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Research Article

SYNTHESIS OF SOME NOVEL METHYL-2-(2- (ARYLIDENEAMINO) OXAZOL-4- YLAMINO) BENZOXAZOLE-5-CARBOXYLATE DERIVATIVES AS ANTIMICROBIAL AGENTS

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ABSTRACT

A series of methyl-2-(arylideneamino) oxazol-4ylamino) benzoxazole-5-carboxylate derivatives (**a–i**) were synthesized and their antimicrobial activities determined in comparison to several control drugs. The synthesized compounds were tested *in vitro* against *Staphylococcus aureus*, and *Bacillus subtilis* as Gram-positive, *S.typhi* and *Escherichia coli* as Gram-negative bacteria and the yeast *Candida albicans* and *A.niger*. Microbiological results showed that the compounds possessed a diffuse spectrum of antibacterial activity against these microorganisms. Compound **VIIe** which bears a methoxy moiety at position 4-of phenyl ring at the 2-position of benzoxazole ring was the most active derivative against *S. aureus, Bacillus subtilis, S.typhi, Escherichia coli, Candida albicans* and *A.niger*. Compound **VIIg** provided higher potency than the other tested compounds against both antibacterial and antifungal organisms.

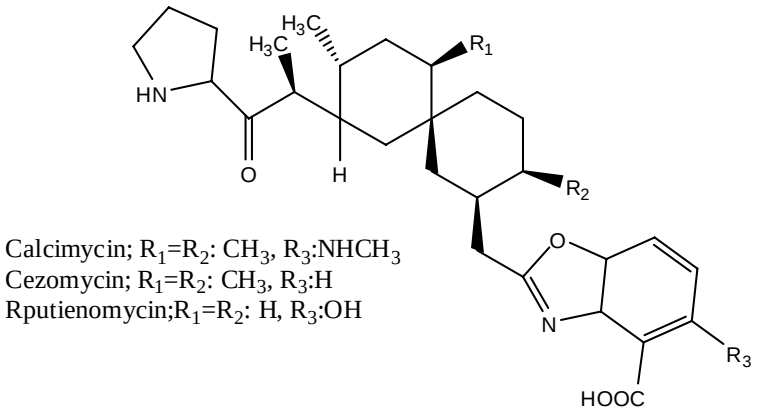
Keywords: Synthesis, Antibacterial activity, Antifungal activity, Benzoxazole

INTRODUCTION

The number of cases of multidrug resistant bacterial infections is increasing at an alarming rate. As well as the clinicians have become reliant on vancomycin as the antibiotic for serious infections resistant to traditional agents there is still need for the new classes of antibacterial agents. Disease-causing microbes that have become resistant to drug therapy are an increasing public health problem. Tuberculosis, gonorrhea, malaria, and childhood ear infections are just a few of the diseases that have become hard to treat with antibiotic drugs. The hospital-acquired infections are resistant to the most powerful antibiotics available, methicillin and vancomycin. These drugs are reserved to treat only the most intractable infections in order to slow development of resistance to them [1]. So there is still need for the new classes of antimicrobial agents.

Benzoxazoles and related fused heterocycles such as benzimidazoles and benzothiazoles were studied for their antitumor, antiviral and antimicrobial activities [2-7].

Benzoxazoles and oxazoles, which are the structural isosters of natural nucleotides and interact easily with the biopolymers, constitute an important class of heterocyclic compounds with antitumor, antiviral, antibacterial and antibiotic activities [8-25]. Therefore, these have been the aim of many researchers for many years. A benzoxazole derivative, calcimycin (Fig. 1), is a carboxylic polyether antibiotic from a strain of *Streptomyces chartreusis* (NRRL 3882). It was found to be very active against Gram-positive bacteria including some *Bacillus* and *Micrococcus* strains [4,26,27]. Two calcimycin analogues, routiennocin and cezomycin (Fig. 1) which are 3-hydroxy- 11, 15-desmethyl and 3-demetylamino derivatives of it, respectively, were found to be highly active against *Bacillus cereus*, *Bacillus negaterium*, *Micrococcus luteus* and *Streptomyces rimosus* [28-30]. Additionally, frankamide, that is 11-demethyl cezomycin, showed some activity against *Bacillus subtilis*, *Staphylococcus a*ureus, *Enterococcus faecalis* and against several plant pathogenic fungal strains [31, 32]. Therefore, it was thought worthwhile to explore of some methyl-2- (arylideneamino) oxazol-4ylamino) benzoxazole -5-carboxylate derivatives as antimicrobial agents. Accordingly the present work is concerned with the synthesis of different methyl-2-(arylideneamino) oxazol-4ylamino) benzoxazole -5-carboxylate derivatives with the objective of discovering novel and potent antimicrobial agents. The compounds were evaluated for their antimicrobial activity using cup-plate method. Moreover, the test compounds showing potent activity. The title compounds were synthesized by treating the methyl-2-(2-aminooxazol-4-ylamino) benzoxazole-5-carboxylates with appropriate aromatic aldehydes to get a new series of methyl-2- (arylideneamino) oxazol-4ylamino) benzoxazole-5-carboxylate derivatives (fig.2).



