Synthesis, characterization and biological evaluation of some isoxazole derivatives from various chalcones

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Abstract : Synthesis and characterization of some isoxazol derivatives has been carried out from chalcone. Initially chalcone were prepared from aromatic aldehyde and ketone in basic medium which then condensed with hydroxylamine hydrochloride. Synthesized compounds were characterized by using NMR, IR and Mass spectroscopic techniques. Spectroscopic data matches with the structure of synthesized compounds. Biological activity of all the synthesized compounds was checked against gram positive and gram negative bacteria. It has been found that all compounds shows good antimicrobial activity. The paper consist of efficient and green method for the synthesis of isoxazole.

Index Terms **– Chalcone, Isoxazole, NMR, IR, Antimicrobial.**

I. INTRODUCTION

The need to reduce the amount of toxic waste and by products arising from chemical processes requires increasing emphasis on the use of less toxic and environmentally compatible materials in the design of new synthetic methods. One of the most promising approaches is the use of water as the reaction medium. Compared to organic solvents the aqueous medium is less expensive, less dangerous, and more environmentally friendly. In recent years, there has been increasing recognition that water is an attractive medium for many organic reactions. Heterocyclic compounds are very important compound in nature, and are essential to life in various ways. These compounds are important because of the their variety of physiological activities associated with this class of substances. Heterocyclic rings are present in several compounds, e. g, most of the members of vitamin B complex, antibiotics, chlorophyll, haemin, other plant pigments, amino acids and proteins, drugs, dye stuffs, enzymes, the genetic material DNA etc. The vast importance of heterocycles in nature product chemistry and pharmacology constantly drive the search for new methods for the construction of heterocyclic unit viz., isoxazoles and pyrazoles. These isoxazoles and pyrazoles were prepared from chalcones which are important intermediate products and they also possess biological and pharmacological activities. Isoxazoles is the five membered ring compound containing nitrogen and oxygen atom and possess interesting medicinal properties and have some industrial utility. Derivatives of Isoxazole have played a crucial role in the history of heterocyclic chemistry and been used extensively important pharmacophores and synthons in the field of organic chemistry. Many biologically active isoxazoles and reduced isoxazole derivatives have been reported. In this paper we have described the synthesis of some chalcone and isoxazole derivatives [1- 4]. Initially chalcones were prepared by condensing aromatic aldehyde and ketone. These chalcone then condensed with hydroxylamine to form isoxazole.

II. EXPERIMENTAL

All melting points were determined in open glass capillaries and are uncorrected. The IR spectra were recorded on KBr disc using Perkin Elmer-1800 intrachord. 1HNMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on Brucker Avance 400MHz spectrophotometer with TMS as internal standard (chemical shifts are expressed in δ ppm). Themass spectra were recorded on a Joel SX-102 (EI/CI/FAB) mass spectrometer at 70 eV. The reactions were monitored by the TLC on silica gel G plates in the solvent system benzene–methanol mixture (9:1). All reagents were purchased from commercial suppliers and used without further purification. The compound includes 2-hydroxy-4-methylacetophenone, benzaldehyde, p-chloro benzaldehyde, anisaldehyde, 4-methyl benzaldehyde.

Synthesis of chalcone:

A mixture of 0.01 mol 2-hydroxy-4- methylacetophenone and 0.01 mol various aldehyde added into ethanol solvent. To this reaction mixture 20 % NaOH added and heated for several minutes' upto formation of solid residue. By keeping overnight residue nuetralized by ice cold HCl solution, filtered and dried in oven [5-7].

Synthesis of isoxazole:

When an equivalent mixture of synthesized chalcone and hydroxylamine hydrochloride was stirred at 50° C in aqueous media, various isoxazole derivatives were obtained in good yields [8-10].

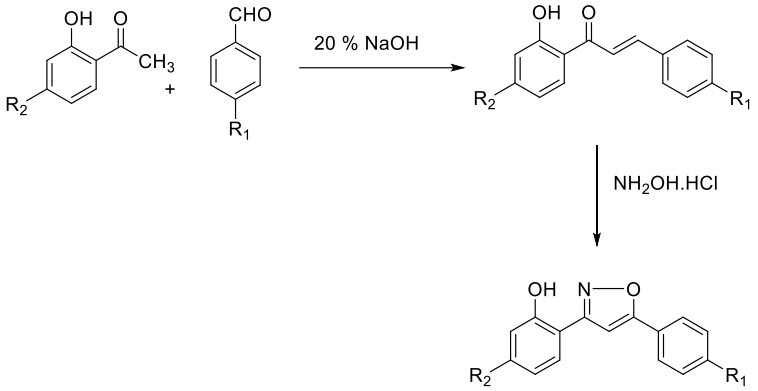

Fig: Scheme of reaction

Sr No	Chalcones	R_1	R_2
1	2-hydroxy-4-methylphenyl-3-phenylprop-2-en-1-one	H	CH_3
2	2-hydroxy-4-methylphenyl-3-(p-tolyl)prop-2-en-1-one	CH_3	CH_3
3	4-chlorophenyl-2-hydroxy-4-methylphenyl-prop-2-en-1-one	Cl	CH_3
4	1-(2-hydroxy-4-methylphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one	OMe	CH_3

III. Result and Discussion

The paper consists of the synthesis and characterization of some isoxazoles.These isoxazoles was prepared from chalcones which are important intermediate products as they possess varied biological and pharmacological activities. They can be obtained by the acid or base catalyzed aldol condensation of O-hydroxy acetophenones with benzaldehydes. Synthesis of various chalcones is reported in the literatures. All the synthesized compounds were found to be pure and dissolved in methanol.

