Synthesis of Some New Isoxazoline and Their Antimicrobial Activity

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Abstract:

Chalcone and their heterocyclic analogues are known to possess a broad spectrum of biological effects. The present study is devoted to the synthesis of new isoxazoline . The newly synthesized compounds where screened for their antimicrobial activities.

Introduction:

Isoxazoline are a class of heterocyclic compound containing two hetero atoms oxygen and nitrogen at one two positions in five membered ring with two double bonds.

Claisen first reported an isoxazole structure from a product of the reaction between 1, 3 diketone and hydroxylamine it was showne to possess typical properties of an aromatic system but under a certain reaction conditions, particularly in reducing or basic media, it become very highly labile.

Various methods for the synthesis ofisoxazolines have been cited in the literature. Ka Young Lee et al. have synthesized indoles and Benzisoxazolines. Synthesized a series of 3-propane 1,2- Benzisoxazoles derivative by microwave assisted eco-friendly method. All the synthesized compound exhibited significant to moderate antimicrobial activity are used as many diseases.

Antimicrobial agents have been used in folk remedies from early times. The earliest sources of medicine comes from 'Egypt' and two kingdoms of 'Assyria' and Babylonia'. The 'Papyri' were the first written account of medical experience from Egypt. The Papyrus discovered by Eder in 1872 was prepared in 1500 B.C. and mention about 700 herbal medicines. A Babylonian Clay-Tablet 700 B.C. has been discovered which mention about 300 drugs.

Modern medicine is considered to date from 'Hippocrates', a Greek Physician (450 B. C.), who far the first time introduced the concept of disease as a pathologic process and tried to organized the science of medicine on the basis of observations and analysis.

Literature shows that much work has been done over many heterocyclic compounds of their antimicrobial activities including the both gram positive and gram negative bacteria. Isoxazoline were known to have bactericidal and fungicidal properties.

Material and Methods

Experimental:

Melting points were determined on Vigo melting point apparatus and are uncorrected. All the compounds were routinely checked for their homogeneity by

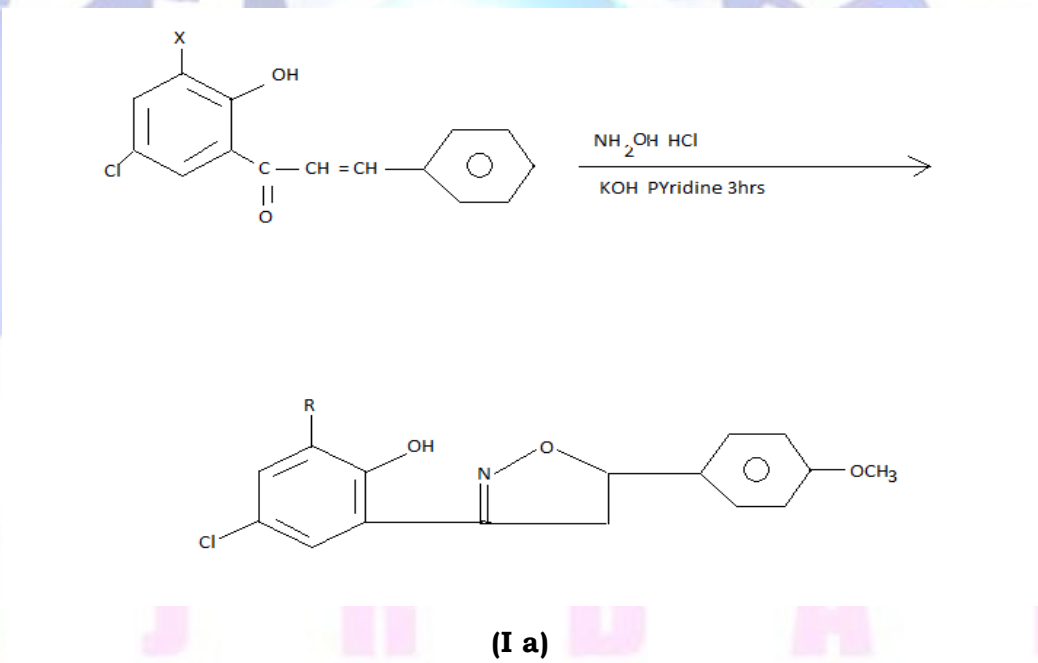
TLC on silica gel plate, IR spectra were recorded in KBr pellets on Perkin-Elmer FT-IR spectrophotometer, ^{1}H NMR spectra were recorded on BRUKER spectrometer on 300 MHz in $CDCL_3$ using TMS as an internal standard. The mass spectra were recorded on FAB mass spectrometer to confirm their structure.