Calcimycin; R_1=R_2: CH_3, R_3:$NHCH_3$
Cezomycin; R_1=R_2: CH_3, R_3:H
Rputienomycin;R_1=R_2: H, R_3:OH

Fig. 1

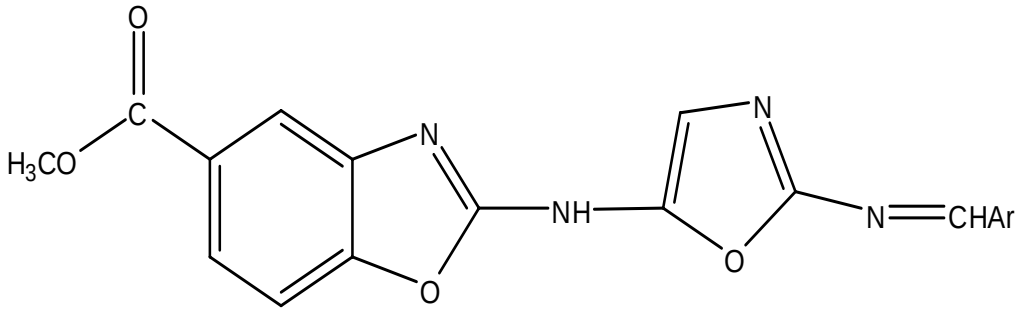


Fig. 2

MATERIALS AND METHODS

All melting points were taken in open capillaries on a veego VMP-1 apparatus and are uncorrected IR spectra were recorded as KBr pellets on a Perkin-Elmer FT IR 240-c spectrometer. The ^{1}H NMR spectra were recorded on Varian-Gemini 200 MHz spectrometer in DMSO-d_6 using TMS as an internal standard and mass spectras were recorded on Schimadzu QP 5050A spectrometer. The targeted compounds were synthesized as shown in Scheme-1.

I. Synthesis of 4-carbomethoxy-2-nitrophenol (II)

To a solution of aluminum nitrate (40g) in acetic acid- acetic anhydride (1:1) mixture (160ml), was added an appropriate phenol (I, 40g) in small portions, while cooling and shaking occasionally. The reaction mixture was left at room temperature for 1.5 h while shaking the contents intermittently to complete the nitration. The resulting brown solution was diluted to complete the nitration. The resulting brown solution was diluted with ice-cold water and acidified with concentrated nitric acid to get a bulky, yellow precipitate. It was filtered washed with small quantity of methanol and purified by recrystallization from alcohol to get a yellow crystalline solid (44g, 85%), m.p 73^{0}C [33].

II. Synthesis of 4-carbomethoxy-2-aminophenol (III)

4-carbomethoxy-2-nitrophenol (II, 10 g) was dissolved in boiling alcohol (50%, 100ml) and sodium dithionite was added to this boiling alcohol solution until it becomes almost colourless. Then the alcohol was reduced to one-third of its volume by distillation and the residual liquid was triturated with crushed ice. The resulting colourless, shiny product was filtered, washed with cold water and dried in the air. Its purification was effected by recrystallization from benzene to get colourless, shiny scales (5.1 g; 60%) m.p 143^{0}C [34].

III. Synthesis of methyl-2-aminobenzoxazole-5-carboxylate (IV)

1.3 mol of 4-carbomethoxy-2-aminophenol (III) was dissolved in 1lit. methyl alcohol and cooled the solution to 5^{0}C by adding chopped ice. A cold suspension of 1.5 mol of cyanogenbromide in 1lit of water was added over a period of 5min with rapid stirring. Continued the stirring for 0.75h at room temperature, 1.3 mol of solid sodium bicarbonate in small portions over a period of 1.5 h was added to bring the p^H 6.5 -7.0. Stirring was continued for another 1h. The solid was separated by filtration, washed with cold water and on recrystallization from ethyl alcohol has resulted white solid, yield 70% m.p 238^{0}C.