Table : Analytical data of synthesized compound

Sr No	Molecular formula	M.P. (ºC)	Yield (%)	C %	H %	N %
1	$C_{16}H_{13}NO_2$ (1a)	112	84	76.48	5.21	5.57
2	$C_{17}H_{15}NO_2$ (1b)	119	78	76.96	5.70	5.28
3	$C_{16}H_{12}ClNO_2$ (1c)	110	76	67.26	4.23	4.90
4	$C_{17}H_{15}NO_3$ (1d)	123	81	72.58	5.37	4.98

5-methyl-2-(5-phenylisoxazol-3-yl)phenol: (1a)
Mp: 112° C; IR (KBr) *v*: 3059(Ar C-H), 1606 (C=O), 2970 (Al C-H), 3345 (O-H), 1590 (C=N), 1226 (C-O). ^{1}H-NMR (400 MHz, CDCl3) δ (ppm) 2.28 (s, 3H, CH3), 9.61 (s, 1H, OH), 6.77 (d, 1H, CH), 6.79 (d,1H), 6.84-7.78 (m, 8H, ArH). MS:(m/z) 251

5-methyl-2-(5-(p-tolyl)isoxazol-3-yl)phenol: (1b)
Mp: 119° C; IR (KBr) *v*: 3064 (Ar C-H), 1630 (C=O), 2982 (Al C-H), 3340 (O-H), 1590 (C=N), 1226 (C-O).
^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 2.28 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 9.61 (s, 1H, OH), 6.77 (d, 1H, CH), 6.79 (d,1H), 6.90-7.78 (m, 7H, ArH). MS:(m/z) 265

2-(5-(4-chlorophenyl)isoxazol-3-yl)-5-methylphenol: (1c)
Mp: 110° C; IR (KBr) *v*: 3024(Ar C-H), 1642 (C=O), 2982 (Al C-H), 3350 (O-H), 1590 (C=N), 1230 (C-O). ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 2.28 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 9.61 (s, 1H, OH), 6.70 (d, 1H, CH), 6.79 (d,1H), 6.90-7.74 (m, 7H, ArH). MS:(m/z) 285

2-(5-(4-methoxyphenyl)isoxazol-3-yl)-5-methylphenol: (1d)
Mp: 123° C; IR (KBr) *v*: 3024(Ar C-H), 1642 (C=O), 2982 (Al C-H), 3350 (O-H), 1590 (C=N), 1230 (C-O).
^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 2.28 (s, 3H, CH_3), 3.81 (s, 3H, OCH_3), 9.57 (s, 1H, OH), 6.70 (d, 1H, CH), 6.79 (d,1H), 6.90-7.74 (m, 7H, ArH). MS:(m/z) 281

IV. Biological Activity

The newly synthesized compounds were subjected to invitro antibacterial activity against by Cup-Plate diffusion method using organisms E.coli and B. subtilis. The compound were tested at concentration of 25, 50 and 100 mg/ml against two gram positive bacterium and two gram negative bacterium. Compound (1a) and (4a) possesses significant while (2a) and (3a) possesses moderate antibacterial activity against B. subtilis and E. coli bacteria [11 & 12].

V. Conclusion

Many methods have been reported for the synthesis of isoxazole but most of them require catalyst, temp etc. In this paper we have developed an efficient synthesis of isoxazole derivatives via the reaction of synthesized chalcone with hydroxylamine hydrochloride in aqueous media without using any catalyst. This method has the advantages of an easier work-up, mild reaction conditions, high yields, and an environmentally benign procedure.

VI. Acknoeledgement

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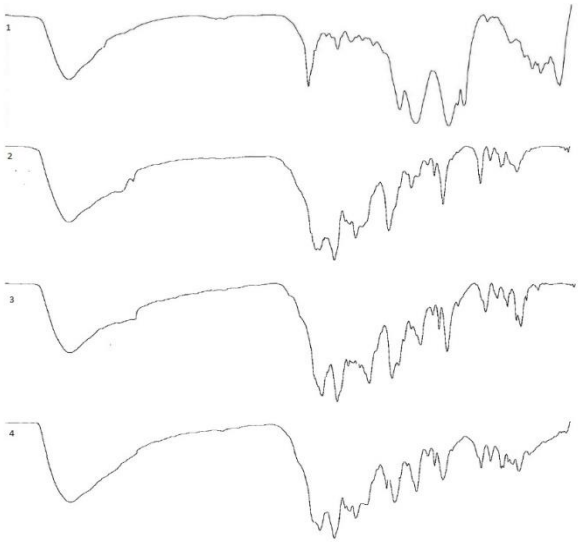
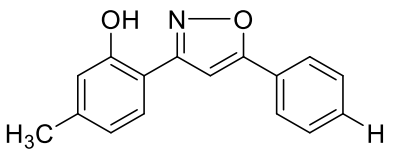


Fig 2: IR spectrum of isoxazole



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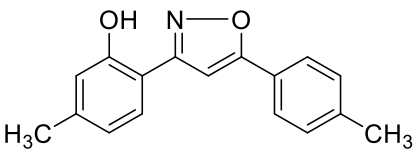

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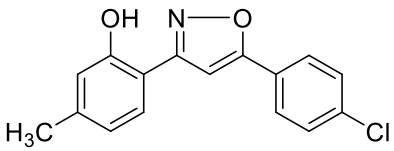

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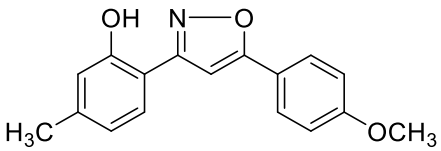

(1d)

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