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# Synthesis and Antibacterial Screening of Some Novel Isoxazoline Derivatives

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## Abstract

The nitrogen and oxygen containing heterocyclic five member isoxazolines have immense synthetic and pharmacological applications. Here we explore the synthesis 5-(3,4-substitutedphenyl)-3-(4-substituted)-4,5-dihydroisoxazole derivatives **2(a-d)** by cyclization of chalcones **1(a-d)** with hydroxalamine hydrochloride in the presence of $B(mim)ClO_4$, affords the excellent yield. The structures of the synthesized compounds were confirmed on the basis of spectral data. These derivatives were screened for their *in vitro* antibacterial activities.

**Keywords:** Chalcones, isoxazolines, antibacterial activity.

## 1. Introduction

Isoxazolines have been reported to possess miscellaneous pharmacological activities like antiinflammatory[1], antibacterial[2], antifungal[3], antibiotic[4], anticonvulsant[5], antitubercular[6], anxeolytic[7] properties. The five member heterocyclic molecules have been attracting the attention of synthetic chemists for their wide range of biological activities ranging anticancer, antiparkinson, anticonvulsant, and anti–HIV,[8-10] insecticidal, antiprotozoal, nitric oxide inhibition, ulcerogenic, and antihyperglycemic.[11-12]

Keeping in view the above particulars, we have designed selected new isoxazoline derivatives and evaluated them for the antibacterial activity.

## 2. Experimental:

The IR spectra of the synthesized compounds were recorded on a Fourier Transform IR spectrometer (model Shimadzu 8700) in the range of 400-4000 cm-1 using KBr pellets.

$^1H$ NMR spectra was recorded on Bruker 400 MHz NMR spectrometer using $CDCl_3$ and the chemical shifts (δ) reported are in ppm downfield using tetramethylsilane (TMS) as internal reference. $^{13}C$ NMR spectra were recorded on Amx-100 MHz NMR spectrometer using $CDCl_3$ and the chemical shifts (δ) reported are in ppm downfield using tetramethylsilane (TMS) as an internal reference. The NMR data is reported as follows: chemical shift, multiplicity (s = single, d = doublet, t = triplet, q = quartet, m = multiplet. The coupling constant (J) is given in Hz. Mass spectra of the compounds were obtained by using LC-MS (SHIMADZU-2010AT, Software class VP).

**Synthesis of 5-(3, 4-substitutedphenyl)-3-(4-substituted)-4,5-dihydroisoxazole:**

The 5-(3, 4-substitutedphenyl)-3-(4-substituted)-4,5-dihydroisoxazole **2(a-d)** were synthesized by reacting a mixture of purified chalcones **1(a-d)** (0.01mol), hydroxylamine hydrochloride (0.03 mol) and a solution of NaOH (0.01 mol) by using $B(mim)ClO_4$ , the completion of the reaction was chwcked by TLC, in 2h, got the product. The excess of the solvent was removed by distillation and the resultant mass was poured into ice water with vigorous stirring. The solution was acidified with dilute HCl. It was kept overnight in cool condition. The resultant solid product was

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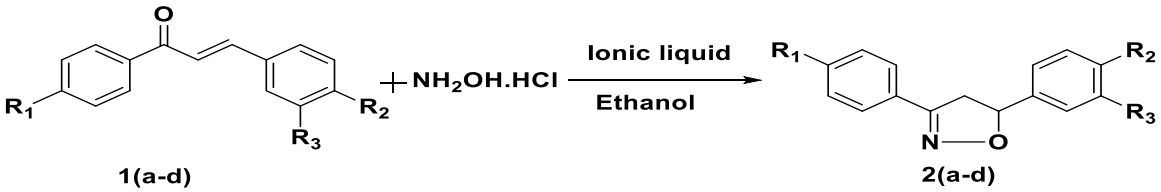
filtered, washed with sufficient cold water, dried, and purified by recrystallization from ethanol.

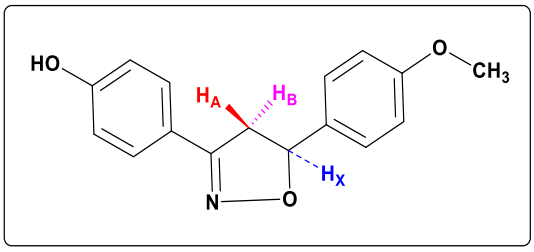
## Scheme I:




1(a-d) 2(a-d)

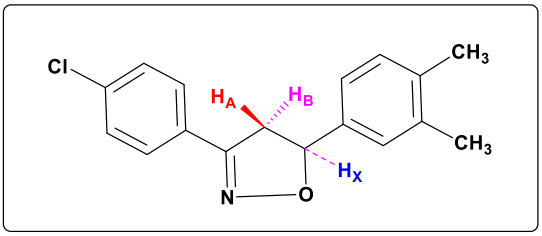
**$R_1$=-OH, -Cl, -Br, H: $R_2$= -OMe, -Me, H, -$NO_2$, $R_3$= H, -Me, H, -Me.**

