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Der Pharma Chemica, 2012, 4(5):2036-2041
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

Synthesis and Antibacterial Activity of Novel Isoxazoline Derivatives

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ABSTRACT

*New isoxazoline derivatives **(4a - 4l)** were prepared from commercially available 2-Hydroxy-Aceto-Naphthanone and their antibacterial activity against four pathogenic bacteria, two Gram negative bacteria and two Gram positive bacteria. Majority of the isoxazoline analogues exhibited antibacterial activity comparable to ampicillin as reference drug.*

Keywords: 2-Hydroxy-Aceto-Naphthanone, Vanillin**,** Isoxazoline, Antibacterial activity, Synthesis, Pathogenic bacteria, bacterial strains.

INTRODUCTION

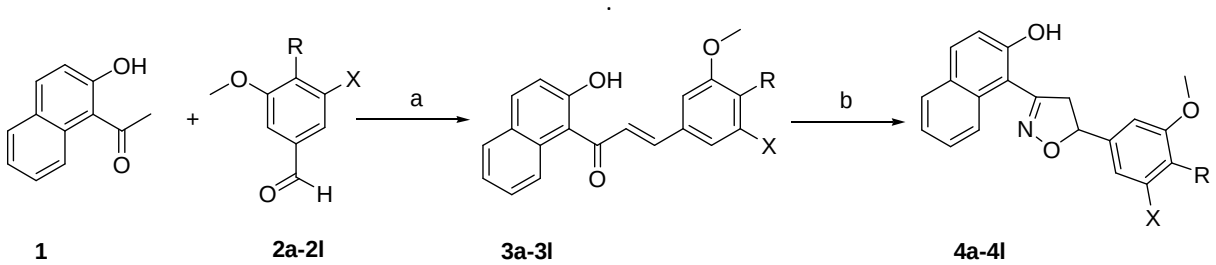
Compounds incorporating heterocyclic ring systems continue to attract considerable interest due to the wide range of biological activities [1-7] they posses. Among the wide range of heterocycles that have been explored for developing pharmacologically important molecule is isoxazolines [8-15], which play a significant role in the field of medicinal chemistry. In addition, isoxazoline derivatives have played a crucial role in the theoretical development of heterocyclic chemistry and are also used extensively in organic synthesis [16-18]. The syntheses of novel isoxazoline derivatives remains a main focus of medicinal research and have been reported to possess antidepressant activity [19], antibacterial [20-21], anti-inflammatory, analgesic activity [22], antioxidant, antituberculosis and anticonvulsant [23]. Encouraged by the diverse biological activities of isoxazoline compounds, it prompted us to synthesize new isoxazoline derivatives from commercially available 2-Hydroxy-Aceto-Naphthanone and evaluate their antimicrobial activity against four pathogenic bacteria.

MATERIALS AND METHODS

All chemicals and solvents were obtained from commercial sources and purified using standard procedures whenever required. The structures of the compounds were confirmed by IR and ^{1}HNMR spectra. IR spectra were recorded on JASCO V500 spectrometer using KBr pellets. ^{1}HNMR spectra were recorded on a Varian Mercury EM-360 spectrometer (400 MHz) and using tetramethylsilane (TMS) as internal standard. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; b, broad. Thin layer chromatography (TLC) was performed on pre-coated aluminium sheets coated with Silica Gel 60 F254, 0.2 mm thickness. The mass spectra were determined on a Micromass, LCT

Experimental methods

The classical synthesis of the title compound involves the base-catalyzed condensation of 2-Hydroxy-Aceto-Naphthanone (**1**) and substituted Vanillin (**2a-l**) to give corresponding chalcones (**3a-3l**).These chalcones were further reacted with hydroxylamine hydrochloride in alkaline medium to yield the corresponding isoxazoline derivatives (**4a-4l**). Compounds (**2a-l**) were prepared, by following the standard literature procedure [24-26] from commercially available vanillin. The reaction sequence for the synthesis of isoxazoline derivatives is shown in **Scheme-1**. The key intermediates, chalcones (**3a-3l**) were prepared by treating 2-Hydroxy-Aceto-Naphthanone (**1**) with aldehydes (**2a-2l**) in presence of 60% of potassium hydroxide (w/v) in ethanol, The crude compounds (**3a-3l**) obtained after the work up were used as such for further reaction. Compounds (**3a-l**) were reacted with hydroxylamine hydrochloride in presence of sodium acetate in ethanol to obtain isoxazoline derivatives (**4a-4l**).