Antibacterial activity (antimicrobial activity) was carried out by Agar cup method. The bacterial strains are identified strains and obtained from National chemical laboratory.

General procedure for synthesis ofIsoxazoline:

Substituted chalcone (0.05 mol) in pyridine (10 ml) and solutions of K-OH (0.25 mol) in 1ml water and hydroxyl amine Hydrochloride (0.09 mol) in 10ml water the reaction mixture reflux for 3 hrs cool and the reaction mixture was acidified with HCL (1:1). The separated solid was filtered and wash with 1% sodium bicarbonate solution again followed by water the product was crystallized from ethanol and glacial acetic acid (1:1) to give yellow colour solid [1]. Yellow solid; Yield 85% m.p:140-150.

Reaction scheme:



(I a)

IR (KBr) v max cm^{-1}:

3084.18 cm^{-1}(CH aromatic stretching), 1564.22 cm^{-1} (C=C aromatic stretching), 1253.74 cm^{-1} (C-O stretching), 1649.15 cm^{-1} (C=N stretching).

^{1}H NMR: [δ $CDCl_3$]:

6.87-8.39 (m 12H, Ar-H), 2.03 (S, 1H, C=CH).

Biological Evaluation

Anti-bacterial activity of (Ia-f):

The study has been conducted according to the method adopted by Cruickshank et al. Nutrient agar broth was melted in a water bath and cooked to 45 ^{0}C with gentle

shaking to bring about uniform cooling. It was inoculated with 0.5-0.6 ml of 24 hrs old culture especially and mixed well by gentle shaking before pouring on the sterilized Petri dish (25 ml each). The poured material was allowed to set (1.5 hrs) and their after the "cups" was made by punching into the agar surface with a sterile cork borer and soaping out the punched part of agar. Into this "cups" 0.1 ml of test solution (prepared by dissolving 100 ml of sample in 10 ml DMF) was added by sterile micropipette. The plates were noted. The antibacterial activities of all compounds are compared against Ampicilinas a standard drugs.

Result and Discussion:

In the present work we have decided to carry out the synthesis of Isoxazoline. The structures were established on the basis of spectral data (IR, NMR and Mass).

All newly synthesized compounds (Ia-f) shown a significant microbial activities.

Table of antimicrobial activity shows that the compound Ia, Ib, Ic more active in S. pyrogenes and Ie and Id having the same activity in both Gram +ve while Ia, Ib, Ic, Id, Ie, If more active in P. aeruginosa compare to E-coli while more active in E-coli compare to P. aeruginosa in Gram –ve.

Table.1- Anti-bacterial activity of (Ia-f):

Compound No.	Zone of Inhibition (in mm)			
	Gram +ve		Gram –ve	
	S. aureus	S. pyrogenes	E. coli	P. aeruginosa
Ia	17	18	15	18
Ib	18	16	15	18
Ic	15	20	17	15
Id	15	14	13	15
Ie	16	15	14	21
If	17	16	15	18
Ampicilline	18	20	18	20
Chloramphenicol	20	21	23	21

Conclusion:

Newly synthesized Isoxazoline (Ia-f) have been tested for their antibacterial activity against the Gram +ve bacteria S. aureus and S. pyrogenes while Gram –ve bacteria E-coli and P. aeruginosa. By punching into the agar surface with a sterile cork borer and soaping out the punched part of agar. Into this "cups" 0.1 ml of test solution, prepared by dissolving 100 ml of sample in 10 ml DMF. Amplicilline, Chloramphenicol were used as reference compound. The entire compound shown good activities against the Gram +ve and Gram –ve bacteria.

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