IV. Synthesis of methyl-2-(2-chloroacetamido) benzoxazole-5-carboxylate (V)

A mixture of methyl-2-aminobenzoxazole-5-carboxylate (IV, 0.01mol) and chloroacetyl chloride (0.01mol) was taken in 20 ml of dry benzene and the reaction mixture was refluxed for 5h on a water bath. The solvent was evaporated and the residue was washed first with benzene and then with petroleum ether. The compound was recrystallized from suitable solvent(s). The compound was found to be containing yield 72% and m.p is 177^{0}C.

IV. Synthesis of methyl-2-(2-aminooxazol-4-ylamino) benzoxazole-5-carboxylate (VI)

Methyl-2-(2-chloroacetamido) benzoxazole-5-carboxylate (VI, 0.01mol) and urea (0.01mol) were dissolved in 10ml of absolute alcohol in conical flask. The conical flask was hanged with a funnel and was subjected to microwave irradiation at 480 Watts for 5min in LG-Microwave oven. The reaction was monitored by TLC. After the completion of the reaction the contents were cooled and triturated with crushed ice the separated solid was filtered, washed with 1% $NaHCO_3$ solution and purified by recrystallization from ethanol and water mixture found to be containing yield 97% and m.p 199^{0}C.

V. Synthesis of methyl-2-(2-(arylideneamino) oxazol-4-ylamino) benzoxazole-5-carboxylate (VII)

Methyl-2-(2-aminoxazol-4-ylamino) benzoxazole-5-carboxylate (XII, 0.01mol) and appropriate aromatic aldehydes; Benzaldehyde, salicyladehyde, *p*-hydroxybenzaldehyde, anisaldehyde, *p*-dimethylaminobenzaldehyde, *p*-chlorobenzaldehyde, veratraldehyde, cinnamaldehyde and 3, 4, 5-trimethylbenaldehyde (0.015mol) were taken into a conical flask and were dissolved in 10ml of absolute alcohol. The conical flask was hanged with a funnel and was subjected to microwave irradiation at 480 Watts for 7min in LG-Microwave oven. The reaction was monitored by TLC. The reaction mixture was cooled and triturated with crushed ice; the separated solid was filtered, washed with 1% $NaHCO_3$ solution and purified by recrystallization from ethanol and water mixture. The compounds were characterized by spectral data. Physical data of all synthesized compounds given in Table-1

CompoundVIIa: Methyl-(2-(4-(dimethylamino) benzylideneamino) oxazol-4-ylamino) benzoxazole-5-carboxylate

