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Synthesis and Biological evaluation of some new oxime, phenyl hydrazone and 2, 4 dinitro phenyl hydrazone derivatives of ketones

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Abstract

Various oximes, phenylhydrazones and 2, 4 dinitrophenylhydrazones have been synthesized by reaction with different ketonic compounds. The structures of these compounds have been confirmed on the basis of spectral data. The antimicrobial activity of the prepared compounds is discussed and some of them are found to be active.

Key words: Oxime, phenylhydrazone, 2, 4 dinitrophenylhydrazone, antimicrobial activity.

Introduction

Oximes, phenylhydrazones and 2, 4 dinitrophenylhydrazones have been demonstrated to possess antimicrobial, anticonvulsant[1] and analgesics, anti inflammatory and antitubercular activities.

Hydrazones possessing an azomethine –NH-N=CH-proton constituent an important class of compounds for new drug development. Therefore, many researchers have synthesized these compounds as target structures and evaluated their biological activities. These observations have been guided us for the development of new oximes, phenylhydrazones and 2, 4 dinitrophenyl hydrazones that possess varied biological activities[2]. Various oximes, phenylhydrazones and di-nitro phenylhydrazone derivatives were synthesized by the reaction between hydroxyl amine, phenyl hydrazine and 2, 4 di-nitro phenyl hydrazine with different ketones. The structures of these compounds were determined using spectral

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data. All the synthesized compounds were evaluated for their antimicrobial activity.

The tissue-lying Staphylococcus aureus, Streptococcus pyogenes, Salmonella typhimurium and Escherichia coli causes food poisoning, rheumatic, salmonellosis and diarrhea; these are the second leading cause of death from bacterial disease worldwide[3]. More than 50 million people worldwide are infected and up to 150,000 die every year due to these bacterial infections[4]. Amoxicillin, norfloxacin, chloramphenicol, ciprofloxacin are the most common drugs used for these bacterial infections but are associated with severe side effects[5]. Toxicity and resistance to the drugs also play important role in the treatment failure[6]. Therefore; there is an urgent need to screen new compounds for the development of new anti-bacterial agents.

Material and Methods Experimental

All the chemicals and solvents used were of A.R. grade. The purity of the compounds was determined by TLC using suitable solvent system. The IR spectra were recorded in KBr on Bruker tensor 27 FTIR Spectrophotometer. ^{1}HNMR spectra were recorded on Nuclear Magnetic Resonance spectrometer using TMS as internal standard. Elemental analyses of the compounds were conducted using Elemental Analysensystem GmbH. Melting points of all synthesized compounds were determined in open glass capillary tubes and are uncorrected.

Synthesis of oximes :

Ketone (4.0 g) and hydroxyl amine hydrochloride (2.4 g) were dissolved in a mixture of ethanol (15 ml) and water (3.0 ml). The solution was continuously stirred and a solution of sodium hydroxide (4.8 g in 5 ml water) was added in portions. In case the reaction becomes vigorous, the flask was cooled under tap water. After the addition was over, the reaction mixture was refluxed for 20 min. It was cooled and diluted with water (40 ml). The separated unreacted ketone was filtered and the filtrate cooled and poured while stirring into dilute HCl (12 ml con. HCl in 75 ml water). The precipitated oxime was filtered and washed with cold water. It was crystallized from methanol. The oxime was stored in vacuum desicator[7].

Synthesis of phenylhydrazones :

Phenyl hydrazine (4.0 g) was dissolved in water and ketone (2.0 g in 5 ml ethanol) was added to it. The reaction mixture was heated for 1 min. Glacial acetic (2 drops) was added and heated for 5 min again. The solid separated after cooling the reaction mixture was collected and crystallized from alcohol[8].

Synthesis of 2, 4 di-nitrophenyl hydrazones:

2, 4 di-nitro phenyl hydrazine (2.0gms) in methanol (10 ml) in conical flask. HCl (10 ml) was added in it. Filter if necessary. The reaction mixture was cooled. The solution of ketone (2.0gm in 5ml methanol) was added in it. The reaction mixture was heated on a water bath for 1-2 min. The solid separated after cooling the reaction mixture was collected and crystallized from alcohol[8].

