# SYNTHESIS AND ANTIMICROBIAL STUDIES OF SOME NOVEL ISOXAZOLINE DERIVATIVES

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**ABSTRACT**: In the present investigation, a series of novel isoxazoline derivatives 4a-i were synthesized by cyclization of 1-(2'-hydroxy phenyl)-5-(6''-methoxynaphthalen)-2-propene-1-one (i.e. Chalcones) 3a-i with hydroxylamine hydrochloride in dimethyl formamide and sodium acetate to obtained 3-(2'-hydroxy phenyl)-5-(6''-methoxynaphthalen)-2-isoxazolines 4a-i. The structures of newly synthesized compounds were confirmed by IR, 1H NMR, mass and elemental analysis. All the compounds were tested for in vitro activities against a panel of Gram-positive and Gram-negative bacteria. Several derivatives of isoxazoline produced good to moderate activities against number of bacteria and fungus.

**Key Words**: Chalcones, Isoxazoline derivatives, Antibacterial, Antifungal activities

## INTRODUCTION

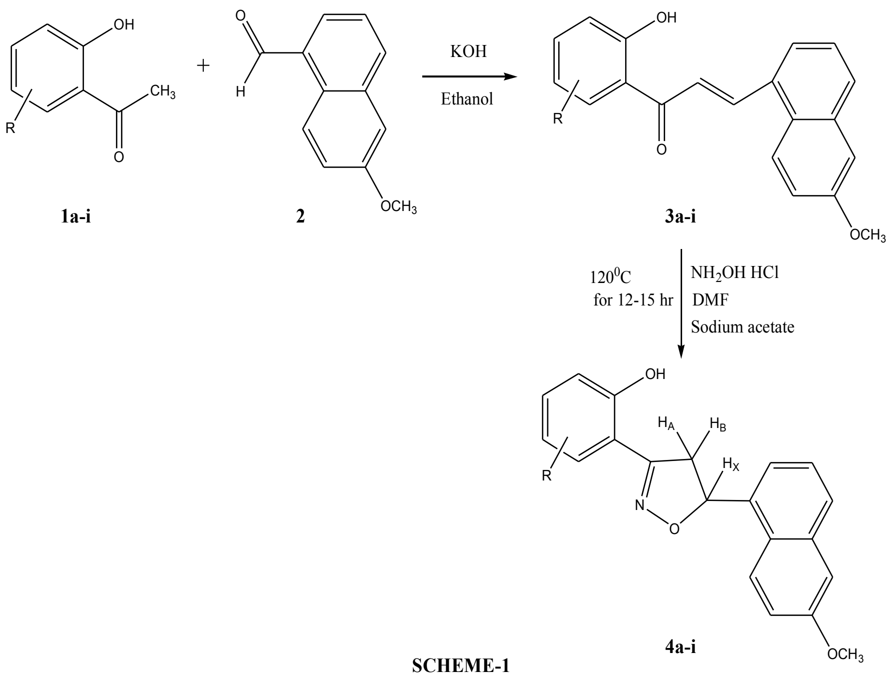
Compounds incorporating heterocyclic ring systems continue to attract considerable interest due to the wide range of biological activities they posses. Amongst them five membered heterocyclic compounds occupy a unique place in the realm of natural and synthetic organic chemistry. Five membered heterocycles like isoxazoline have found wide application as pharmaceutical and agrochemical agents. In recent years, attention has increasingly been given to the synthesis of isoxazoline derivatives as a source of new antibacterial agents. The synthesis of novel isoxazoline derivatives remain a main focus of medicinal research. Isoxazoline derivatives have been reported to possess antifungal[1], antibacterial[2], anticonvulsant[3], anti-inflammatory[4], anti-viral[5], analgesic[6], antitumar[7], chemotherapy[8] activity. Penicillin derivatives containing isoxazole ring are found to be antibacterial [9] active. Isoxazoline derivatives also show a good potency in animal models of thrombosis[10]. In addition, isoxazoline derivatives have played a crucial role in the theoretical development of heterocyclic chemistry and are also used extensively in organic synthesis[11, 12].