1 **2a-2l** **3a-3l** **4a-4l**

a. R = -OCH2CH3, X = H
b. R = -OCH2CH2CH3, X = H
c. R = -OCH2CH2-morpholine, X = H
d. R = -OCH2CH2-piperidine, X = H
e. R = -OCH2CH2-pyrollidine, X = H
f. R = -OCH2CH2-diethyl amine, X = H
g. R = -OCH2CH3, X = I
h. R = -OCH2CH2CH3, X = I
i. R = -OCH2CH2-morpholine, X = I
j. R = -OCH2CH2-piperidine, X = I
k. R = -OCH2CH2-pyrollidine, X = I
l. R = -OCH2CH2-diethyl amine, X = I

Scheme 1. Reagents and Conditions: a) 60% KOH (w/v), Ethanol, rt, 24h; b) $NH_2OH.HCl$, NaOAc, Ethanol, 80 °C, 4h

General Procedure for the Preparation of Isoxazoline Derivatives (4a-4l)

To an ethanol solution containing appropriate chalcones **3a-3l** (348 mg, 1.0 mmol) was added hydroxylamine hydrochloride (2.0 mmol), and sodium acetate (4.0 mmol). The contents were stirred at reflux temperature for 4 h under argon atmosphere; the reaction mixture was cooled to room temperature and poured into water and extracted with ethyl acetate. The organic layer was washed with brine solution, dried over anhydrous sodium sulphate filtered and concentrated under reduced pressure, to obtain the crude compounds. The crude compounds were purified by column chromatography using silica gel (60-120 mesh). Yields of the products varied between 58.0 and 77.5%.

1-(5-(4-ethoxy-3-methoxyphenyl)-4,5-dihydroisoxazol-3-yl)napthalen-2-ol ***(4a)***

Yellow liquid; Yield: 261 mg, 75%; IR (neat): ν_{max} 3100, 1650, 1590, 1230,1150 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.30 (t, 3H, *J* = 6.8 Hz), 2.98 (dd, 1H, *J* = 7.7 & 16.9 Hz), 3.62 (dd, 1H, *J* = 2.2 & 16.9 Hz), 3.81 (s, 3H), 4.12 (q, 2H, *J* = 6.8 Hz), 5.22 (dd, 1H, *J* = 1.4 & 12.0 Hz),7.02-7.91 (m, 8H), 9.34 (d,1H , *J* = 9Hz), 11.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 14.72, 42.73, 56.22, 65.12, 80.88, 111.84, 112.14, 115.62, 118.38, 120.16, 123.92, 126.41, 126.81, 128.22, 129.14, 132.62, 133.34, 135.24, 145.54, 150.18, 156.31, 158.91; EI MS: m/z (rel.abund.%) 349 (M^+, 100).

1-(4,5-dihydro-5-(3-methoxy-4-propoxyphenyl)isoxazol-3-yl)napthalen-2-ol ***(4b)***

Yellow liquid; Yield: 260 mg, 72.3%; IR (neat): ν_{max} 3150, 1645, 1610, 12360, 1150 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.04 (t, 3H, *J* = 6.8 Hz), 1.72 (q, 2H, *J* = 6.8 Hz), 3.02 (dd, 1H, *J* = 7.7 & 16.9 Hz), 3.58 (dd, 1H, *J* = 2.2 & 16.8 Hz), 3.82 (s, 3H), 3.98 (t, 2H, *J* = 6.6 Hz), 5.24 (dd, 1H, *J* = 1.22 & 12.02 Hz), 6.98 -7.92 (m, 8H), 9.32 (d,1H , *J* = 8.8Hz), 11.4 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 10.42, 22.76, 42.91, 56.32, 71.81, 80.92, 111.81, 112.12, 115.64, 118.42, 120.21, 123.91, 126.40, 126.82, 128.12, 129.12, 132.42, 133.32, 135.21, 145.52, 150.12, 156.21, 158.92; EI MS: m/z (rel.abund.%) 362 (M^+, 100).

