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Research Article

EVALUTION AND SYNTHESIS OF 5-CHLORO BENZOFURAN DERIVATIVES FOR ANTIBACTERIAL ACTIVITY

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ABSTRACT

In the present work, some new benzofuran derivatives were prepared 5-Chloro benzofuran -2-carbohydrazide synthesized, by ethyl 5-Chloro benzofuran -2-caboxylate with various substituated aromatic aldehyde to give schiff base and obtained compound were cyclized with carbon disulphide and alcoholic potassium hydroxide to obtain various 5-Chloro benzofuran derivatives.The structure of the products was characterized by spectral data. All the compounds were evaluated for antibacterial activity against *Staphylococcus aureus* and *Escherichia coli.*

Keywords: Antibacterial activity, Synthesis, 5-Chloro Benzofuran derivatives

INTRODUCTION

Benzofuran are the important group of heterocyclic compound, several derivatives of which have been marked as biologically and pharmacologically active product. The literature survey revealed that, benzofuran also possess different biological activities such as anti-inflammatory [1], antimicrobial [2] , analgesic [3], antihypertensive [4] activity . These observations stimulated us to synthesize some new Benzofuran derivatives for better activities.

MATERIALS AND METHOD

Melting point of all derivatives was determined by open capillary method and are uncorrected..The IR spectra were recorded with KBR pellets on Shimadzu FT-IR-8400S Spectrophotometer.H1 NMR were recorded on Bruker spectrospin-200 NMR spectrophotometer and the Mass spectral analysis of the compounds was carried out by using Turbospray Mass spectrometer.

Synthesis of Ethyl 5-Chloro benzofuran-2-carboxylate (iii)

5-Chloro Salicyladehyde (20.0ml, 0.164mol) and diethylbromomalonate (40.0ml, 0.168mol) in ethyl methyl ketone (40.0ml, 0.555mol) was treated with anhydrous potassium carbonate (20.0g, 0.869mol).The reaction mixture was refluxed for 18 hours on steam bath.

Ethyl methyl ketone was distilled off under reduced pressure and the residue formed was dissolved in 400ml of water and cooled in an ice-bath.It was acidified with dil H_2SO_4.The product formed was extracted with 25ml portion of solvent ether twice and the extract was washed with sodium bicarbonate solution. It was dried over calcium chloride. Solvent was removed and the residue ethyl 5-Chloro bezofuran-2-carboxylate was dried.

Synthesis of 5-Chloro Benzofuran-2-carbohydrazide (iv)

Ethyl 5-Chloro benzofuran-2-carboxylate (17.40g, 0.1mol) and hydrazine hydrate 99 %(4.8ml, 0.1mol) in methanol (35.0ml) was refluxed for 8 hours.The reaction mixture was concentrated a solid which was formed filtered and recrystallized from methanol.The precipitate obtained is 5-Chloro benzofuran-2-carbohydrazide.

Synthesis of shift base (v)

In a 100ml Round bottom flask, 5-Chloro Benzofuran-2-carbohydrazide (2.5g, 0.01mol) was treated with different aromatic aldehyde (1.72g, 0.01mol) in methanol(35.0ml) containing a drop of glacial acetic acid as a catalyst was refluxed for 4hours and cooled. Methanol was distilled off under pressure.The solid thus obtained shiff base were filtered and recrystallized from toluene.

Synthesis of 5-Chloro benzofuran derivatives (via-e)

Shift base in ethanol (12.0ml) to this solution potassium hydroxide (0.5g, 0.008mol) and carbon disulphide (1.0 ml, 0.013mol) were added. The mixture was refluxed on steam bath for 10hours.The solution was allowed to cool overnight and then concentrated. The solution was again cooled at room temp and then dissolved in 150.0ml ice cold water. The resulting solution was acidified with dil HCl and allowed to stand for 12hours.The solid which was filtered and it was air dried and recrystalized from ethanol.

(via) IR : (in cm^{-1}): 3304.50 cm^{-1}(O-HAr), 3022.20 cm^{-1} (C-HAr),

2940.63cm^{-1} (C-H Aliphatic), 1592.97 cm^{-1} (C=N str), 1321.65 cm^{-1} (C-N str),

1046.36 cm^{-1} (C=S str), 651 cm^{-1} (Cl-Ar),1117.15 cm^{-1}(C-O-C str).

^{1}H NMR :(in δ, ppm) δ 6.61-8.65(m, 10H, ArH), δ3.84(s, 2H, CH_2)

δ 4.87(s, 1H,OH).

(vib) IR: (in cm^{-1}): 3264.97 cm-1 (C-HAr), 2950.32cm-1 (C- H Aliphatic), 1591.70 cm-1 (C=N str), 1305.23 cm-1 (C-N str),1035.89 cm-1 (C=S str), 655 cm^{-1} (Cl-Ar),1090.51 cm-1(C-O-C str).