Encouraged by the diverse biological activities of isoxazoline compounds and in continuation of our work on synthesis of biological active heterocycles containing isoxazoline[13], hence it was decided to prepare a new series of 3-(2'-hydroxy phenyl)-5-(6''-methoxynaphthalen)-2-isoxazolines (4a-i) and evaluated for their antibacterial and antifungal activities.

## Experimental Section

### General procedure for preparation of Chalcones from substituted o-hydroxy acetophenone and 6-methoxy napthaldehyde (3a-i)

A mixture of **1a-i** (0.01 mmol) and **2** (0.01 mmol) was stirred in ethanol (30 ml) and then potassium hydroxide solution (15 ml, 0.02 mmol) was added to it. The reaction mixture was kept over night at room temperature and then it was poured on crushed ice and acidified with dilute hydrochloric acid. The Chalcones derivative precipitates out as solid. Then it was filtered and purified by recrystalization from acetic acid (Scheme 1).



SCHEME-1

1-(2'-hydroxy phenyl)-5-(6''- methoxynaphthalen)-2-propene-1-one (3a)

Yellow crystals (Acetic acid) Yield: 94%; m.p. 156 $^{O}$C; Anal. Calc. for ($C_{20}H_{16}O_3$); C, 78.93; H, 5.30; found: C, 78.89; H, 5.25 %; $^1$H NMR (DMSO, 400 MHz), δ 12.4 (s, 1H, OH), 8.1-7.4 (m, 10H, Ar-H), 7.3-7.1 (dd, 1H, >C=CH$_B$), 6.95-6.90 (dd, 1H, CH$_A$=C<), 3.82 (s, 3H, $OCH_3$), IR (KBr pellets Cm$^{-1}$): 3600 (Ar-OH), 1625 (CH=CH), 1645 (>C=O).

## General procedure for preparation of 2-isoxazolines (4a-i)

A mixture of propenones (i.e. chalcones), 3a-i (0.01 mmol), hydroxylamine hydrochloride (0.012 mmol) and sodium acetate (0.04 mmol) in 20 ml of dimethylformamide was heated on oil bath at 120$^0$C for 12-15 hr. The reaction mass was then poured into 250 ml of ice-cold water. The solid obtained was filtered, washed with water, dried, and purified by recrystalization from acetic acid to give 4a-i physical and elemental data of 4a-i are listed in Table I.

## RESULT AND DISCUSSION

The reaction sequences for the synthesis of isoxazoline are shown in Scheme-1. The key intermediates 1-(2'-hydroxy phenyl)-5-(6''-methoxynaphthalen)-2-propene-1-one (3a-i) were prepared by treating 2-hydroxy acetophenones (1a-i) with 6-methoxy napthaldehyde in presence of potassium hydroxide according to Claisen-Schmidt condensation method. The Propenones (3a-i) are used as suitable precursor for the synthesis of isoxazolines (4a-i). The intermediates (3a-i) on treatment with hydroxylamine hydrochloride in dimethylformamide and sodium acetate yielded 3-(2'-hydroxy phenyl)-5-(6''-methoxynaphthalen)-2-isoxazolines (4a-i). The structure of synthesized compounds was confirmed by IR, $^1$H NMR, mass spectra and elemental analysis. The compounds are insoluble in water but soluble in methanol, ethanol and DMSO.

The formulas, melting point, yield of the compounds are listed in Table 1. Selected diagnostic bands of the IR spectra of 4a showed useful information about the structure of the compound. It showed C=N stretching band at 1610 $cm^{-1}$ because of ring closure and 1540 $cm^{-1}$ of C=C. In addition, the absorption bands at 1230 $cm^{-1}$ were attributed to the –C-O-N stretch vibrations which also confirm the formation of desired isoxazoline ring. The compound 4a showed additional sharp band appearing in the region 3610 $cm^{-1}$ due to Ar-OH stretch. In the $^1H$ NMR spectra, $H_A$, $H_B$ and $H_X$ protons of the isoxazoline ring were seen as 2.88-2.81 (dd, 1H, $J$ = 10.8 Hz, $H_A$), 3.62-3.56 (dd, 1H, $J$ = 10.8 Hz, $H_B$), 5.22-5.16 (dd, 1H, $J$ = 10.2, Hx) respectively.