1-(5-(4-(2-morpholinoethoxy)-3-methoxyphenyl)-4,5-dihydroisoxazol-3-yl)napthalen-2-ol ***(4c)***
Brown liquid; Yield: 300 mg, 70.1%; IR (neat): ν_{max} 3080, 1655, 1595, 1235,1145 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.44 (m, 4H), 2.72 (t, 2H, *J* = 6.8 Hz), 3.58 (m, 4H), 4.14 (t, 2H, *J* = 6.8 Hz), 3.16 (dd, 1H, *J* = 7.8 & 16.6 Hz), 3.62 (dd, 1H, *J* = 2.0 & 16.8 Hz), 3.80 (s, 3H), 4.12 (t, 2H, *J* = 6.9 Hz), 5.34 (dd, 1H, *J* = 2.0 & 11.8 Hz), 7.0 -7.8 (m, 8H), 9.32 (d,1H , *J* = 9.0 Hz), 11.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 25.91 (3C), 42.71, 54.62 (2C), 54.72, 67.22, 56.21, 80.93, 111.83, 112.11, 115.62, 118.12, 120.16, 123.92, 126.61, 126.72, 128.22, 129.0, 132.38, 133.34, 135.11, 145.54, 150.18, 156.22, 158.72; EI MS: m/z (rel.abund.%) 433 (M^+, 100).

1-(5-(4-(2-(piperidin-1-yl)ethoxy)3-methoxyphenyl)-4,5-dihydroisoxazol-3-yl)napthalen-2-ol ***(4d)***
Brown liquid; Yield: 280 mg, 65.1%; IR (neat): ν_{max} 3120, 1640, 1598, 1232,1180, cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.48 (m, 6H), 2.2 (m, 4H) 2.74 (t, 2H, *J* = 6.7 Hz), 3.15 (dd, 1H, *J* = 8.2 & 16.0 Hz), 3.62 (dd, 1H, *J* = 2.2 & 16.6 Hz), 3.87 (s, 3H), 4.15 (t, 2H, J = 6.7 Hz), 5.22 (dd, 1H, *J* = 1.6 & 12.0 Hz), 6.9 -7.94 (m, 8H), 9.34 (d, 1H, *J* = 9.0 Hz), 11.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 42.6,53.62 (2C), 54.81,56.3, 66.41 (2C), 67.12, 80.91, 111.81, 112.12, 115.81, 118.14, 120.12, 123.91, 126.60, 126.76, 128.12, 129.12, 132.41, 133.21, 135.21, 145.51, 150.12, 156.32, 158.37; EI MS: m/z (rel.abund.%) 431 (M^+, 100).

1-(5-(4-(2-pyrrolidin-1-yl)ethoxy)-3-methoxyphenyl)-4,5-dihydroisoxazol-3-yl)napthalen-2-ol ***(4e)***
Light yellow viscous liquid; Yield: 250 mg, 62.3%; IR (neat): ν_{max} 3110, 1660, 1600, 1220,1150 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.82 (m, 4H), 2.45 (m, 4H) 2.87 (t, 2H, *J* = 6.7 Hz), 3.05 (dd, 1H, *J* = 7.8 & 16.6 Hz), 3.58 (dd, 1H, *J* = 1.6 & 16.2 Hz), 3.82 (s, 3H), 4.25 (t, 2H, J = 6.7 Hz), 5.25 (dd, 1H, *J* = 2.0 & 12.0 Hz), 7.15 -7.88 (m, 8H), 9.324 (d,1H,J = 9.0 Hz), 11.5(s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 25.89(2C), 42.68,54.42,56.21, 58.24 (2C), 67.22, 80.92, 111.78, 112.10, 115.84, 118.16, 120.16, 123.81, 126.40, 126.66, 128.14, 129.22, 132.21, 133.32, 135.41, 145.54, 150.22, 156.22, 158.34; EIMS:m/z (rel.abund.%) 417 (M^+, 100).

1-(5-(4-(2-diethylamino)ethoxy)-3-methoxyphenyl)-4,5-dihydroisoxazol-3-yl)napthalen-2-ol ***(4f)***
Brown liquid; Yield: 250 mg, 60%; IR (neat): ν_{max} 3100, 1650, 1590, 1231,1150 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.05 (t, 6H, *J* = 6.7 Hz), 2.25 (q, 4H, *J* = 6.7 Hz), 2.76 (t, 2H, *J* = 6.9 Hz), 3.02 (dd, 1H, *J* = 7.28 & 16.0 Hz), 3.58 (dd, 1H, *J* = 1.2 & 16.2 Hz), 3.88 (s, 3H), 4.22 (t, 2H, *J* = 6.9 Hz), 5.32 (dd, 1H, *J* = 2.6 & 12.4 Hz), 7.12 -7.92 (m, 8H), 9.32 (d,1H,J = 9.0 Hz), 11.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 13.92 (2C), 42.82, 49.48 (2C), 54.41, 67.19, 80.91, 111.72, 112.14, 115.64, 118.10, 120.12, 123.68, 126.42, 126.62, 128.24, 129.21, 132.41, 133.22, 135.38, 145.34, 150.26, 156.24, 158.32; EI MS: m/z (rel.abund.%) 419 (M^+, 100).

