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Synthesis, Characterization of 3, 4, 5 - Isoxazolines and Antimicrobial Screening

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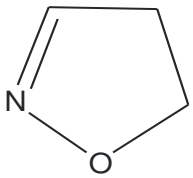
Abstract

A series of 3, 4, 5 – substituted isoxazolines were synthesized via flavanone. Flavanones reacting with hydroxyl amine hydrochloride to form substituted of 3, 4, 5 – isoxazolines. All these compounds are characterized by resources of their UV, IR, ^{1}H NMR spectroscopic information. Synthesized compounds evaluate for their antimicrobial bustle. All the compounds exhibited weak to reasonable bustle against all organisms except three which shows strong bustle.

Keywords: Isoxazoline, Antimicrobial screening.

Introduction

The importance of heterocycles like flavanones, isoxazoles and Isoxazolines mendacity in the actuality that they can be efficiently used as antibacterial, antitubercular, antiviral, antifungal, herbicidal, insecticidal and antidepressant agents[1-5]. The dihydroderivatives of Isoxazoles are known as Isoxazoline.



Isoxazoline

Isoxazoline are important pharmacophores in several pharmacologically important molecule. They are also useful intermediates for the synthesis of a broad multiplicity of bioactive natural products[6]. Isoxazoline derivatives have played a vital role in the hypothetical growth of heterocyclic chemistry and be also used widely in organic synthesis[7].

In current years, thought has increasingly been given to the synthesis of isoxazoline derivative as a source of novel antibacterial agent.

The synthesis of new isoxazoline derivatives stay behind a major focus of medicinal research. Isoxazoline derivatives reported posses antifungal, antibacterial, anticonvulsant, anti-inflammatory, antiviral and analgesic activities[8].

Quan et al design and synthesized isoxazoline derivatives as factor xa- inhibitors[9]. Maurya et al Synthesized 3, 5-disubstituted Isoxazoline as protein Tyrosine Phsophatase 1 B inhibitators[10]. Mugesh et al used oxazoline derivatives as active ligands to synthesized selenolato complexes which posse's antioxidant, anticancer and antiHIV activity[11]. Sharma et al synthesized derivatives of isoxazoline 3-phenyl amino-5-(substituted phenyl) isoxazoline and found to possess antifungal activity[12]. Arai et al found that isoxazoline compound having macrophage migration inhibitatory factor as asymmetric ligand[13].

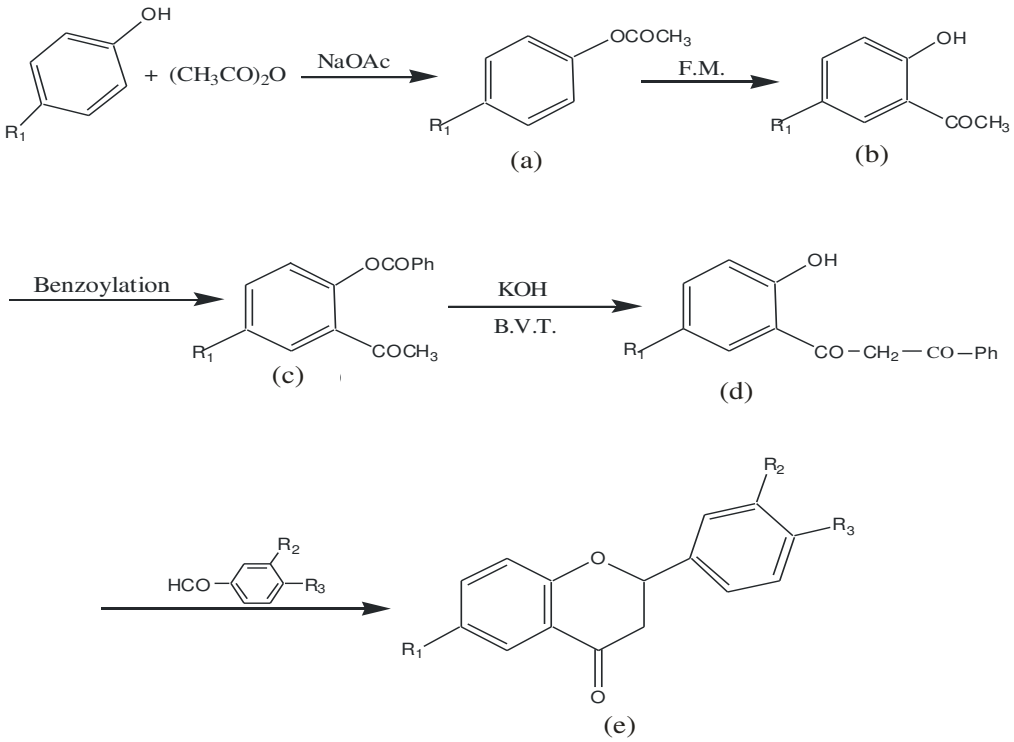
Raekyu Chang etal synthesized 2- Isoxazolines[14]. Jadhav et al synthesized and studied antimicrobial bustle of some novel pyrazoline and isoxazoline derivatives[15]. Tejas Kumar etal synthesized some novel isoxazolines and studies antibacterial activities[16].