Further evidence for the formation of isoxazoline 4a was obtained by recording the mass spectra. The mass spectrum of compound 4a showed a molecular ion peak at *m/z* 319.35 which is in conformity with the molecular formula $C_{20}H_{17}NO_3$. The characterization data of other isoxazoline derivatives (4a-i) are also provided in this paper.

**Table 1 Melting points, yield percentage, molecular formulae, and molecular weights of compounds (4a-i)**

| Compound | R | M.p ($^oC$) | Yield (%) | Mol. formula (Mol. wt) |
|---|---|---|---|---|
| **4a** | H | 140 | 85 | $C_{20}H_{17}NO_3$ (319.35) |
| **4b** | 3’-Cl, 5’-Cl | 180 | 80 | $C_{20}H_{15}Cl_2NO_3$ (388.24) |
| **4c** | 5’-Cl | 154 | 75 | $C_{20}H_{16}ClNO_3$ (353.8) |
| **4d** | 3’-Cl | 135 | 82 | $C_{20}H_{16}ClNO_3$ (353.8) |
| **4e** | 5’-Br | 160 | 80 | $C_{20}H_{16}BrNO_3$ (398.25) |
| **4f** | 3’-$CH_3$, 5’-$CH_3$ | 172 | 70 | $C_{22}H_{21}NO_3$ (347.41) |
| **4g** | 3’-$CH_3$ | 148 | 78 | $C_{21}H_{19}NO_3$ (333.38) |
| **4h** | 5’-$CH_3$ | 150 | 80 | $C_{21}H_{19}NO_3$ (333.38) |
| **4i** | 3’-$CH_3$, 5’-Cl | 165 | 82 | $C_{21}H_{18}ClNO_3$ (367.83) |

## Biological Activity

### *Antibacterial studies*

The newly synthesized compounds were screened for their antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeuroginosa* and *Streptococcus pyogenes* (recultured) bacterial strains by disc diffusion method[14, 15]. Discs measuring 6.25 mm in diameter were punched from Whatman no.1filter paper.The test compounds were prepared with different concentrations using dimethylformamide. One milliliter containing 100 times the amount of chemical in each disc was added to each bottle, which contains 100 discs. The discs of each concentration were placed in triplicate in nutrient agar medium seeded with fresh bacteria separately. The incubation was carried out at 37° C for 24 h. ciprofloxacin was used as a standard drug. Solvent and growth controls were prepared and kept. Zones of inhibition and minimum inhibition concentrations (MICs) were noted. The results of antibacterial studies are given in Table 2.

The investigation of antibacterial screening data reveled that all the tested compounds showed moderate to good bacterial inhibition.

Compounds 4b, 4c, 4d, 4e, and 4i showed good activity against Gram-negative bacteria *E. coli* (inhibition zone >15 mm), while compounds 4a, 4f, 4g and 4h were moderate activity (inhibition zone 11-14 mm). Compounds 4b, 4c, 4e, and 4i showed strong activity against Gram-positive bacteria *S. aureus* (inhibition zone >15 mm), while compounds 4d, 4f, 4g and 4h were moderately active (inhibition zone 12-14 mm). Compounds 4b, 4c, 4e, and 4i showed good activity against *P. aeuroginosa* (inhibition zone 14-20 mm), while compounds 4d, 4f, 4g, and 4h were moderately active (inhibition zone 10-13 mm)

Compounds 4b, 4c, 4e and 4i showed good activity against *S. pyogenes* (inhibition zone >15 mm), while compounds 4a, 4d, 4f and 4g were moderately active (inhibition zone 13-14 mm). None of the tested compounds were found to be superior to the Ciprofloxacin.