1-(5-(4-ethoxy-3-iodo-5-methoxyphenyl)-4,5-dihydroisoxazol3-yl)napthalen-2-ol ***(4g)***
Yellow liquid; Yield: 364 mg, 77%; IR (neat): ν_{max} 3600, 1610, 1540, 1230,1155 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.38 (t, 3H, *J* = 6.8 Hz), 2.99 (dd, 1H, *J* = 6.8 & 17.0 Hz), 3.58 (dd, 1H, *J* = 2.0 & 16.6 Hz), 3.82 (s, 3H), 4.02 (q, 2H, J = 6.7 Hz), 5.25 (dd, 1H, *J* = 2.2 & 12.4 Hz),7.2-7.9 (m, 7H), 9.30 (d,1H , *J* = 9.0 Hz), 11.5 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 14.62, 42.72, 56.22, 64.22, 80.18, 87.12, 110.68, 112.21, 118.61, 123.71, 126.41, 126.62, 126.81, 128.22, 129.41, 130.92, 134.34, 135.32, 149.22, 151.18, 156.41, 158.61; EI MS: m/z (rel.abund.%) 474 (M^+, 100).

1-(4,5-dihydro-5-(3-iodo-5-methoxy-4-propoxyphenyl)isoxazol-3-yl)napthalen-2-ol ***(4h)***
Light yellow liquid; Yield: 366 mg, 75.2%; IR (neat): ν_{max} 3615, 1615, 1535, 1232,1145 cm^{-1} ; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.22 (t, 3H, *J* = 6.7 Hz), 1.85 (q, 2H, *J* = 6.7 Hz), 2.99 (dd, 1H, *J* = 7.2 & 17.2 Hz), 3.72 (dd, 1H, *J* = 4.0 & 17.0 Hz), 3.91 (s, 3H), 4.02 (q, 2H, J = 6.7 Hz), 5.15 (dd, 1H, *J* = 4.2 & 13.4 Hz), 7.08 -7.88 (m, 7H), 9.22 (d,1H , *J* = 8.8Hz), 11.5 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 10.44, 22.68, 42.68, 56.42, 70.56, 80.34, 87.14, 110.64, 112.24, 118.64, 123.68, 126.44, 126.66, 126.84, 128.42, 129.44, 130.91, 134.38, 135.34, 149.20, 151.21, 156.44, 158.56; EI MS: m/z (rel.abund.%) 488 (M^+, 100).

1-(5-(4-(2-morpholinoethoxy)-3-iodo-5-methoxyphenyl)-4,5-dihydroisoxazol-3-yl)napthalen-2-ol ***(4i)***
Brown liquid; Yield: 352 mg, 63.4%; IR (neat): ν_{max} 3618, 1612, 1530, 1220,1160 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.39 (m, 4H), 2.70 (t, 2H, *J* = 6.9 Hz), 3.5 (m, 4H), 4.0 (t, 2H, *J* = 6.9 Hz), 3.06 (dd, 1H, *J* = 6.8 & 16.98 Hz), 3.58 (dd, 1H, *J* = 2.6 & 16.92 Hz), 3.82 (s, 3H), 4.10 (t, 2H, *J* = 6.9 Hz), 5.2 (dd, 1H, *J* = 3.6 & 12.8 Hz), 6.98 -7.8 (m, 7H), 9.25 (d,1H , *J* = 9.0 Hz), 11.5 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 42.81, 53.74 (2C), 54.74, 56.42, 66.28, 66.84(2C), 80.34, 87.12, 110.54, 112.26, 118.44, 123.64, 126.42, 126.62, 126.44, 128.22, 129.34, 130.90, 134.34, 135.24, 149.22, 151.24, 156.42, 158.46; EI MS: m/z (rel.abund.%) 559 (M^+, 100).

