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SYNTHESIS, CHARACTERIZATION AND ANTI-MICROBIAL ACTIVITY OF SUBSTITUTED BENZOXAZOLE DERIVATIVES

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ABSTRACT

A Series of some novel benzoxazole compounds were synthesized and evaluated for anti-microbial activity. The reaction of o-aminophenol with dicarboxylic acid yield substituted benzoxazole. The title compounds were synthesized by treating substituted benzoxazole with oxalic acid,cinnamicacid, succinic acid,phthalic acid,salicylic acid.Their structures were confirmed by IR, ^{1}HNMR, and ^{13}CNMR. Anti-microbial activity against *staphylococclus aureus* was studied for the synthesized compounds.

KEY WORDS: Benzoxazole, o-aminophenol, dicarboxylic acid, Anti-microbial.

INTRODUCTION

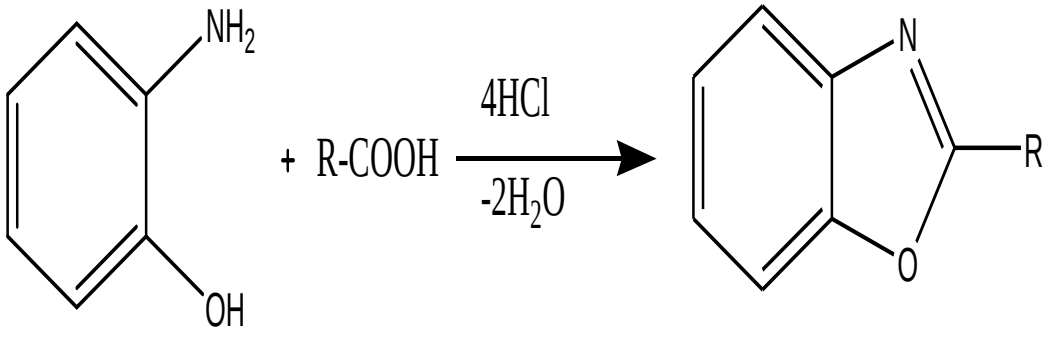
The small and simple benzoxazole nucleus is present in compounds involved in research possess interesting biological activities like antifungal[1] , antihistaminic[2], antitumor[3] , antinuclear[4] anti-inflammatory[5] anti-HIV[6] and anti-cancer[7]. Benzoxazole is used primarily in industry and research, and has no household use. Being a heterocyclic compound, benzoxazole finds use in research as a starting material for the synthesis of larger, usually bioactive structures [8-9]. Benzoxazole can be considered as structural isosteres1 of the naturally occurring nucleic bases adenine and guanine, which allow them to interact easily with polymers of living systems[10].In the present study is it planned to synthesize benzoxazole compounds and characterize these compounds by IR, ^{1}H NMR and ^{13}C NMR spectral analysis. Since these compounds contain highly biological active benzoxazole nucleus, it is also aimed at carrying out anti-microbial activity [11].

MATERIALS AND METHODS

All melting points were taken in open capillaries and are uncorrected. Elemental analysis was performed on aPerkin-Elmer analyzer. IR spectral[12]were recorded in KBr on Shimadzu spectrometer, ^{1}H-NMR[13] and ^{13}C-NMR[14]in DMSO-d6 on a Bruker AC-400 spectrometer using TMS as an internal standard. The microorganisms were obtained from National Chemical Laboratory, Pune

General procedure for the synthesis of benzoxazole compounds(A-E)

O-aminophenol (4.0 g) was condensed with dicarboxylic acids (oxalic acid, succinic acid, salicylic acid, phthalic acid, cinnamic acid) in 50ml of 4N HCL. The reaction mixture was stirred for about 4hours with magnetic stirrer at 80°C. The product were precipitated by adding concentrated ammonia solution, filtered through suction and washed with cold water. The synthesized compounds were recrystallized from water and ethanol.**Scheme 1**



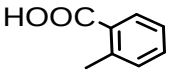
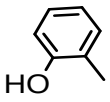
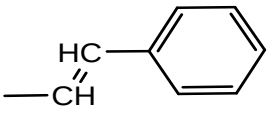
	R
A	-COOH
B	-CH2-CH2-COOH
C	
D	
E	

Table1:Analytical data of benzoxazole compounds (A-E)

Compound	%yield	Molecular Formula	Molecular Weight
A	56	$C_8H_5N_1O_3$	163
B	78	$C_{10}H_9N_1O_3$	191
C	79	$C_{14}H_9N_1O_3$	239
D	74	$C_{13}H_9N_1O_2$	211
E	67	$C_{15}H_{11}N_1O$	221

IR Spectral data of the synthesizedcompounds(A-E)

Table 2: The IR frequencies of the synthesized benzoxazole compounds (A-E) [15] are tabulated (Table 2) as follows:

Compounds	Frequency in cm^{-1}						
	C-H	C=N	C-N	C-O	C=O	C-C	O-H
A	3063	1761	1271	1404	1730	742	2852
B	3055	1598	1273	1404	-	744	2852
C	3055	1730	1267	1400	1874	761	2850
D	2924	1780	1267	1406	-	742	2852
E	2958	1739	1267	1408	1722	742	2852

NMR data of the synthesized compounds(A-E)

Table 3:The ^1H NMR frequencies of the synthesized compounds (A-E) are tabulated (Table3) as follows:

Compounds	Chemical shift In ppm			
	Ar-H	-COOH	$-CH_2$	OH
A	6.669	8.971	-	-
B	6.669	9.003	2.500	-
C	6.674	9.034	-	-
D	6.652	-	-	8.988
E	6.671	9.005	-	-

Table 4: The following table (Table 4) shows the ^{13}C NMR frequencies of the synthesized compounds(A-E) [16].

Compounds	Chemical shift of sp2 Carbon in ppm	Chemical shift of carbonyl Carbon in ppm
A	39.44	139.96
B	39.66	143.96
C	39.41	139.96
D	39.37	143.94
E	39.55	143.97

Antimicrobial study

The purified compounds A, B, C, D and E were tested for their antimicrobial activity against *Staphylococcus aureus.*The results suggest that the synthesized compound A, exhibit high antimicrobial activity against *Staphylococcus aureus,[17]*.