**Table 2. Antibacterial activities of pyrazolines (4a-i)**

| Compd. no. | Diameter of growth inhibition zone (mm) | | | |
|---|---|---|---|---|
| | *Escherichia coli* | *Staphylococcus aureus* | *Pseudomonas aeruginosa* | *Streptococcus pyogenes* |
| **4a** | 12 | 10 | 09 | 13 |
| **4b** | 18 | 17 | 18 | 17 |
| **4c** | 17 | 15 | 15 | 15 |
| **4d** | 15 | 13 | 12 | 14 |
| **4e** | 16 | 15 | 16 | 16 |
| **4f** | 12 | 12 | 12 | 13 |
| **4g** | 11 | 14 | 10 | 13 |
| **4h** | 12 | 07 | 11 | 09 |
| **4i** | 15 | 16 | 14 | 15 |
| Standard | 20 | 19 | 25 | 20 |

### *Antifungal studies*

Newly prepared compounds were screened for their antifungal activity against *Aspergillus flavus*, *Aspergillus fumigatus*, *Candida albicans* and *Penicillium marneffei* (recultured) in DMSO by serial plate dilution method[16, 17]. Sabourands agar media were prepared by dissolving peptone (1 g), D-glucose (4 g) and agar (2 g) in distilled water (100 mL) and adjusting pH to 5.7. Normal saline was used to make a suspension of spore of fungal strain for lowning. A loopful of particular fungal strain was transferred to 3 mL saline to get a suspension of corresponding species. Agar media (20 mL) were poured into each petri dish. Excess of suspensions was decanted and the plates were dried by placing in an incubator at 37° C for 1 h using an agar punch, wells were made and each well were labeled. A control was also prepared in triplicate and maintained at 37° C for 3-4 days. Zone of inhibition and minimum inhibitory concentration (MIC) were noted. The activity of each compound was compared with flucanazole as the standard drug. The results of antifungal studies are given in Table 3.

The antifungal screening data showed moderate to good activity but compounds particularly 4b, 4c, 4e and 4i emerged as very active against *A. fumigatus* and *A. flavus*. Similarly, compounds 4b, 4c, 4e and 4i showed good activity against *P. marneffei* and *C. albicans*. Remaining compounds were moderately active against all the fungal strains.

## Spectral analysis of compounds (4a-i)

### *3-(2'-hydroxy phenyl)-5-(6''-* methoxynaphthalen*)-2-isoxazoline (4a)*

White crystals (Acetic acid); Anal. Calc. for ($C_{20}H_{17}NO_3$); C, 75.22; H, 5.37; N, 4.39 found: 75.11; H, 5.25; N, 4.35 %; $^1$H NMR (DMSO, 400 MHz), δ 11.2 (s, 1H, OH), 8.64-8.40 (m, 4H, Ar-H), 7.38-7.28(m, 4H, Ar-H), 7.50-7.47 (d, 1H, $J$ =1.6 Hz, Ar-H), 7.16-7.14 (d, 1H, $J$ = 2.8 Hz, Ar-H), 5.22-5.16 (dd, 1H, $J$ = 10.2, Hx), 3.84 (s, 3H, -$OCH_3$), 3.62-3.56 (dd, 1H, $J$ = 10.8 Hz, $H_B$), 2.88-2.81 (dd, 1H, $J$ = 10.8 Hz, $H_A$), IR (KBr pellets Cm$^{-1}$): 3610 (Ar-OH), 1610 (C=N of isoxazoline ring), 1155 (-$OCH_3$), 1540 (C=C), 1230 (-C-O-N of isoxazoline).