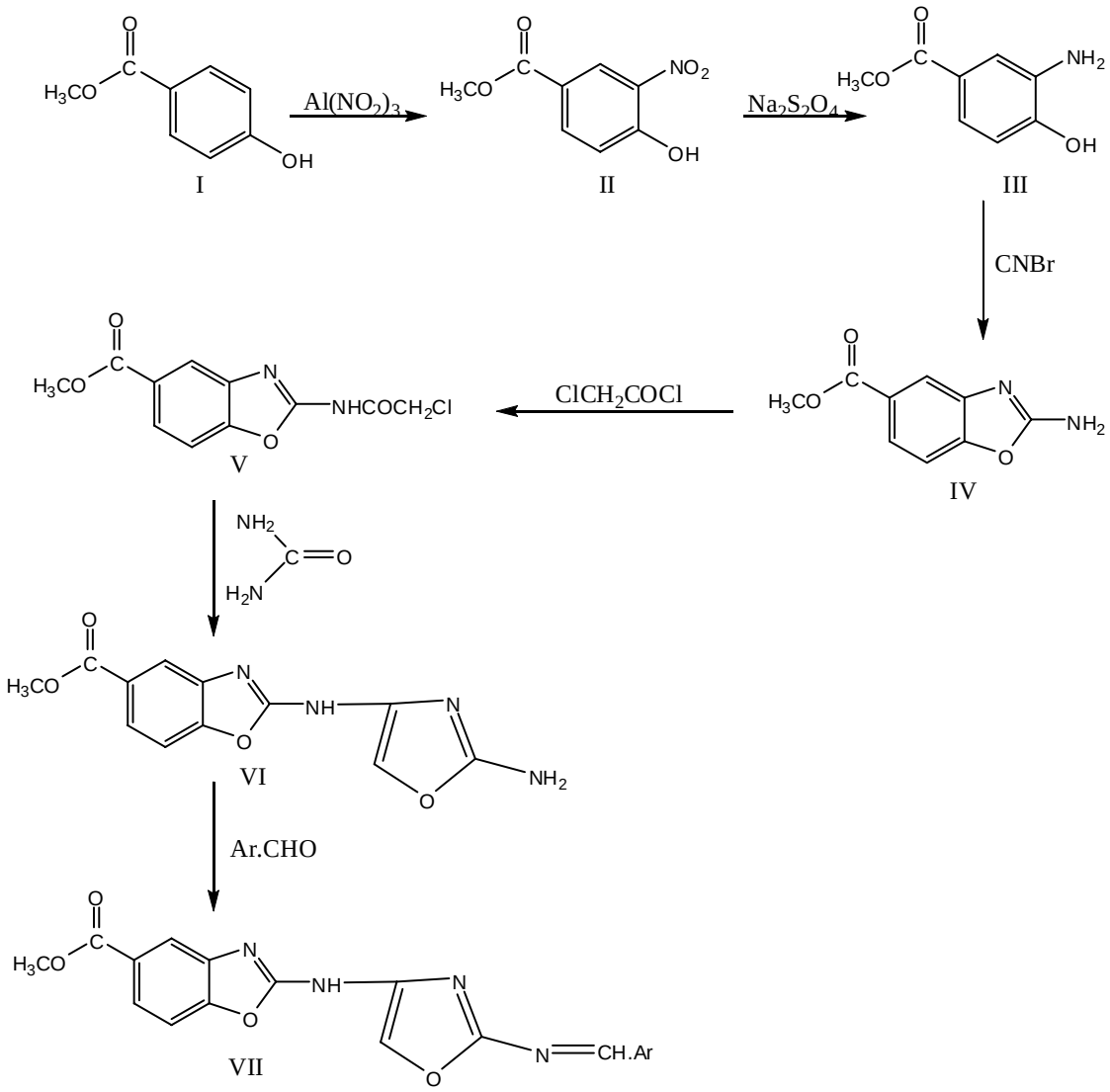
IR (KBr, cm-1): 3133(NH), 1693 (C=N), 1610 (C=C), 1582 (C=N), 1249 (C-O-C);

^{1} H-NMR (DMSO-d6) δ: 8.8 (s, 1H, CH), 8.6 (s, 1H, Ar-H), 8.1(d, 1H, Ar-H), 8.0(d, 1H, Ar-H), 7.6(s, 1H, Ar-H oxazole ring), 7.5(d, 2H, Ar-H), 6.8(d, 2H, Ar-H) 5.3(s, 1H, NH), 3.8(s, 3H, OCH_3), 3.0(s, 6H, CH_3); MS (*m/z):* M+: 406.1

Compound VIIb: Methyl-2-(2-(benzylideneamino) oxazol-4-ylamino) benzoxazole-5-carboxylate

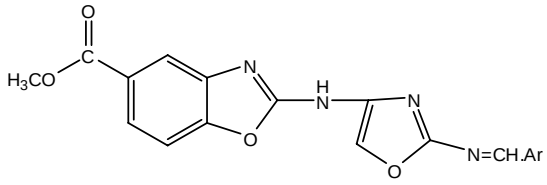
IR (KBr, cm-1): 3138(NH), 1696 (C=N), 1602 (C=C), 1576 (C=N), 1233 (C-O-C).

^{1} H-NMR (DMSO-d6) δ: 8.6 (s, 1H, CH), 8.5 (s, 1H, Ar-H), 8.1(d, 1H, Ar-H), 8.0(d, 1H, Ar-H), 7.8 (d, 2H, ArH), 7.7 (s, 1H, Ar-H oxazole ring), 7.5(t, 3H, Ar-H), 6.8(d, 2H, Ar-H) 5.3(s, 1H, NH), 3.8(s, 3H, OCH_3); MS (*m/z):* M+: 363.1



Scheme 1

Table 1: Physical data of methyl-2-(2-(arylideneamino) oxazol-4-ylamino) benzoxazole-5-carboxylates (VII)