Synthesized compounds :

KIJ 1: 2 - [(2-(hydroxymino) (phenyl) methyl]

benzoic acid

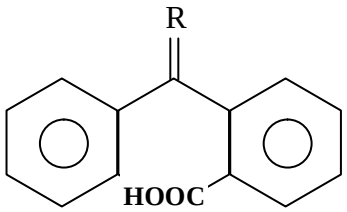
KIJ 2: 2 - [2-phenyl (2-phenylhydrazono) (phenyl)methyl] benzoic acid

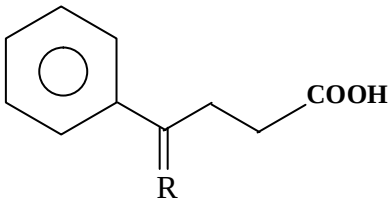
KIJ 3: 2 - [(2-(2, 4 dinitro phenyl) hydrazono) (phenyl)methyl] benzoic acid

KIJ 4: 4 - (hydroxyimino) - 4 -phenylbutanoic acid

KIJ 5: 4 - phenyl – 4- (2-phenylhydrazono) butanoic acid

KIJ 6: 4 - [2- (2, 4 dinitrophenyl) hydrazono] - 4 - phenyl butanoic acid

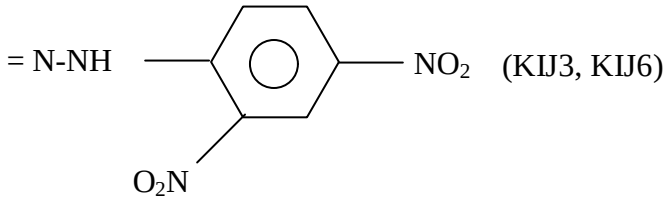




1 **2**

R = NOH (KIJ1, KIJ4)

= N-NHC$_6$H$_5$ (KIJ2, KIJ5)



(KIJ3, KIJ6)

Scheme 1. Synthesis of oxime, phenylhydrazone and 2, 4 dinitrophenylhydrazone derivatives of ketones (KIJ1-KIJ6).

Table 1. Physico-chemical Characterization Data of the Compound

Compound	M.F.	M. W.	M.P(^{o}C)	% yield	Rf
KIJ 1	$C_{14}H_{11}O_3N$	241	95	65.13	0.54
KIJ 2	$C_{20}H_{16}O_2N_2$	316	62	75.80	0.88
KIJ 3	$C_{20}H_{14}O_6N_4$	406	77	69.49	0.76
KIJ 4	$C_{10}H_{10}O_3N$	193	92	67.06	0.65
KIJ 5	$C_{16}H_{16}N_2O_2$	268	98	71.55	0.77
KIJ 6	$C_{16}H_{14}O_6N_4$	358	119	74.67	0.85

Antimicrobial Activity :

All the newly synthesized oximes3, phenylhydrazones and 2, 4 dinitrophenylhydrazones were subjected to antimicrobial activity against two bacterial strains *Escherichia coli* and *Staphylococcus aureus at 10 g/ml*. The soaked discs were incubated at 37ºC for 24 hours. Diameters of the zones of inhibition (in mm) were measured by disc diffusion method. The results are reported in Table 3.

Table 3. Antimicrobial Activity of synthesized compounds

Com-pound	Zone of Inhibition in mm E. Coli	S. aureus
KIJ 1	+	+
KIJ 2	+	++
KIJ 3	+	+++
KIJ 4	Nil	Nil
KIJ 5	Nil	Nil
KIJ 6	Nil	Nil

+++ significant activity, ++,+ moderate activity

Results and Discussion

Oxime, phenylhydrazones and 2, 4 dinitrophenylhydrazones were prepared from various ketone using appropriate reagents. These synthesized compounds were identified by physico-chemical and spectral data and purity was checked by TLC.

Among these compound KIJ 3 showed significant inhibitory. Compounds KIJ 1 and KIJ 2 showed moderate activity. While the remaining compounds showed no activity against E.coli and S.aureus bacteria.

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