ANTIBACTERIAL ACTIVITY OF 5-BROMO-3-(HYDROXYIMINO)-1,3-DIHYDRO-2H-INDOL-2-ONE

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ABSTRACT

Reaction of 5-Bromo-1*H*-indole-2,3-dione with hydroxyl amine hydrochloride gave (3Z)-5-bromo-3-(hydroxyimino)-1,3-dihydro-2*H*-indol-2-one in a good yield. The synthesized compound was characterized by IR and ^{1}H NMR , melting point also detected . The prepared component was reported for antibacterial efficacy contra *staphylococcus aureus*, *Escherichia coli*, *Streptococcus*, and *klebsiella pneumoniae,* which manifest effective antibacterial activity versus *staphylococcus aureus* and *klebsiella pneumoniae* and medium activity versus *Escherichia coli* and *Streptococcus.*

INTRODUCTION

Bacterial resistance to antibiotics is considered one of the most important health problems at the present time, and it has become necessary to prepare new organic compounds and test their effectiveness against microorganisms, which are necessary to overcome the resistance of microorganisms to known drugs.

An oxime is an imine-related chemical compound with the general formula RR'C=NOHH. Gao and co-workers were prepared oxime esters from dihydrocumic acid. Antibacterial activity displayed better antibacterial activity against Gram-negative bacteria compared with bromogeramine (1). A series of oxime carbamat derivatives of 3-Aryl-2-thioquinazolin-4(3H)-one were synthesized and screened for their antifungal and antibacterial activity. All compounds have good activity against bacterial and fungal species (2). Data from literature on the synthesis and structure of nucleoside oximes and related pyrimidine and purine nitrogen bases were reviewed(3). The synthesis of novel heterocyclic systems similar to

pyrimidine oximes from nucleoside oximes has been described. The biological activity of nucleoside and nitrogen base oxime derivatives was also reviewed (3).

In this work, a derivative of oxime was prepared and its biological effectiveness as an antibacterial was tested for a number of positive and negative gram bacteria.

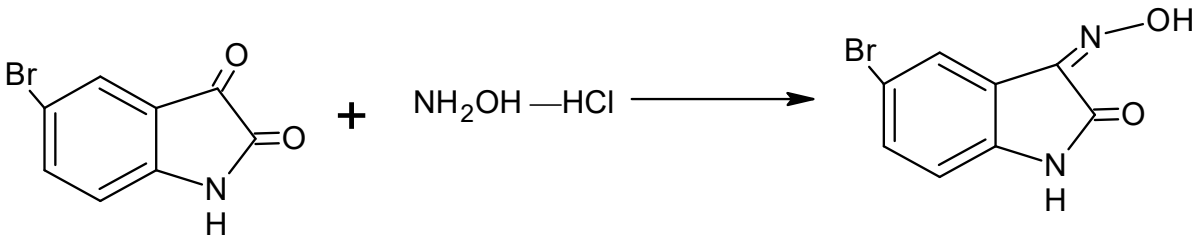
MATERIALS AND METHODS

Instrumentation: Technique of infrared spectroscopy is conducted with an instrument a Pye-Unicam SP3-300 spectrometer which registered in (4000-200 cm^{-1}) wave numbers. Determination of ^{1}H and ^{13}C by Nuclear magnetic resonance is showed at 600 MHz (Bruker, Al-albayt University in Jordan). And by using Philip Harris instrument the melting point is determinate.

Synthesis

Synthesis of (3Z)-5-bromo-3-(hydroxyimino)-1,3-dihydro-2*H*-indol-2-one: 5-Bromo-1*H*-indole-2,3-dione with hydroxyl amine hydrochloride (4.4 mmol, 1.0 g) within 15 ml ethyl alcohol to hydroxylamine hydrochloride (4.4 mmol, 0.3 g), 10% mole of sodium acetate was compile and performing sol. was refluxed to 3 hrs at 70-80 ^{0}C and then put for 24h in cooler. After that filtering, washing with ethanol and re-crystallization by using chloroform:ethanol (8:2, v:v) to give brown crystals of 5-bromo-3-(hydroxyimino)-1,3-dihydro-2*H*-indo-2-one.

Color : Brown crystals, Yield : 79%. M.p. : 119 -122°C. FT-IR (KBr, ν, cm^{-1}): 3255 (OH), 3068 and 3024 (CH-Ar-H); 1710 (C=O) 1610,1635 (C=C, C=N). ^{1}H NMR (300 MHz, $CDCl_3$,δ ppm): 8.1 -6.68(m, 3H, Ar-H), 3.30 (s, 1H, NH), 1.50 (s, 1H, N-OH).



Scheme 1: Preparation of (3Z)-5-bromo-3-(hydroxyimino)-1,3-dihydro-2*H*-indol-2-one

Antibacterial activity: The antibacterial activity of synthesized product was assigned against four bacteria species *(staphylococcus aureus*, *E. coli*, *klebsiella pneumoniae* and *streptococcus*) employing the technique of (5). Bacterial suspension was diluted with sterile physiological solution. Petri plates containing 20 ml of Mueller Hinton Agar were then used .

Discs (Whatman, no. 3) were saturated in 20ml of (50,100,200) conc. Of prepared substance under 37degree. Then discs sited onto the face of the agar. overnight incubation, confluent bacterial growth was observed. Inhibition zone of the bacterial growth was measured in mm.

