=C with elimination of water. IR spectra of 5-(4-hydroxy-3-methoxybenzylidene)-2-imino-3-(4-methoxyphenyl) oxazolidin-4-one displayed bands corresponding to υ C=C, υ O-H, υ C=O, υ C=N, υ C-H, υ C-O, and υ (=C-H) vibration in 1670-1590 $cm^{-1}$, 3353-3274 $cm^{-1}$, 1657-1742

$cm^{-1}$, 1664-1592 $cm^{-1}$ , 2856-2741 $cm^{-1}$ , 1336- 1121 $cm^{-1}$ and 3108-2937 $cm^{-1}$ regions, respectively of products obviously confirming the existence of condensation products of 2-imino-3-(4-methoxyphenyl) oxazolidin-4-one.

With a view to receive further $^{13}C$ NMR and $^{1}H$ NMR of 5-(4-hydroxy-3-methoxybenzylidene)-2-imino-3-(4-methoxyphenyl) oxazolidin-4-one has also been analyzed. Proton chemical shifts in δ6.3-8.3, δ4.5-6.3 and δ4-3.5 regions indicated the presence of aromatic proton, olefin and $OCH_3$ groups, respectively. The $^{13}C$ NMR spectral data of the compounds also conform of proposed structure of these 5-(4-hydroxy-3-methoxybenzylidene)-2-imino-3-(4-methoxyphenyl) oxazolidin-4-one, a proton signal at 55 ppm indicate the presence of $OCH_3$ group and a signal at 108 ppm clearly show the presence of olefinic methine carbon due to new C=C bond formation between 2-imino-3-(4-methoxyphenyl) oxazolidin-4-one and vanillin. A signal at 169 ppm shows the presence of carbonyl group (keton in ring), a signal at 158 ppm is due to C=NH group. Aromatic carbons show different chemical shifts due to different substituting groups in benzene ring. From IR, $^{1}H$ NMR and $^{13}C$ NMR clearly show the formation of C=C bond from 2-imino-3-(4-methoxyphenyl) oxazolidin-4-one and vanillin. IR $^{1}H$ NMR and $^{13}C$ NMR spectral assignments of these compounds were in good agreement with those reported in literature [9]

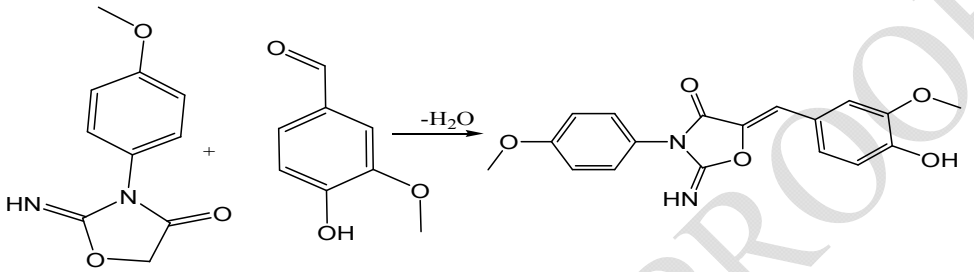
**Antimicrobial Effects**

The in vitro antimicrobial activity of compound 5-(4-hydroxy-3-methoxybenzylidene)-2-imino-3-(4-methoxyphenyl) oxazolidin-4-one, was performed using the disk diffusion method. Ampiciln was used as standard drugs for bacteria. The compound was tested for anti-bacterial activities by disk-diffusion method using nutrient broth medium. Perusals of antibacterial data of 5-(4-hydroxy-3-methoxybenzylidene)-2-imino-3-(4-methoxyphenyl) oxazolidin-4-one show activity of against both *E. coli* and S. aureus bacteria. The compound show high activity against both S. aureus and E. coli bacteria in 20 µl concentrations, the compound also show medium in both S. aureus and E. coli bacteria in 10 µl concentrations. From this activity it could be easily inferred that bactericidal activity is dependent on position of substituent, concentration and nature compound. The outcome of this study is presented in table-2.

**Table2. Zone of bacterial growth inhibition (mm)**

| S.N. | Compound | Zone of inhibition (mm) | | | |
|---|---|---|---|---|---|
| | | *S. aureus* | | *E. coli* | |
| | | 10 µl | 20 µl | 10 µl | 20 µl |
| 1 | $C_{18}H_{16}N_2O_5$ | 7.5 | 9.5 | 10.5 | 11 |
| 2 | Ampiciln | 8 | 10 | 12 | 12.5 |
| 3 | DMSO | - | - | - | - |

**Key**: all results mean of three replications




**Scheme1: Reaction root for synthesis of 5-(4-hydroxy-3-methoxybenzylidene)-2-imino-3-(4-methoxyphenyl) oxazolidin-4-one.**

## SUMMARY AND CONCLUSIONS

An efficient reaction of 2-imino-3-(4-methoxyphenyl) oxazolidin-4-one with vanillin yield 5-(4 hydroxy-3-methoxybenzylidene)-2-imino-3-(4-methoxyphenyl) oxazolidin-4-one. IR, $^{1}H$ NMR and $^{13}C$ NMR spectra were used to elucidate structures of the 5-(4-hydroxy-3-methoxybenzylidene)-2-imino-3-(4-methoxyphenyl) oxazolidin-4-one. It can be concluded that Oxazolidinones class of compound certainly holds great promise towards the good antibacterial activity leads in medicinal chemistry.

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## REFERENCE

1. Jennifer F, Pankaj K, and Abhishek K, Int. Journal of Pharmaceutical Sciences and Drug Research, 2013; 5(3): 101-104.
2. Ford L, Overman L, Ricca D and Trost B, Pergamon Press, Oxford, 1997; 2: 1007.
3. Willam W, Grover H, Roy C, Turnbull B, and John D., J. Med. Chem, 1973;16(10): 1129.

4. Yumiko O, Yuka H, Yoko S, Kouichi T, Yoshihiro I, Shuichi H, and Hiroshi N., J. Org. Chem, 2005;70: 5737-5740.
5. Yoshida Y, and Inoue S, Chem. Soc. perkin Trans, 19791; 3146.
6. Jain S, Ph.D Thesis, C.C S. University, manual. 2009.
7. Tesfahun B, Aman, Shilashi B and Hanna S., Synthesis, Characterization And Antibacterial Evaluation Of 2-Imino-3-(4-Methoxyphenyl) Oxazolidin-4-One,wjpps, 2014:1143-1149.
8. Amare A, Germany university of Gottinge., 2002: 112.
9. John C, A Practical Approach Encyclopedia of Analytical Chemistry, 2000, 10815-10837.
10. Willam JW, Grover CH, Roy TC. Turnbull LB and John PD., J. Med. Cem, 1973; 16: 1129.
11. Seoung J, Myung H, Jung H and Chang H., Bioorg & Med Chem Lett, 2008; 40: 5815–18.
12. Park C, Brittelli D, Wang CL, Marsh F, Gregory WA and Wuonola MA., J Med Chem, 1992; 35: 1156-1165.