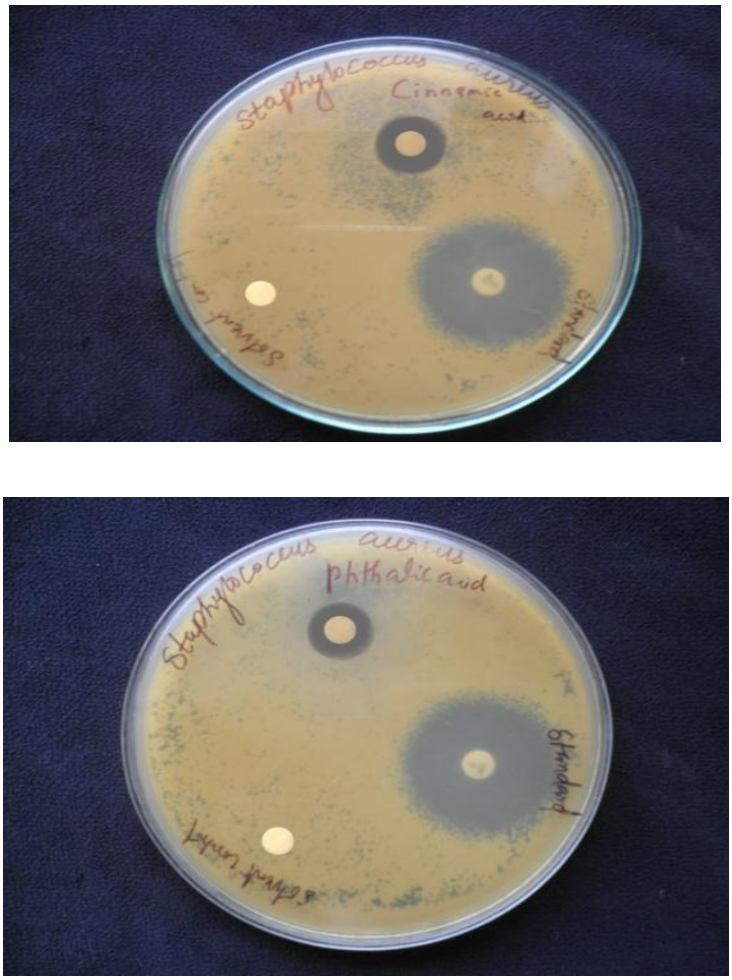


Fig 1. Anti-microbial activity of compound A&B

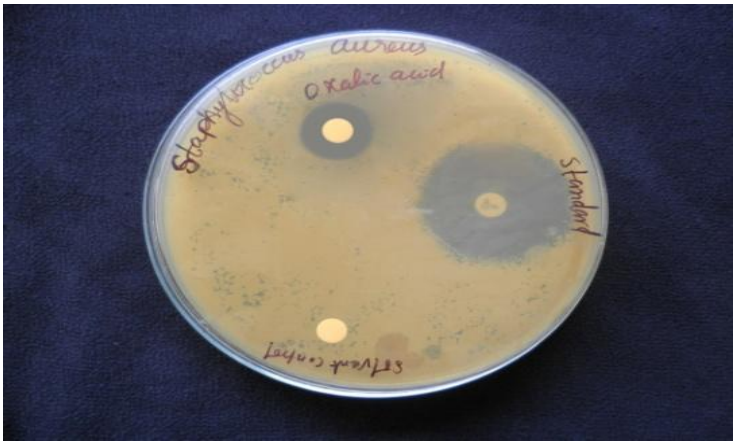


Fig 2. Antimicrobial activity of Compound C&D

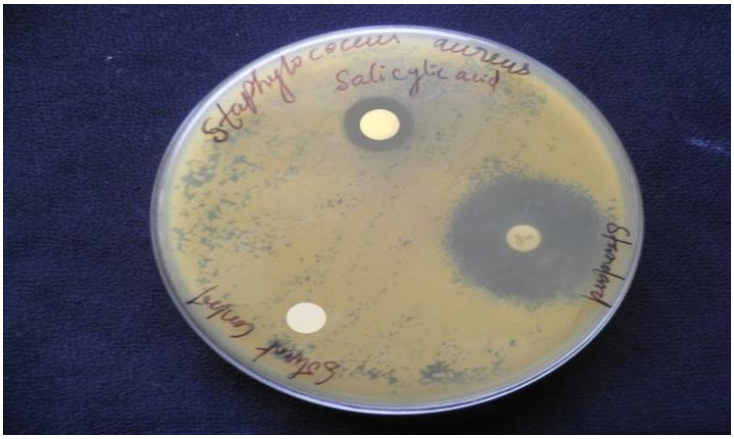


Fig 5. Anti-microbial activity of Compound E

RESULTS AND DISCUSSION

The anti-microbial activity for the given sample was carried out by disc diffusion technique. The test microorganisms of *Staphylococcus aureus*, were obtained from National Chemical Laboratory (NLC) Pune and maintained by periodical sub culturing on nutrient agar medium for bacteria. The effect produced by the sample was compared with the effect produced by the positive control (reference standard ciprofloxacin 5 µg/disc [18-20].

Table 5:The following table(Table 5) shows the antimicrobial activity of the synthesized compounds(A-E).

Name of the Micro organisms	**Zone of inhibition in mm**					
	A	B	C	D	E	Std
Staphylococcus aureus (NCIM 2079)	25	20	24	18	18	35

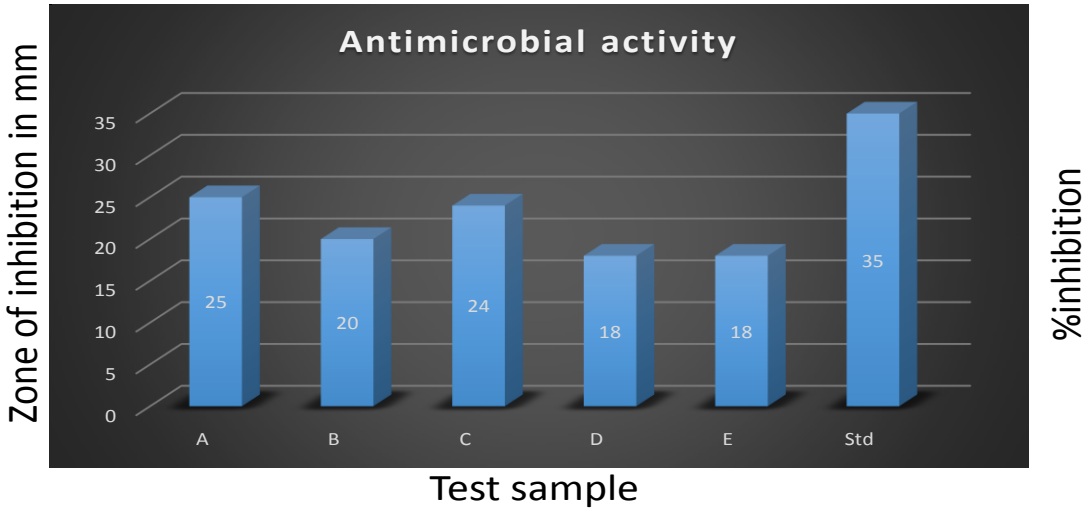


Fig 6.Antimicrobial activity (Staphylococcus aureus)