SNo	Compd	Ar	Chemical formula	MeltingPoint (ºC)	Yield (%)	Elemenyal analysis (C; N; H; O)
1	**VIIa**	4-dimethylaminophenyl	$C_{21}H_{19}N_5O_4$	228	94	62.22;4.72;17.27;15.79
2	**VIIb**	Phenyl	$C_{19}H_{14}N_4O_4$	211	95	62.98; 3.89; 15.46; 17.66
3	**VIIc**	2-hydroxyphenyl	$C_{19}H_{14}N_4O_5$	229	90	60.23; 3.73; 14.81; 21.14
4	**VIId**	4-chlorophenyl	$C_{19}H_{13}N_4O_4Cl$	204	91	57.51; 3.30; 14.12, 16.13, 8.94(Cl)
5	**VIIe**	4-methoxyphenyl	$C_{20}H_{16}N_4O_5$	235	96	61.22; 4.11; 14.28; 20.39
6	**VIIf**	4-hydroxyphenyl	$C_{19}H_{14}N_4O_5$	236	98	60.23; 3.73; 14.81; 21.14
7	**VIIg**	2-hydroxy-4-methoxyphenyl	$C_{20}H_{16}N_4O_6$	222	92	58.82; 3.95; 13.72; 23.51
8	**VIIh**	Cinnamalyl	$C_{21}H_{16}N_4O_4$	233	95	64.64; 4.15; 14.43; 16.48
9	**VIIi**	3,4,5-trimethylphenyl	$C_{22}H_{20}N_4O_4$	207	93	65.34; 4.98; 13.85; 15.82
7	**VIIg**	2-hydroxy-4-methoxyphenyl	$C_{20}H_{16}N_4O_6$	222	92	58.82; 3.95; 13.72; 23.51
8	**VIIh**	Cinnamalyl	$C_{21}H_{16}N_4O_4$	233	95	64.64; 4.15; 14.43; 16.48
9	**VIIi**	3,4,5-trimethylphenyl	$C_{22}H_{20}N_4O_4$	207	93	65.34; 4.98; 13.85; 15.82

Compound VIIc: methyl-2-(2-(2-hydroxybenzylideneamino) oxazol-4-ylamino) benzoxazole-5-carboxylate

IR (KBr, cm-1): 3137(NH), 1669 (C=N), 1620 (C=C), 1585 (C=N), 1241 (C-O-C).

^{1}H-NMR (DMSO-d6) δ: 11.2(s, 1H, OH), 8.8 (s, 1H, ArH), 8.3 (s, 1H, CH), 8.1(d, 1H, Ar-H), 8.0(d, 1H, Ar-H), 7.9 (s, 1H, ArH oxazole ring), 7.7 (d, 1H, Ar-H), 7.5(t, 1H, Ar-H), 7.1(t, 1H, Ar-H), 7.0(d, 1H, Ar-H), 5.5(s, 1H, NH), 3.9(s, 3H, OCH_3); MS (*m/z):* M+: 379.1

Compound VIId: Methyl-2-(2-(4-chlorobenzylideneamino) oxazol-4-ylamino) benzoxazole-5-carboxylate

IR (KBr, cm-1): 3112(NH), 1685 (C=N), 1609 (C=C), 1564 (C=N), 1223 (C-O-C).

^{1}H-NMR (DMSO-d6) δ: 8.6(s, 1H, ArH), 8.3 (s, 1H, CH), 8.2(d, 1H, Ar-H), 8.0(d, 1H, Ar-H), 7.9 (s, 1H, ArH oxazole ring), 7.8 (d, 2H, Ar-H), 7.5(d, 2H, Ar-H), 5.1(s, 1H, NH), 3.6(s, 3H, OCH_3); MS (*m/z):* M+: 397.1

Compound VIIe: Methyl-2-(2-(4-methoxybenzylideneamino) oxazol-4-ylamino) benzoxazole-5-carboxylate

IR (KBr, cm-1): 3114(NH), 1647 (C=N), 1615 (C=C), 1543 (C=N), 1212 (C-O-C).