1-(5-(4-(2-(piperidin-1-yl)ethoxy)-3-iodo-5-methoxyphenyl)-4,5-dihydroisoxazol-3-yl)napthalen-2-ol ***(4j)***
Yellow liquid; Yield: 334 mg, 60 %; IR (neat): ν_{max} 3612, 1610, 1590, 1260,1150 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.46 (m, 6H), 2.14 (m, 4H) 2.72 (t, 2H, *J* = 6.7 Hz), 3.14 (dd, 1H, *J* = 7.4 & 16.8 Hz), 3.58 (dd, 1H, *J* = 2.2 & 16.8 Hz), 3.89 (s, 3H), 4.14 (t, 2H, J = 6.7 Hz), 5.20 (dd, 1H, *J* = 2.4 & 13.2 Hz), 6.89 -7.9 (m, 7H), 9.34 (d,1H,J = 9.0 Hz), 11.5 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 25.89 (3C), 42.9, 54.42(2C), 54.92, 56.24, 66.26, 80.24, 87.18, 110.52, 112.24, 118.42, 123.66, 126.46, 126.42, 126.48, 128.23, 129.24, 130.92, 134.38, 135.28, 149.27, 151.20, 156.43, 158.44; EI MS: m/z (rel.abund.%) 557 (M^+, 100).

1-(5-(4-(2-pyrrolidin-1-yl)ethoxy)-3-iodo-5-methoxyphenyl)-4,5-dihydroisoxazol-3-yl)napthalen-2-ol ***(4k)***
Pale yellow viscous liquid; Yield: 331 mg, 61.2%; IR (neat): ν_{max} 3610, 1615, 1545, 1235,1155 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.80 (m, 4H), 2.45 (m, 4H) 2.87 (t, 2H, *J* = 6.7 Hz), 3.05 (dd, 1H, *J* = 7.0 & 16.2 Hz), 3.58 (dd, 1H, , *J* = 2.8 & 16.4 Hz), 3.82 (s, 3H), 4.25 (t, 2H, J = 6.7 Hz), 5.25 (dd, 1H, *J* = 2.6 & 13.4 Hz), 7.0 -7.8 (m, 7H), 9.30 (d,1H,J = 9.0 Hz), 11.52 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 25.82 (2C), 42.6, 54.62, 58.42(2C), 56.41, 66.21, 80.42, 87.22, 110.42, 112.20, 118.22, 123.56, 126.36, 126.34, 126.44, 128.22, 129.28, 130.12, 134.39, 135.24, 149.31, 151.24, 156.42, 158.41; EIMS:m/z (rel.abund.%) 543 (M^+, 100).

1-(5-(4-(2-diethylamino)ethoxy)-3-iodo-5-methoxyphenyl)-4,5-dihydroisoxazol-3-yl)napthalen-2-ol ***(4l)***
Pale yellow liquid; Yield: 316 mg, 58.3%; IR (neat): ν_{max} 3600, 1650, 1535, 1230,1160, cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.02 (t, 6H, *J* = 6.7 Hz), 2.26 (q, 4H, *J* = 6.7 Hz), 2.72 (t, 2H, *J* = 6.9 Hz), 3.05 (dd, 1H, *J* = 7.6 & 16.8 Hz), 3.54 (dd, 1H, *J* = 3.2 & 16.8 Hz), 3.89 (s, 3H), 4.2 (t, 2H, *J* = 6.9 Hz), 5.3 (dd, 1H, *J* = 2.8 & 13.2 Hz), 7.1 -7.9 (m, 7H), 9.32 (d, 1H, *J* = 9.0 Hz), 11.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 13.2 (2C), 42.81, 49.4(2C), 54.62, 56.20, 66.42, 80.20, 87.20, 110.40, 112.22, 118.20, 123.52, 126.32, 126.38, 126.40, 128.20, 129.24, 130.16, 134.41, 135.32, 149.34, 151.28, 156.40, 158.42; EI MS: m/z (rel.abund.%) 545 (M^+, 100).

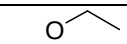
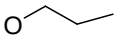
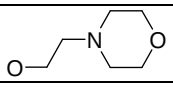
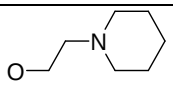
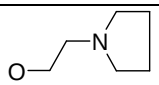
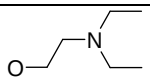
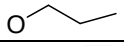
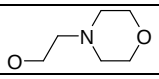
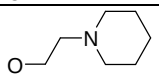
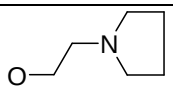
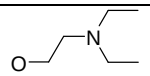
Antibacterial activity
Isoxazoline analogues (**4a–4l**) were dissolved in dimethyl sulphoxide at 250 µg/mL concentration. The composition of nutrient agar medium was Bactotryptone (10 g), yeast extract (5 g), NaCl (10 g), final pH 7.4. After 18 h the exponentially growing cultures of the six bacteria in nutrient broth at 37 ^{o}C were diluted in sterile broth. From each of these diluted cultures, 1mL was added to 100 mL sterilized and cooled nutrient agar media to give a final bacterial count of 1 x 10^6 cell/ml. The plates were set at room temperature and later dried at 37 ^{o}C for 20h. Paper discs (6mm, punched from whatmann no 41 paper) were ultraviolet sterilized and used for the assays. Discs were soaked in different concentration of the test solution and placed on the inoculated agar media at regular intervals of 6-7 cm, care was taken to ensure that excess solution was not on the discs. All the samples were taken in triplicates. The plates were incubated at 37 ^{o}C in an inverted fashion. Activity was determined by zones showing complete inhibition (mm). Growth inhibition was calculated with reference to positive control.