**Table 3 Antifungal activities of pyrazolines (4a-i)**

| Compound no. | Diameter of growth inhibition zone (mm) | | | |
|---|---|---|---|---|
| | *Aspergillus fumigatus* | *Aspergillus flavus* | *Penicillium marneffei* | *Candida albicans* |
| **4a** | 14 | 09 | 10 | 08 |
| **4b** | 19 | 16 | 16 | 17 |
| **4c** | 18 | 14 | 16 | 16 |
| **4d** | 11 | 11 | 10 | 12 |
| **4e** | 15 | 15 | 14 | 15 |
| **4f** | 14 | 11 | 10 | 09 |
| **4g** | 14 | 13 | 12 | 14 |
| **4h** | 07 | 09 | 10 | 11 |
| **4i** | 16 | 15 | 13 | 15 |
| Standard | 20 | 16 | 18 | 20 |

### 3-(2'-hydroxy-3', 5'-dichloro phenyl)-5-(6''- methoxynaphthalen)-2-isoxazoline *(4b)*

White crystals (Acetic acid); Anal. Calc. for ($C_{20}H_{15}Cl_2NO_3$); C, 61.87; H, 3.89; N, 3.61 found: C, 61.85; H, 3.84; N, 3.55 %; $^1$H NMR (DMSO, 400 MHz), δ11.4 (s, 1H, OH), 8.40 (s, 1H, Ar-H), 7.36-7.31(m, 4H, Ar-H), 7.48-7.46 (d, 1H, $J$ = 1.8 Hz, Ar-H), 7.24 (s, 1H, Ar-H), 7.18-7.16 (d, 1H, $J$ = 2.6 Hz, Ar-H), 5.21-5.15 (dd, 1H, $J$ = 10.00, Hx), 3.86 (s, 3H, $OCH_3$), 3.62-3.55 (dd, 1H, $J$ = 10.6 Hz, $H_B$), 2.86-2.79 (dd, 1H, $J$ = 10.8 Hz, $H_A$), ), IR (KBr pellets Cm$^{-1}$): 3615 (Ar-OH), 1600 (C=N of isoxazoline ring), 1165(-$OCH_3$), 1535 (C=C), 1235 (-C-O-N of isoxazoline), 842(C-Cl).

### 3-(2'-hydroxy-5'-chloro phenyl)-5-(6''- methoxynaphthalen)-2-isoxazoline *(4c)*

White crystals (Acetic acid); Anal. Calc. for ($C_{20}H_{16}ClNO_3$); C, 67.90; H, 4.56; N, 3.96 found: C, 67.80; H, 4.52; N, 3.94 %; $^1$H NMR (DMSO, 400 MHz), δ 11.1 (s, 1H, OH), 8.30-8.36 (d, 1H, $J$ = 10.6 Hz, Ar-H), 8.20-8.18 (d, 1H, $J$ = 10.4 Hz, Ar-H), 7.38-7.27(m, 4H, Ar-H), 7.49-7.46 (d, 1H, $J$ = 1.6 Hz, Ar-H), 7.15-7.12 (d, 1H, $J$ = 2.6 Hz, Ar-H), 7.26 (s, 1H, Ar-H), 5.24-5.18 (dd, 1H, $J$ = 10.2, Hx), 3.85 (s, 3H, $OCH_3$), 3.60-3.54 (dd, 1H, $J$ = 10.8 Hz, $H_B$), 2.90-2.83 (dd, 1H, $J$ = 10.8 Hz, $H_A$), IR (KBr pellets Cm-$^1$): 3612 (Ar-OH), 1615 (C=N of isoxazoline ring), 1160 (-$OCH_3$), 1540 (C=C), 1230 (-C-O-N of isoxazoline), 840(C-Cl).

### 3-(2'-hydroxy-3'-chloro phenyl)-5-(6''- methoxynaphthalen)-2-isoxazoline *(4d)*

White crystals (Acetic acid); Anal. Calc. for ($C_{20}H_{16}ClNO_3$); C, 67.90; H, 4.56; N, 3.96 found: C, 67.81; H, 4.53; N, 3.93 %; $^1$H NMR (DMSO, 400 MHz), δ 11.2 (s, 1H, OH), 8.60-8.45 (m, 3H, Ar-H), 7.38-7.29 (m, 4H, Ar-H), 7.48-7.46 (d, 1H, $J$ = 1.8 Hz, Ar-H), 7.14-7.12 (d, 1H, $J$ = 2.8 Hz, Ar-H), 5.24-5.15 (dd, 1H, $J$ = 10.6, Hx), 3.86 (s, 3H, $OCH_3$), 3.62-3.55 (dd, 1H, $J$ = 11.0 Hz, $H_B$), 2.92-2.84 (dd, 1H, $J$ = 10.8 Hz, $H_A$): IR ( KBr pellets Cm$^{-1}$): 3610 (Ar-OH), 1610 (C=N of isoxazoline ring), 1145 (-$OCH_3$), 1545 (C=C), 1232 (-C-O-N of isoxazoline), 845(C-Cl),.