^{1}H-NMR (DMSO-d6) δ: 8.8(s, 1H, ArH), 8.5 (s, 1H, CH), 8.0(d, 1H, Ar-H), 7.8(d, 1H, Ar-H), 7.6 (s, 1H, ArH oxazole ring), 7.4 (d, 2H, Ar-H), 7.3(d, 2H, Ar-H), 5.4(s, 1H, NH), 3.9(s, 3H, OCH_3), 3.6(s, 3H, OCH_3); MS (m/z): M+: 393.1

Compound VIIf: Methyl-2-(2-(4-hydroxybenzylideneamino) oxazol-4-ylamino) benzoxazole-5-carboxylate

IR (KBr, cm-1): 3133(NH), 1690 (C=N), 1602 (C=C), 1592 (C=N), 1259 (C-O-C).

^{1}H-NMR (DMSO-d6) δ: 9.4(s, 1H, OH), 8.8(s, 1H, ArH), 8.6(s, 1H, CH), 8.1(d, 1H, Ar-H), 8.0(d, 1H, Ar-H), 7.9 (s, 1H, ArH oxazole ring), 7.8 (d, 2H, Ar-H), 6.8(d, 2H, Ar-H), 5.0(s, 1H, NH), 3.6(s, 3H, OCH_3); MS (m/z): M+: 379.1

Compound VIIg: methyl-2-(2-(2-hydroxy-4-methoxybenzylideneamino)oxazol-4-ylamino)benzoxazole-5-carboxylate

IR (KBr, cm-1): 3141(NH), 1659 (C=N), 1612 (C=C), 1568 (C=N), 1217 (C-O-C).

^{1}H-NMR (DMSO-d6) δ: 11.5(s, 1H, OH), 8.8(s, 1H, ArH), 8.7(s, 1H, CH), 8.4(d, 1H, Ar-H), 8.3(d, 1H, Ar-H), 7.7 (s, 1H, ArH oxazole ring), 7.6 (d, 1H, Ar-H), 6.6(d, 1H, Ar-H), 6.4(s, 1H, ArH), 5.2(s, 1H, NH), 3.9(s, 3H, OCH_3), 3.3(s, 3H, OCH_3); MS (m/z): M+: 409.0

CompoundVIIh: methyl-2-(2-(3-cinnamylideneamino) oxazol-4-ylamino) benzoxazole-5-carboxylate

IR (KBr, cm-1): 3103(NH), 1640 (C=N), 1600 (C=C), 1590 (C=N), 1219 (C-O-C).

^{1}H-NMR (DMSO-d6) δ: 8.6 (s, 1H, ArH), 8.1 (d, 1H, Ar-H), 8.0(d, 1H, Ar-H), 7.7(s, 1H, Ar-H oxazole ring), 7.6(d, 2H, Ar-H),7.5 (s, 1H, CH), 7.4(t, 1H, Ar-H), 7.3(t, 1H, Ar-H), 7.0 (s, 1H, CH), 5.3 (s, 1H, CH), 4.6 (s, H, NH), 3.8(s, 3H, OCH_3); MS (m/z): M+: 389.0

CompoundVIIi: methyl-2-(2-(3, 4, 5-trimethylbenzylideneamino) oxazol-4-ylamino) benzoxazole-5-carboxylate

IR (KBr, cm-1): 3201(NH), 1670 (C=N), 1628 (C=C), 1588 (C=N), 1219 (C-O-C).

^{1}H-NMR (DMSO-d6) δ: 8.8 (s, 1H, ArH), 8.5 (d, 1H, CH), 8.1(d, 1H, Ar-H),8.0(s, 1H, ArH), 7.8(s, 1H, Ar-H oxazole ring), 7.3(s, 2H, Ar-H), 5.2 (s, 1H, CH), 5.3 (s, H, NH), 3.9(s, 3H, OCH_3), 2.3(s, 6H, CH_3), 2.13.9(s, 3H, CH_3); MS (m/z): M+: 405.0

Antibacterial activity by cup plate method [35]

The antibacterial activity of synthesized compounds was conducted against two gram-positive bacteia viz., *Bacillus subtilis* and *Staphylococcus aureus* and two gram-negative bacteia viz., *Escherichia coli* and *Salmonella typhi* by using cup plate method. Ampicillin sodium was employed as standard to compare the results.

Culture medium: Nutrient broth was used for the preparation of inoculum of the bacteria and nutrient agar was used for the screening method.

