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Ecofriendly Synthesis, Characterization and Antibacterial Assay of Some Chlorosubstituted Isoxazoles

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Abstract

The concept of green chemistry is now widely adopted to meet the scientific challenges in order to protect the human health and environment. Nowadays researchers are working extensively to synthesize new compounds using ecofriendly solvents and other conditions. Literature survey reveals that isoxazoles are very useful units in the fields of medicinal, pharmaceutical and agriculture. Isoxazoles have been reported to exhibit a broad spectrum of biological activities. In this regard, in the present study, we have undertaken synthesis and characterization of new chlorosubstitutedisoxazole derivatives by the action of chlorosubstituted flavones, which were prepared from chalcones in a ecofriendly single step, with hydroxylamine hydrochloride in good yields. The newly synthesized compounds are screened against some bacteria with special reference to study antipathogenic activities.

Keywords: *Chlorosubstitutedisoxazoles, flavones, chalcones, antibacterial assay, antipathogenic activities.*

Introduction

Literature survey shows that the chlorosubstituted heterocycles[1] have antifungal[2], antimicrobial[3], antitubercular[4], antiviral[5], and antibacterial[6] activity. Taking into account the widespread applications of chlorosubstituted heterocycles such as pyrazoles, thiazoles, isoxazoles[7] in the fields of pharmaceutical, medicine and agriculture, it was thought interesting to synthesize some new chlrosubstituted isoxazoles and study their impact on plant pathogens especially bacteria. The isoxazoles are the compounds having five membered ring containing both oxygen & nitrogen atoms in the 1,2 positions. It has been observed that flavones are the best starting compounds for the preparation of isoxazole derivatives. These flavones are prepared from chalcones in a ecofriendly single step.

Experimental

Scheme-I

Preparation of 2,4-dichloro phenyl acetate(*1a*): 2,4-dichlorophenol (10gm) was mixed with acetic anhydride (12ml) and anhydrous sodium acetate (1gm). The mixture was refluxed for about an hour. The

mixture was cooled and poured into cold water. Acetate layer was separated and then washed with water several times. It was finally collected by distillation.

Preparation of 1-(3,5-dichloro-2-hydroxyphenyl)ethanone(2a): 2,4-dichlorophenol (10ml) was mixed with anhydrous $AlCl_3$(24gm) and heated at 120^0C for 45 minutes. The reaction mixture was decomposed with ice cold water containing a little HCl. A greenish solid thus separated was recrystallised by ethanol to get compound 2a.

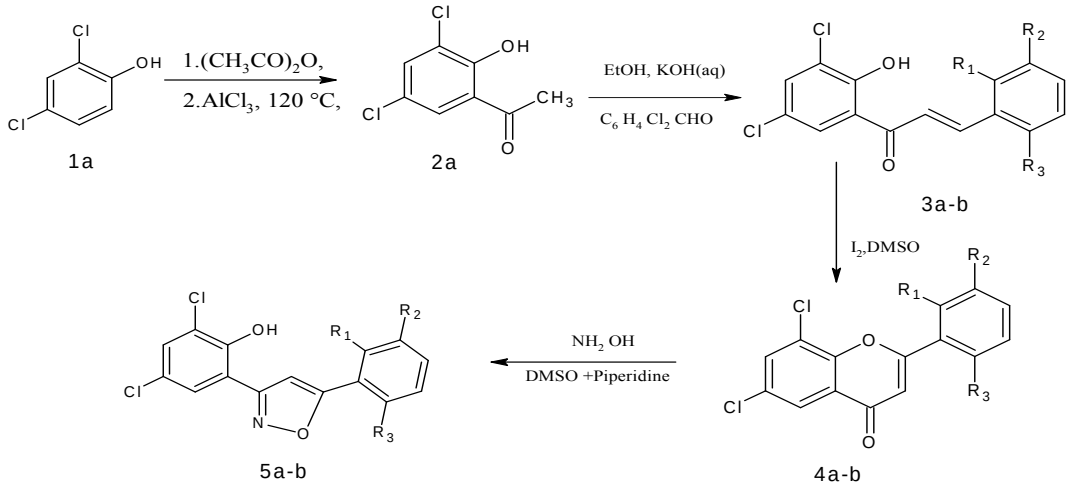
IR(KBr ν_{max})(cm^{-1}) 3050cm^{-1}(-OH phenolic str),1665(C=Ostr), 1300(C-Ostr), 730(C-Clstr)

NMR: δ12.73(s,1H,Ar-H) , δ7.25-7.63(m,2H,Ar-H) , δ2.60,(s,3H,-CH_3).