^{1}H NMR (in δ, ppm) : δ 6.74-8.35(m, 6H, ArH), δ3.94(s, 3H, OCH_3) δ 4.30(s, 2H,CH_2).

(vic) IR: (in cm^{-1}): 3060.18 cm^{-1} (C-HAr), 2919.22cm^{-1} (C-H Aliphatic), 1598.11 cm^{-1} (C=N str), 1291.69 cm^{-1} (C-N str), 1090.51 cm^{-1} (C=S str), 659 cm^{-1} (Cl-Ar),1180.61 cm^{-1}(C-O-C str).

^{1}H NMR (in δ, ppm) δ 6.74-8.86(m, 8H, ArH), δ3.71(s, 3H, OCH_3) δ 4.21(s, 2H,CH_2).

Mass spectrum of the compounds exhibited the characteristic signals at: m/z= 402.4

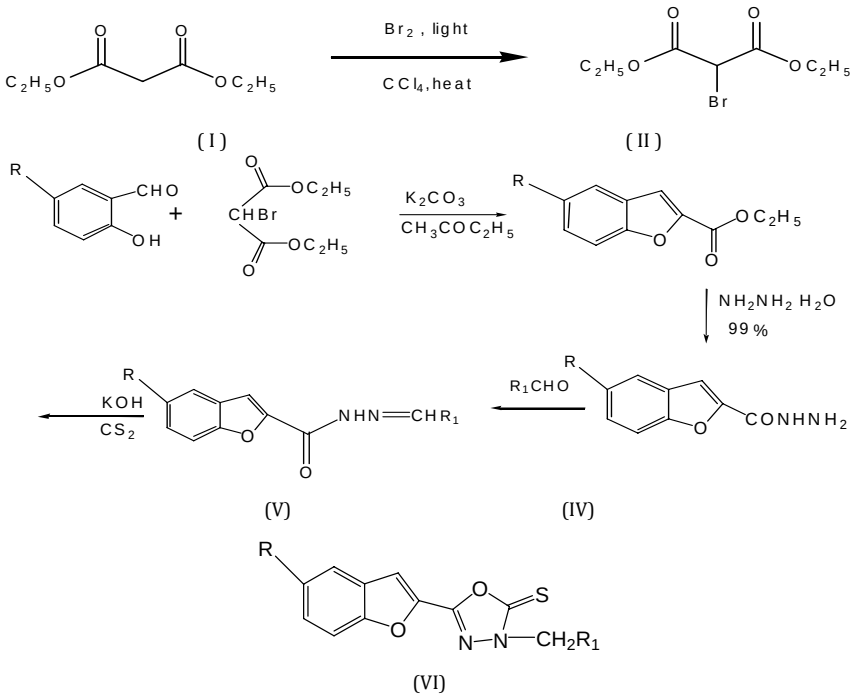
(vid) IR: (in cm^{-1}): 3440.89cm^{-1}(O-HAr), 3082.57 cm^{-1} (C-HAr), 2816.70cm^{-1} (C-H Aliphatic), 1576.71 cm^{-1} (C=N str), 1291.05 cm^{-1} (C-N str), 1089.29 cm^{-1}(C=S str), 591 cm^{-1} (Cl-Ar),1192.65 cm^{-1}(C-O-C str).

^{1}H NMR (in δ, ppm): δ 6.94-8.85(m, 8H, ArH), δ3.84(s, 2H, CH_2), δ4.24(q, 2H, CH_2),

δ 1.52(t, 3H, CH_3)

(vie) IR: (in cm^{-1}): 3088.05 cm-1 (C-HAr), 2940.16cm-1 (C- H Aliphatic), 1527.21 cm-1 (C=N str), 1279.95 cm-1 (C-N str), 1081.71 cm-1 (C=S str), 656 cm^{-1} (Cl-Ar), 1169.03 cm-1(C-O-C str).

^{1}H NMR (in δ, ppm) δ 6.74-8.38 (m, 8H, ArH), δ 4.31(s, 2H,CH_2).



SCHEME -1

Compound no.	R	R1
via	Cl	2-hydroxy1-naphthaldehyde
vib	Cl	3,4,5 trimethoxy benzaldehyde
vic	Cl	2-methoxy benzaldehyde
vid	Cl	4-hydroxy3-ethoxy benzaldehyde
vie	Cl	pyridine1-carboxyaldehyde

RESULT AND DISCUSSION

Anti-bacterial activity: All the synthesized compounds (via-vie) were screened for their anti-bacterial activity by cup plate diffusion technique[6-9] .The prepared microbial suspension was added in the media and mixed with and transferred into petridish.16µg/ml solution of ciprofloxacin and ampicillin 32µg/ml in DMSO was prepared as standard and 30µg/ml in DMSO was prepared as sample. The zone of inhibition was measured in millimeter (Fig : 1 and Fig : 2) and reported in Table-2 .