Composition of Nutrient agar medium: Peptone 5.0 gm; Sodium chloride 5.0 gm;

Beef extract 1.5 gm; Yeast extract 1.5 gm; Agar 15.0 gm; Distilled water upto1000 ml; pH 7.4 $\pm$ 0.2

The test organisms were subcultured using nutrient agar medium. The tubes containing sterilized medium were inoculated with respective bacterial strain. After incubation at 37°C $\pm$ 1°C for 24 h, they were stored in refrigerator. The stock cultures were maintained. Bacteria inoculum was prepared by transferring a loopful of stock culture to nutrient broth (100 ml) in conical flasks (250 ml). The flasks were incubated at 37°C $\pm$ 1°C for 48 h before the experimentation. Solution of the test compounds were prepared by dissolving 10 mg each in normal saline (10 ml, AnalaR grade). A reference standard for both gram-positive and gram-negative bacteria was made by dissolving accurately weighed quantity of ampicillin sodium in normal saline separately. The nutrient agar medium was sterilized by autoclaving at 121°C (15 lb/sq. inch) for 15 min. The petriplates, tube and flasks plugged with cotton were sterilized in hot-air oven at 160°, for an hour. Into each sterilized petriplate (10 cm diameter), about 27 ml of molten nutrient agar medium was poured and inoculated with the respective strain of bacteria (6 ml of inoculum to 300 ml of nutrient agar medium) was transferred asceptically. The plates were left at room temperature to allow the solidification. In each plate, three cups of 6 mm diameter were made with sterile borer. Then 0.1 ml of the test solution was added to the respective cups asceptically and labeled, accordingly. The plates were kept undisturbed for atleast 2 hours in refrigerator to allow diffusion of the solution properly into nutrient agar medium. After incubation of the plates at 37° $\pm$ 1°C for 24 h, the diameter of zone of inhibition surrounding each of the cups was measured with the help of an antibiotic zone reader. All the experiments were carried out in triplicate. Simultaneously, controls were maintained employing 0.1 ml of dimethyl formamide to observe the solvent effects. The results are presented in Table2.

Antifungal activity [36]

All those compounds screened for antibacterial activity were also tested for their antifungal activity. The fungi employed for screening were: *Candida albicans* and *Aspergillus niger*. The test organisms were sub-cultured using potato-dextrose-agar medium. The tubes containing sterilized medium were inoculated with test fungi and after incubation at 25°C for 48 h, they were stored at 4°C in refrigerator. The inoculum was prepared by taking a loopful of stock culture to about 100 ml of nutrient broth, in 250 ml conical flasks. The flasks were incubated at 25°C for 24 h before use. The solutions of test compounds were prepared by a similar procedure described under the antibacterial activity. A reference standard (1 mg/ml conc.) was prepared by dissolving 10 mg of Clotrimazole in 10 ml of normal saline (AnalaR grade). Further, the dilution was made with normal saline itself to obtain a solution of 100 μg/ml concentration. The potato-dextrose-agar medium was sterilized by autoclaving at 121°C (15 lb/sq. inch) for 15 minutes. The petriplates, tubes and flasks with cotton plugs were sterilized in hot-air oven at 150°, for an hour. In each sterilized petriplate, about 27 ml of molten potato-dextrose-agar medium inoculated with respective fungus (6 ml of inoculum in 300 ml of potato-dextrose medium) was added, aseptically. After solidification of the medium at room temperature three discs of 6 mm diameter were made in each plate with a sterile borer. Accurately 0.1 ml (100 μg/disc) of test solution was transferred to the discs aseptically and labelled, accordingly. The

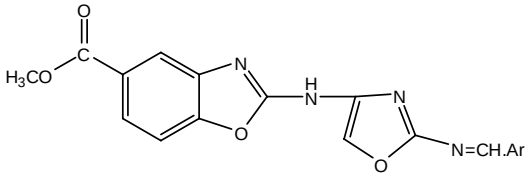
reference standard, 0.1 ml (10 μg/disc) was also added to the discs in each plate. The plates were kept undisturbed at room temperature for 2 h, atleast to allow the solution to diffuse properly into the potato-dextrose-agar medium. Then the plates were incubated at 25°C for 48 h. The diameter of the zone of inhibition was read with the help of an antibiotic zone reader. The experiments were performed in triplicate in order to minimize the errors. The results are presented in Table-3.