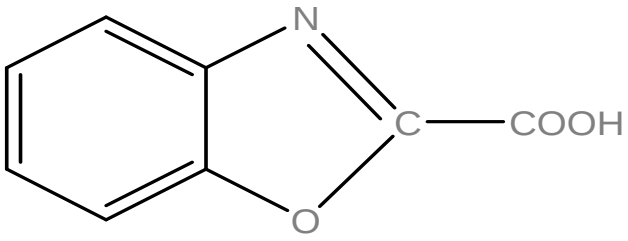
DISCUSSION

The reaction o-aminophenol with of with dicarboxylic acids (oxalic acid, cinnamic acid, succinic acid, phthalic acid, salicylic acid) yield substituted-benzoxazole [21].The title compounds were synthesized by treating substituted benzoxazolewith 4HCl and $2H_2O$. Their structures were confirmed by IR,^{1}H-NMR and ^{13}CNMR. Antimicrobial activity against *Staphylococcus aureus*,was studied for the synthesized compounds. The purity and homogeneity of all the synthesized compounds were confirmed by their column chromatography [22]. The aromatic stretching frequencies for all the derivatives were found to be at the range of 2900-3100 cm-1.The presence of NH stretching was confirmed by the peaks at 3100-3200 cm^{-1}. NH 1730 cm^{-1}, C=O 1630 cm^{-1}, C=N 3084 cm^{-1}, Ar–H 877 cm^{-1}[21]. Also 1H-NMR spectra were useful for identifying protons.The peaks at the frequency range 6.0 – 8.0 confirm the aromatic protons.O-H 12.4ppm, CH 8.4ppm, Ar-H 7.0-7.6ppm, CH_3 3.9ppm [23].Compound A (Benzooxazole-2-carboxylic acid) shows more activity than the other compounds against *Staphylococcus aureus[23-25]*.

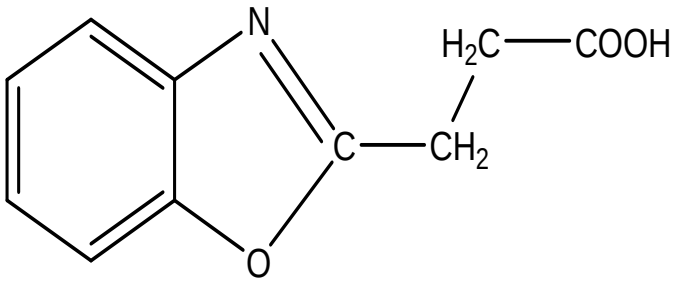
CONCLUSION

1. **Co**mpounds A-E are prepared using scheme 1.
2. IR, 1H NMR, 13 C NMR spectra are taken. The results are in good agreement with the reported results.
3. The Anti-microbialactivity is studied and the compound A shows maximum activity.

   Hence from the above results and discussion, the structure of the newly synthesized compounds are as follows:

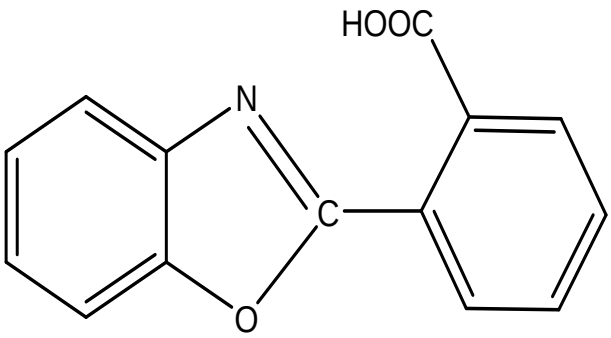


Benzooxazole-2-carboxylic acid



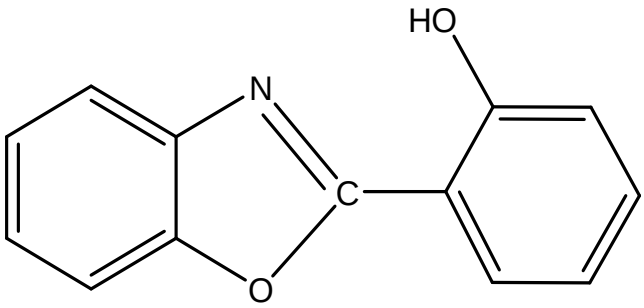
3-Benzooxazol-2-yl-propionic acid

Fig 7. Compound A&B

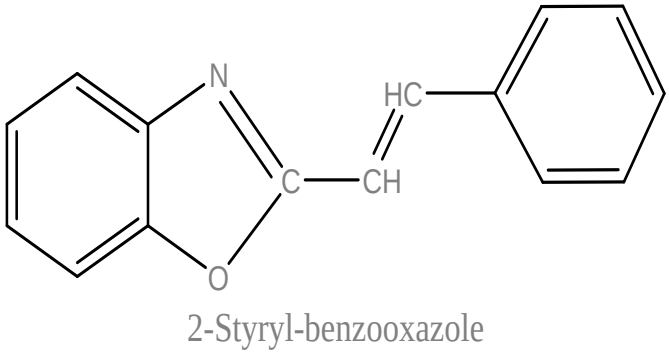


2-Benzooxazol-2-yl-benzoic acid

Fig 8. Compound C&D



2-Benzooxazol-2-yl-phenol



2-Styryl-benzooxazole

Fig 9. Compound E

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