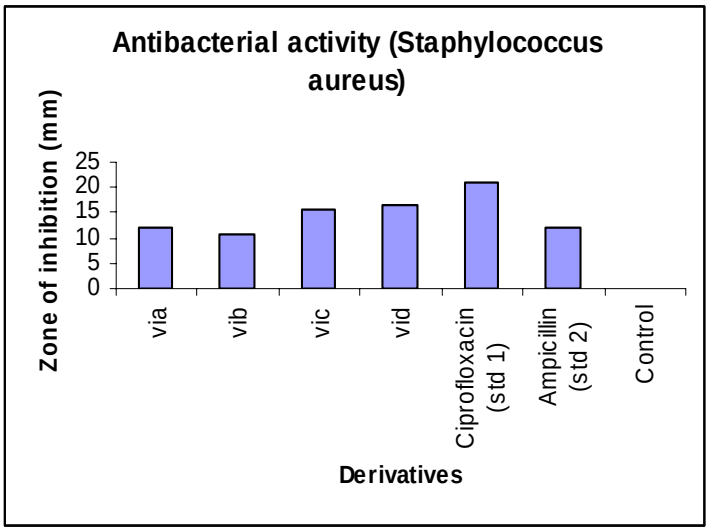


Fig. 1

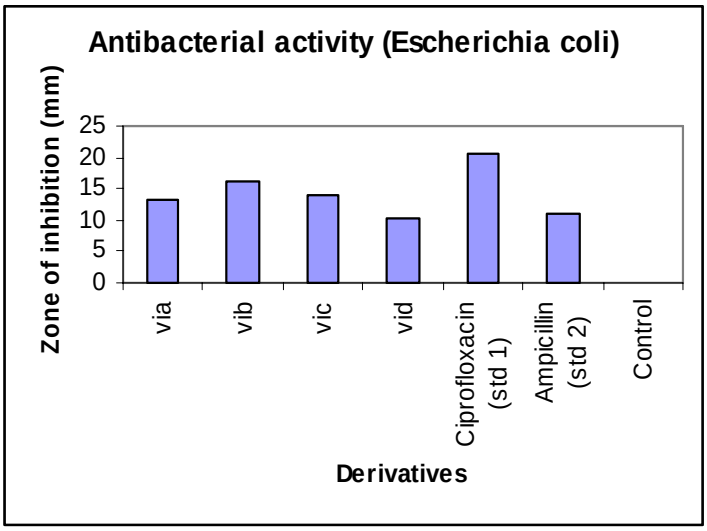


Fig. 2

Table 1: Characterization data of 5-chlorobenzofuran derivatives

Compound code	Molecular formula	Molecular weight	MP ^{O}C	% Yield	Rf	Anti-bacterial activity
via	$C_{18}H_{13}N_2O_3SCl$	372.8	145-147	56%	0.50	Active
vib	$C_{20}H_{17}N_2O_5SCl$	432.93	180-182	60.3%	0.35	Active
vic	$C_{19}H_{15}N_2O_4SCl$	402.9	168-170	64.7%	0.45	Inactive
vid	$C_{17}H_{10}N_2O_4SCl_2$	377	170-173	59.3%	0.48	Active
vie	$C_{16}H_{10}N_3O_2SCl$	309.34	165-168	53.2%	0.55	Active

Table 2: Antibacterial activity 0f 5-Chloro benzofuran derivatives

	Zone of inhibition(mm)	
Compounds	***Staphylococcus aureus***	***Escherichia coil***
via	12.243±0.211**	13.323±0.212**
vib	10.521±0.344**	16.125±0.320**
vic	15.632±0.324**	13.838±0.278**
vid	16.552±0.276**	10.463±0.148**
Ciprofloxacin (std 1)	21.186±0.057**	20.753±0.242**
Ampicillin (std 2)	12. 142±0.143**	11.180±0.027**
Control	0.037±0.023	0.037±0.023

Values are Mean ± SEM, n=5 , ** P < 0.01, when compared with control.

CONCLUSION

A total number of ten Benzofuran derivatives were subjected to anti-bacterial activity using specific gram positive and gram negative bacteria like S.aureus, E.coli. From the above result it can be concluded that the various derivatives that were synthesized were confirmed by various analytical methods & the anti-bacterial activity screening showed that derivatives vi (a-d)] had significant activity comparable to that of standard.

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