Materials and Methods

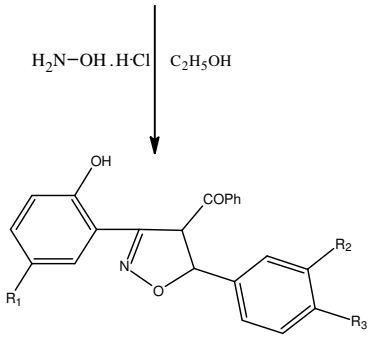
3-aroyl falvanones prepared from phenols by literature method. i. Phenols when treated with acetic anhydride will give phenyl acetate (a), ii. Compound (a) on Fries migration will give 2-hydroxy-acetophenone (b), iii. Compound (b) on benzoylation will give 2-benzoyl-5-methyl-acetophenone (c). iv. Compound (c) on treatment with alkali undergoes transformation to form 1, 3, Substituted 1, 3 - propanedione (d). v. The propanedione (d) on treatment with aromatic aldehydes will gives different flavanones (e). vi. These flavanones will be treated with hydroxyl amine hydrochloride to form Isoxazolines (f).

All the melting points are drawn on VEEGO Melting point apparatus and are accurate. UV spectra are recorded on UV-VIS Spectrometer (Perkin Elmer) using DMSO as a solvent. IR spectra are recorded on Perkin FTIR Spectrometer using KBr pelletes. ^{1}H NMR spectra are recorded on 300MHZ using TMS as reference in $CDCl_3$ at Chemical Technology Matunga Mumbai.

All synthesized compounds are screen for their antimicrobial activity by disc diffusion method using DMSO as control.



Synthesis of 3, 4, 5 substituted isoxazoline



(f) (6)
3, 4, 5 substituted isoxazoline
Scheme-1

Table-1
Physical data of compounds 6a - 6f

Compound code.	Mol. Formula.	R_1	R_2	R_3	M.P. ^0C	Yield %
6a	$C_{22}H_{17}O_3N$	H	H	H	150	55
6b	$C_{23}H_{19}O_4N$	H	H	OCH_3	134	70
6c	$C_{20}H_{15}O_4N$	H	H	H	160	65
6d	$C_{23}H_{19}O_3N$	CH_3	H	H	152	50
6e	$C_{24}H_{21}O_4N$	CH_3	H	OCH_3	171	65
6f	$C_{21}H_{17}O_4N$	CH_3	H	H	147	60

Table-2
Antimicrobial screening of synthesized compounds against test organisms

Sr. No.	Compound code.	Name of compound.	Zone of inhibition (mm)			
			Ec	Pm	Sc	Stc
0	Control	Control	….	…	….	….
1	6a	3-(2-hydroxyphenyl)-4-benzoyl- 5-phenyl isoxazoline	8.3	6.0	8.0	10
2	6b	3-(2-hydroxyphenyl)-4-benzoyl- 5-(4-methoxyphenyl) isoxazoline	6.6	5.6	5.6	8.2
3	6c	3-(2-hydroxyphenyl)-4-benzoyl- 5-(2'furyl) isoxazoline	9.2	8.2	7.4	5.0
4	6d	3-(2-hydroxy-5-methylphenyl)-4-benzoyl- 5-phenyl isoxazoline	8.9	6.3	5.4	9.4
5	6e	3-(2-hydroxy-5-methylphenyl)-4-benzoyl- 5-(4-methoxyphenyl) isoxazoline	6.1	5.7	7.3	6.0
6	6f	3-(2-hydroxy-5-methylphenyl)-4-benzoyl- 5-(2'furyl) isoxazoline	12.0	6.4	7.0	7.6

Ec – Escherechia coli, Pm – Pseudomonas floresae, Sc – Staphylococcus aruaes, Stc–Strptococcus

Table-3
Comparison of Antimicrobial activity of compounds

Organisms	Activity of compounds against tested organism		
	Strong	Moderate	Weak
Escherichia Coli	6f	6c	6e
Pseudomonas floresae	6c	6d,6f	6b,6e
Staphylococcus spp.	6a	6c,6e	6d,6b
Streptococcus spp.	6a	6d	6c

Present investigation results were recorded and compared according to Tejas kumar Shah and Vikas Desai[16].

Results and Discussion

The structure of compounds 6a-f is established on the basis of spectral investigation. UV λ_{max} values for 6a-f found in the range 309.12nm-339.82nm. The infra red Spectrum of 6a-f exhibit a band owing to phenolic O-H str (3340 cm^{-1}), =CH str. (3100-3000 cm^{-1}), C=C str. (1635-1495 cm^{-1}), Aromatic C-H str.(3060cm^{-1}), C=N (ring) (1650-1580 cm^{-1}) stretching vibration bands which show presence of isoxazoline nucleus. Aromatic C = str. (1613cm^{-1}), N-O str. (1215cm^{-1}). Additional in their ^{1}H-NMR ($CDCl_3$) spectrum the emergence of a signal at δ 3.75(s, 3H,-O-CH_3), δ 5.13(d, 1H, CH-CH-C=O, isoxazoline), δ 5.93(d, 1H,-O-CH-Ar, isoxazoline) δ 6.82-7.94(m, 13 H, Ar-H) confirms the presence of isoxazoline ring.

Conclusion

The entire synthesized compound shows inhibition zones against the tested organisms (Table-2), from this may be concluded that these compounds are active at concentration of 0.01mole per wet-disc and DMSO was used as control. All the compounds shows weak to moderate activity against all organisms except 6a, 6c and 6f which shows strong activity against all four tested organisms(Table-3) and compounds 6c,6d,6e and 6f shows moderate activity and remaining shows weak activity against tested organisms. 3, 4, 5 – substituted isoxazolines are good antimicrobial agents and good ligands also hence in future they can be used for the synthesis of their metal complexes, which may shows good antimicrobial activity.

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