RESULTS AND DISCUSSION

All the newly synthesised compounds methyl-2- (arylideneamino) oxazol-4ylamino) benzoxazole -5-carboxylate derivatives (VIIa-h) have been evaluated for their antibacterial activity against both gram-positive and gram-negative bacteria and the results are presented in Table2. The results of the evaluation have been viewed by taking Ampicillin, a broad spectrum antibiotic as the standard drug. Table-2 pertaining to the antibacterial activity data of methyl-2- (arylideneamino)oxazol-4ylamino) benzoxazole -5-carboxylate derivatives **(VII)** indicates that all the compounds showed excellent antibacterial activity against all the four strains except compound VIIh and VIIi. Compound VIIb with simple phenyl group the activity was mild with a zone of inhibition of 13mm, 11mm, 12mm, and 11mm respectively. In case compound VIIa there is a dimethyl amino group at 4th position of phenyl ring also showed mild activity with a zone of inhibition of 12mm, 11mm, 10mm, 12mm respectively.

In case compound VIIc and VIIf hydroxyl group substituted on phenyl ring almost showed same acitivity with a zone of inhibition of 19mm, 18mm, 15mm, 15mm and 19mm, 17mm, 18mm, 18mm respectively. In case of compound VIIi three bulkier methyl groups substituted on the phenyl ring might have reduced the activity, this compound showed activity only against two strains *B. subtilis* and *S. aureus*. In case of compound VIIh the unsaturation on the phenyl ring might have reduced the activity. But the compounds VIIe and VIIg showed a potent activity against all four strains with a zone of inhibition of 23mm, 21mm, 20mm, 18mm, and 24mm, 22mm, 21mm, 20mm respectively, these compounds showed activity greater than the standard drug Ampicillin with a zone of inhibition of 22mm, 20mm, 18mm and 17mm respectively. Results are summarized in Table-2.

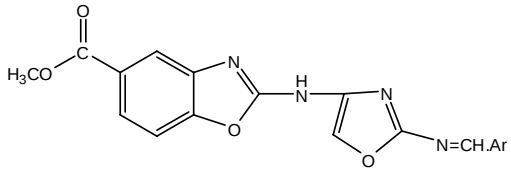
Table 2: Antibacterial activity of methyl-2-(2-(arylideneamino) oxazol-4-ylamino) benzoxazole-5-carboxylates (VII).



S No	Compd	Ar	Zone of inhibition (in mm)			
			B. subtilis	*S. aureus*	*E. coli*	*S. typhi*
1	**VIIa**	4-dimethylaminophenyl	12	11	10	12
2	**VIIb**	Phenyl	13	11	12	11
3	**VIIc**	2-hydroxyphenyl	19	18	15	15
4	**VIId**	4-chlorophenyl	20	15	17	16
5	**VIIe**	4-methoxyphenyl	23	21	20	18
6	**VIIf**	4-hydroxyphenyl	19	17	18	18
7	**VIIg**	2-hydroxy-4-methoxyphenyl	24	22	21	20
8	**VIIh**	Cinnamalyl	12	--	--	11
9	**VIIi**	3,4,5-trimethylphenyl	13	10	--	--
10	**std**	Ampicillin (10 μg/cup)	22	20	18	17

Concentration of the test compound: 100 μg/cup

Table 3: Antifungal activity of methyl-2-(2-(arylideneamino) oxazol-4-ylamino) benzoxazole-5-carboxylates (VII).



SNo	Compd	Ar	Zone of inhibition (in mm)	
			C. albicans	*A. niger*
1	**VIIa**	4-dimethylaminophenyl	15	16
2	**VIIb**	Phenyl	--	12
3	**VIIc**	2-hydroxyphenyl	19	15
4	**VIId**	4-chlorophenyl	21	15
5	**VIIe**	4-methoxyphenyl	28	20
6	**VIIf**	4-hydroxyphenyl	26	17
7	**VIIg**	2-hydroxy-4-methoxyphenyl	30	21
8	**VIIh**	Cinnamalyl	14	15
9	**VIIi**	3,4,5-trimethylphenyl	16	13
10	**std**	Clotrimazole (10 μg/cup)	27	19

Concentration of the test compound: 100 μg/cup

In case antifungal activity all the compounds showed mild to higher antifungal activity. The compound VIIb with simple phenyl group showed activity against only *A. niger*. But remaining compound VIIa, VIIc, VIId, VIIf, VIIh and VIIi showed moderate activity against two strains *C.albicans* and *A.niger*. But the compounds VIIe and VIIg showed a very high activity than the standard drug clotrimazole with a zone of inhibition of 26mm, 17mm and 30mm, 21mm respectively. Results are summarized in Table-3.

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