### 3-(2'-hydroxy-5'-bromo phenyl)-5-(6''- methoxynaphthalen)-2-isoxazoline *(4e)*

White crystals (Acetic acid); Anal. Calc. for ($C_{20}H_{16}BrNO_3$); C, 60.32; H, 4.05; N, 3.52 found: C, 60.25; H, 3.85; N, 3.47 %; $^1$H NMR (DMSO, 400 MHz), δ11.1 (s, 1H, OH), 8.32-8.38 (d, 1H, $J$ = 10.6 Hz, Ar-H), 8.22-8.16 (d, 1H, $J$ = 10.4 Hz, Ar-H), 7.36-7.32 (m, 4H, Ar-H), 7.52-7.48 (d, 1H, $J$ = 1.8 Hz, Ar-H), 7.14-7.12 (d, 1H, $J$ = 2.8 Hz, Ar-H), 7.28 (s, 1H, Ar-H), 5.22-5.16 (dd, 1H, $J$ = 10.2, Hx), 3.84 (s, 3H, $OCH_3$), 3.62-3.56 (dd, 1H, $J$ = 10.8 Hz, $H_B$), 2.86-2.79 (dd, 1H, $J$ = 10.8 Hz, $H_A$), IR (KBr pellets Cm-$^1$): 3615 (Ar-OH), 1615 (C=N of isoxazoline ring), 1150 (-$OCH_3$), 1530 (C=C), 1220 (-C-O-N of isoxazoline), 610(C-Br).

### 3-(2'-hydroxy-3', 5'-dimethyl phenyl)-5-(6''- methoxynaphthalen)-2-isoxazoline *(4f)*

White crystals (Acetic acid); Anal. Calc. for ($C_{22}H_{21}NO_3$); C, 76.06; H, 6.09; N, 4.03 found: C, 75.96; H, 5.99; N, 4.00 %; $^1$H NMR (DMSO, 400 MHz), δ11.4 (s, 1H, OH), 8.38 (s, 1H, Ar-H), 7.38-7.28(m, 4H, Ar-H), 7.52-7.49 (d, 1H, $J$ = 1.6 Hz, Ar-H), 7.26 (s, 1H, Ar-H), 7.14-7.12 (d, 1H, $J$ = 2.8 Hz, Ar-H), 5.23-5.17 (dd, 1H, $J$ = 10.20, Hx), 3.86 (s, 3H, $OCH_3$), 3.61-3.54 (dd, 1H, $J$ = 10.6 Hz, $H_B$), 2.90-2.83 (dd, 1H, $J$ = 10.8 Hz, $H_A$), ), 2.66 (s, 6H, $CH_3$): IR (KBr pellets Cm$^{-1}$): 3612 (Ar-OH), 1610 (C=N of isoxazoline ring), 1160 (-$OCH_3$), 1532 (C=C), 1235 (-C-O-N of isoxazoline).