Preparation of 1-(3,5-dichloro-2-hydroxyphenyl)-3-(2,3-dichlorophenyl)prop-2-en-1-one(3a): 1-(3,5-dichloro-2-hydroxyphenyl) ethanone (0.01M) and 2,3-dichlorobenzaldehyde(0.01M) were added to ethanol(20ml). To this mixture KOH solution(40%,10ml) was added drop wise . The reaction mixture was kept for overnight, then poured on ice containing little HCl. The product was filtered and recyrstallised from ethanol to obtain the compound 3a.

IR(KBr ν_{max})(cm^{-1}) 3417cm^{-1}(O-Hstr),1645(C=Ostr),308cm^{-1}(ArC-Hstr),1648cm^{-1} (C=Cstr),738cm^{-1}(C-Clstr).

NMR: δ8.17(d,1H,CH=CH) , δ7.39(d,1H,CH=CH), δ6.7-7.5(m,5H,Ar-H), δ5.0(s,1H,Ar-OH).



where a; R_1=Cl, R_2=H,R_3=Cl and b ; R_1=Cl, R_2=Cl,R_3=H

Preparation of 6,8-dichloro-2-(2,3-dichlorophenyl)-4*H*-chromen-4-one (4a) -

1-(3,5-dichloro-2-hydroxyphenyl)-3-(2,3-dichlorophenyl)prop-2-en-1-one (0.01M) was dissolved in 20ml DMSO, To this few crystals of Iodine were added. The mixture was refluxed for 10 min. Then the

mixture was poured on the crushed ice. The product was filtered and recrystallised from chloroform to get compound 4a.

IR(KBr ν_{max})(cm^{-1}):3400cm^{-1}(O-Hstr), 1650cm(C=Ostr),1310cm^{-1}(C-Osrt),730cm^{-1}(C-Clstr).

NMR: δ9.1(m,2H,Ar-H) , δ7.9(m,2H,Ar-H),δ7.3(s,1H,Ar-H),δ7.1(m,4H,Ar-H), δ5.1(s,1H,Ar-OH), δ4.8(m,1H,CH), δ2.0(d,1H,-CH_2), δ1.8(d,1H,-CH_2).

Preparation of 2,4-dichloro-6-[5-(2,3-dichlorophenyl)-1,2-oxazol-3-yl]phenol (5a) : 6,8-dichloro-2-(2,3-dichlorophenyl)-4*H*-chromen-4-one (0.01M) and hydroxylamine hydrochloride(0.01) dissolved in 20ml DMSO with a few drops of pipyridine. The mixture was refluxed for 1.5 hrs. The product was filtered and recrystallised from chloroform to get compound 5a.

IR(KBr ν_{max})(cm^{-1}) :3400cm^{-1}(O-Hstr),1584cm^{-1} (C=Nstr),1310cm^{-1}(C-Osrt), ,730cm-1(C-Clstr).

NMR: δ8.3(s,1H,C-H),δ7.1-7.3(m,5H,Ar-H),δ5.2(s,1H,Ar-H).

Antibacterial Study

The newly synthesized compounds(5a and 5b) were screened for their antibacterial activity against some *Gram positive* pathogens viz. *Staphylococcus aureas* and *Streptococcus sp.* and some *Gram negative* pathogens viz. *Pseudomonas sp.* and *Solmonella Typhi.* at conc.of 1000 µm gentamycine as a standard. DMF was used as solvent control using agar plate techniques. The chlorosubstituted isoxazoles synthesized when screened for antibacterial activity, it was noticed that all these compounds had shown remarkable inhibitory activity.

Results And Discution

Physical characterization data of all the compounds are given in Table-1.

TABLE-1

CHARACTERIZATION DATA OF NEWLY SYNTHESIZED COMPOUNDS

Compound	Mol. Formula	M.P.(^{0}C)	Yield(%)	R_f
1a	$C_8 H_6 Cl_2 O_2$	214(B.P.)	85	0.75
2a	$C_8 H_6 Cl_2 O_2$	91-92	70	0.80
3a	$C_{15} H_8 Cl_4 O_2$	84-86	80	0.77
3b	$C_{15} H_8 Cl_4 O_2$	95-97	82	0.73
4a	$C_{15} H_7 Cl_4 O_2$	160-162	59	0.74
4b	$C_{15} H_7 Cl_4 O_2$	183-185	57	0.82
5a	$C_{15} H_7 Cl_4 NO_2$	195-197	63	0.72
5b	$C_{15} H_7 Cl_4 NO_2$	186-188	61	0.81

The synthetic routes which furnished the target compounds are shown below along with their IR and NMR data. The newly synthesized compounds (5a and 5b) were found to be active against test pathogens. A further detailed study in the light of Medical sciences is advised.

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