RESULTS AND DISCUSSION

Chemistry

The present work describes the synthesis of the novel oxime derivative by 5-bromo-1H-indole-2,3-dione reaction with hydroxyl amine hydrochloride in a ratio of 1:1 to yield the oxime derivative in good yield (Scheme 1). IR spectra revealed common features in some regions and distinctive fingerprint bands and other regions. The IR spectrum supports the hydroxyl group (OH) stretching around 3258cm^{-1} (6) . ^{1}H NMR spectra of synthesized compounds show hydroxyl proton (OH) signals at 1.5 ppm, ^{1}H NMR spectra of synthesized compounds show a singlet at 3.30 ppm due to (NH) and aromatic protons (Ar) signals at 6.68-8.10 ppm range .

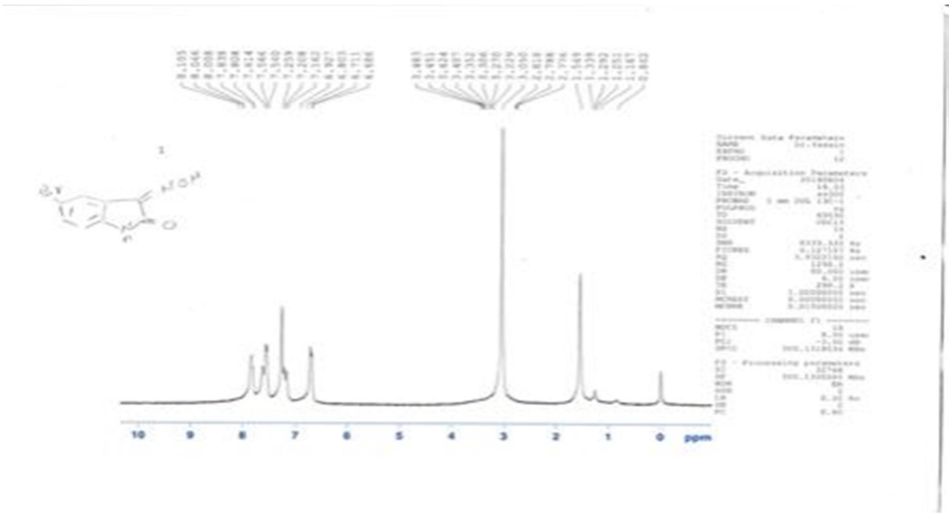


Figure 1: ^{1}H-NMR of (3Z)-5-bromo-3-(hydroxyimino)-1,3-dihydro-2H-indol-2-one 5-bromo-1H-indole-2,3-dione

Antibacterial activity

The antibacterial activity results are shown in Table 1, Figure 2, The prepared compound was active against all the selected bacteria species with some difference values according to concentration increment. The activity in all concentration of our compound, showed high activity against *staphylococcus aureus* and *klebsiella pneumoniae,* at all concentrations but it exhibit a moderate activity against *E.coli* and *Streptococcus sp*. With no activity at 50 µg/ml concentration. This study clearly demonstrated that a prepared component showed significant antibacterial activity, particularly against *staphylococcus aureus* and *klebsiella pneumoniae.*

Table 1: Antibacterial Activity of oxime derivative

Bacteria	**Inhibition zone of antibacterial sensitivity test to compound (mm)**		
	oxime conc.(µg/ml)		
	50	100	200
E. coli	7	15	18
S.aureus	10	12	13
Streptococcus	7	8	11
K. pneumoniae	10	13	15

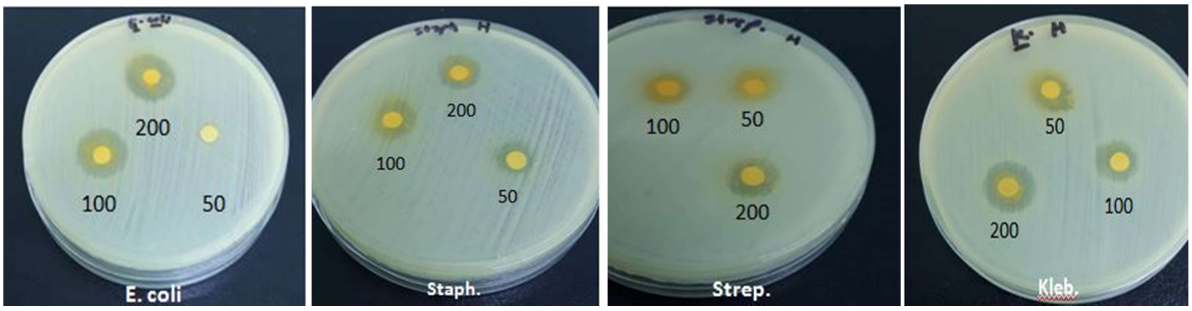


Figure 2: Antibacterial activity screen of oxime derivative

الفعالية المضادة للبكتريا لمركب

5-Bromo-3-(hydroxyimino)-1,3-dihydro-2H-indol-2-one

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الخلاصة

ان تفاعل ال 5-Bromo-1H-indole-2,3-dione مع hydroxyl amine hydrochloride نتج عنه المركب (3Z)-5-bromo-3-(hydroxyimino)-1,3- dihydro-2H-indol-2-one 5-bromo-1H-indole-2,3-dione بحصيله انتاجية جيدة. تم تشخيص المركب المحضر بالطرق الطيفية المتمثلة بطيف الاشعة تحت الحمراء والرنين المغناطيسي للبروتون، وكذلك تحديد درجة الانصهار، وتم اختبار فعالية المركب المصنع ضد بعض انواع البكتريا مثل: klebsiella pneumonia ,Staphylococcus aureus, Escherichia coli, حيث اضهر المركب فعالية متوسطة ضد *staphylococcus aureus* and *klebsiella pneumonia* و فعالية عالية ضد *Escherichia coli* and *Streptococcus* .

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