### 3-(2'-hydroxy-3'-methyl phenyl)-5-(6''- methoxynaphthalen)-2-isoxazoline *(4g)*

White crystals (Acetic acid); Anal. Calc. for ($C_{21}H_{19}NO_3$); C, 75.66; H, 5.74; N, 4.20 found: C, 75.63; H, 5.70; N, 4.18 %; $^1$H NMR (DMSO, 400 MHz), δ 11.4 (s, 1H, OH), 8.62-8.46 (m, 3H, Ar-H), 7.36-7.30 (m, 4H, Ar-H), 7.49-7.46 (d, 1H, $J$ = 1.6 Hz, Ar-H), 7.16-7.14 (d, 1H, $J$ = 2.8 Hz, Ar-H), 5.24-5.18 (dd, 1H, $J$ = 10.2, Hx), 3.86 (s, 3H, $OCH_3$), 3.62-3.56 (dd, 1H, $J$ = 10.8 Hz, $H_B$), 2.90-2.83 (dd, 1H, $J$ = 10.8 Hz, $H_A$), 2.65 (s, 3H, $CH_3$): IR ( KBr pellets Cm$^{-1}$): 3618 (Ar-OH), 1612 (C=N of isoxazoline ring), 1160 (-$OCH_3$), 1540 (C=C), 1231 (-C-O-N of isoxazoline).

### 3-(2'-hydroxy-5'-methyl phenyl)-5-(6''- methoxynaphthalen)-2-isoxazoline *(4h)*

White crystals (Acetic acid); Anal. Calc. for ($C_{21}H_{19}NO_3$); C, 75.66; H, 5.74; N, 4.20 found: C, 75.62; H, 5.71; N, 4.17 %; $^1$H NMR (DMSO, 400 MHz), δ 11.6 (s, 1H, OH), 8.30-8.36 (d, 1H, $J$ = 10.6 Hz, Ar-H), 8.21-8.15 (d, 1H, $J$ = 10.4 Hz, Ar-H), 7.40-7.30 (m, 4H, Ar-H), 7.50-7.46 (d, 1H, $J$ = 1.8 Hz, Ar-H), 7.14-7.12 (d, 1H, $J$ = 2.8 Hz, Ar-H), 7.28 (s, 1H, Ar-H), 5.21-5.15 (dd, 1H, $J$ = 10.2, Hx), 3.85 (s, 3H, $OCH_3$), 3.60-3.54 (dd, 1H, $J$ = 10.8 Hz, $H_B$), 2.88-2.81 (dd, 1H, $J$ = 10.8 Hz, $H_A$), 2.60 (s, 3H, $CH_3$): IR (KBr pellets Cm-$^1$): 3612 (Ar-OH), 1610 (C=N of isoxazoline ring), 1155 (-$OCH_3$), 1535 (C=C), 1232 (-C-O-N of isoxazoline).

### 3-(2'-hydroxy-5'-chloro-4'-methyl phenyl)-5-(6''- methoxynaphthalen)-2-isoxazoline *(4i)*

White crystals (Acetic acid); Anal. Calc. for ($C_{21}H_{18}ClNO_3$); C, 68.57; H, 4.93; N, 3.81 found: C, 68.54; H, 4.89; N, 3.78 %; $^1$H NMR (DMSO, 400 MHz), δ 11.4 (s, 1H, OH), 8.28 (s, 1H, Ar-H), 7.37-7.29(m, 4H, Ar-H), 7.49-7.46 (d, 1H, $J$ = 1.6 Hz, Ar-H), 7.36 (s, 1H, Ar-H), 7.14-7.12 (d, 1H, $J$ = 2.8 Hz, Ar-H), 5.25-5.19 (dd, 1H, $J$ = 10.2 Hz, Hx), 3.87 (s, 3H, $OCH_3$), 3.62-3.56 (dd, 1H, $J$ = 10.8 Hz, $H_B$), 2.90-2.83 (dd, 1H, $J$ = 10.8 Hz, $H_A$), ), 2.64 (s, 3H, $CH_3$): IR (KBr pellets Cm$^{-1}$): 3610 (Ar-OH), 1615 (C=N of isoxazoline ring), 1155 (-$OCH_3$), 1540 (C=C), 1230 (-C-O-N of isoxazoline), 842(C-Cl).

## Conclusion

The synthesized 2-isoxazoline 4a-i all are novel. Compounds with electron releasing groups such as methoxy and compounds having pharmacophores such as chloro, bromo groups and both these groups are present in one moiety exhibited best antimicrobial activity. The data reported in this article may be helpful guide for the medicinal chemist who is working in this area.

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