RESULTS AND DISCUSSION

The structure of synthesized compounds was confirmed by IR,^{1}H NMR,^{13}C NMR and Mass spectra. Compounds (**4a-l)** were screened against screened against four pathogenic bacteria, two Gram negative strains viz., *i) Pseudomonas aeruginosa,and* ii) *Escherichia coli* and two Gram positive strains viz., *iii) Staphylococcus aureus iv) Streptococcus pyogenes,* following agar well diffusion procedure as per the reference [27]. The antibacterial activity of the synthesized isoxazolines **4a-4l** was correlated with the zone of inhibition of ampicillin as a reference drug (**Table 1)**. The antibacterial test results for the newly synthesized isoxazoline analogues revealed that most of the compounds exhibited moderate to good activity against the Gram +ve (*Streptococcus pyogenes and Staphylococcus aureus)* and Gram –ve bacteria (*Escherichia coli and Pseudomonas aeruginosa*). *Staphylococcus aureus*: compounds **4a, 4b, 4c, 4e, 4f, 4j, 4k and 4l** (having zone of inhibition: 17-18 mm) exhibited good to excellent activity while the remaining compounds displayed moderate activity. *Streptococcus pyogenes*: compounds **4a, 4f, 4k and 4l** (zone of inhibition: 18 mm) displayed good to excellent activity while the remaining compounds showed moderate activity. *Pseudomonas aeruginosa*: compounds **4a,4d,** and **4i** (zone of inhibition: 22 mm) displayed excellent activity, while **4c, 4e, 4h and 4j** showed good to moderate activity and remaining compounds **4b, 4f,4g,4k, and 4l** showed less activity. In case of inhibition of *Escherichia coli* compounds **4d** and **4e** showed excellent activity with a zone of inhibition 22 mm and remaining compounds showed moderate and less active. As all the compounds showed antibacterial activity against the bacteria tested, it indicates that this basic moiety can be a potential scaffold for anti bacterial drugs. It may be suggested that the isoxazoline derivative with a suitable R group

may lead to a good antibacterial agent for all the *Escherichia coli*, *Pseudomonas aeruginosa*, *Streptococcus pyogenes* and *Staphylococcus aureus* bacterial strains. Thus further lead optimization is required to get wide spectrum of activity.

Table 1: Results of Antibacterial Bioassay of Compounds 4a-4l (Concentration used 250 µg/mL of DMSO) Zones of inhibition of compounds 4a-4l

Compound no.	R	X	*Gram negative bacteria*		*Gram positive bacteria*	
			E. coli MTCC 443	*P. aeruginosa MTCC 424*	*S.aureus MTCC 96*	*S.pygenes MTCC 442*
4a		H	17	22	17	18
4b		H	19	16	17	16
4c		H	20	18	17	17
4d		H	22	22	16	17
4e		H	22	18	17	17
4f		H	20	16	18	18
4g		I	19	17	16	16
4h		I	20	18	16	17
4i		I	20	22	16	16
4j		I	18	18	17	17
4k		I	19	18	17	18
4l		I	19	18	17	18
SD* ampicillin (Conc. 250 µg/mL)	SD* ampicillin		20	20	18	19

CONCLUSION

We have synthesized new Isoxazoline derivatives **4 (a-l)** from commercially available 2-Hydroxy-Aceto-Naphthanone and screened for the antibacterial activity against Escherichia coli (MTCC-443), Staphylococcus aureus (MTCC-96), Pseudomonas aeruginosa (MTCC-424) and Streptococcus pyogenes (MTCC-442) bacterial strains. All of the screened compounds exhibited good to excellent activity when compared to the standard ampicillin drug. In case of inhibition of *Escherichia coli* compounds **4d and 4e** showed excellent activity with a zone of inhibition 22 mm. Thus further lead optimization is required to get wide spectrum of activity.

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