### 3. Spertral data of 5-(3, 4-substitutedphenyl)-3-(4-substituted)-4,5-dihydroisoxazole:4-(5-(4 methoxyphenyl)-4,5-dihydroisoxazol-3-yl)phenol (2a):



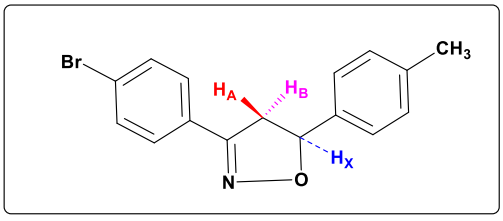

Solid, yield = 75%, mp 165-167 °C; **IR (KBR $cm^{-1}$):** 3331, 1630 $cm^{-1}$; **$^1$H-NMR (400 MHz, $CDCl_3$):** $\delta$ 13.55 for (s, 1H, -OH), 7.14-7.85 (m, 6H, Ar-H), 5.75(dd, 1Hx, Jcis = 10.8 Hz, Jtrans = 8.4 Hz), 3.77 (dd, 1Ha, Jgem = 16.8 Hz, Jcis = 10.8 Hz), 3.32 (dd, 1H, Jgem = 16.5 Hz, Jtrans = 8.4 Hz), 2.37 (s, 3H, $OCH_3$). **LCMS:** 270 [M +1]. **Elemental analysis** (CHN) Calculated for **$C_{16}H_{15}NO_3$** : C, 71.36; H, 5.61; N, 5.20; found C, 71.24; H, 5.55; N, 5.23.

### 2.3-(4-chlorophenyl)-5-(3,4-dimethylphenyl)-4,5-dihydroisoxazole (2b):




Solid, yield = 767, mp 155-157 °C; **IR (KBR $cm^{-1}$):** 3331, 1633, 745 $cm^{-1}$; **$^1$H-NMR (400 MHz, $CDCl_3$):** $\delta$ 7.90-7.20 (m, 6H, Ar-H), 5.90 (dd, 1Hx, Jcis = 10.8 Hz, Jtrans = 8.4 Hz), 3.81 (dd, 1Ha, Jgem = 16.8 Hz, Jcis = 10.8 Hz), 3.29 (dd, 1H, Jgem = 16.5 Hz, Jtrans = 8.4 Hz), 2.34 (s, 6H, $CH_3$). **LCMS:** 286 [M +1];
**Elemental analysis** (CHN) Calculated for **$C_{17}H_{16}ClNO$**: C, 71.45; H, 5.64; N, 4.90; found C, 71.40; H, 5.70; N, 4.88.

### 3. 3-(4-bromophenyl)-5-(p-tolyl)-4,5-dihydroisoxazole (2c):




Solid; yield: 93 %; mp 142-143 °C. **IR (KBR $cm^{-1}$):** 1645, 532 $cm^{-1}$; **$^1$H NMR (300 MHz,**

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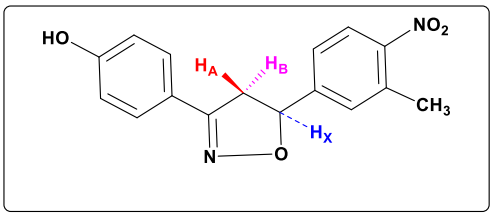
**$CDCl_3$):** δ 7.65-7.17 (m, 8H, Ar), 5.80 (dd, 1Hx, Jcis = 10.8 Hz, Jtrans = 8.4 Hz), 3.81 (dd, 1Ha, Jgem = 16.8 Hz, Jcis = 10.8 Hz), 3.33 (dd, 1H, Jgem = 16.5 Hz, Jtrans = 8.4 Hz), 2.33 (s, 3H, $CH_3$); **$^{13}$C NMR (75.5 MHz, $CDCl_3$):** δ 154.5, 137.3, 136.7, 131.1, 130.6, 128.7, 128.3, 125.1, 123.5, 82.1, 40.9, 20.3; **LCMS**: 317 [M +1]; **Elemental analysis** (CHN) Calculated for **$C_{16}H_{14}BrNO$**: C, 60.78; H, 4.46; N, 4.43; found C, 60.80; H, 4.44; N, 4.45.

### 4. 5-(3-methyl-4-nitrophenyl)-3-phenyl-4,5-dihydroisoxazole (2d):




Solid; yield: 85 %; mp 150-152 °C; **IR (KBR $cm^{-1}$):** 1627 $cm^{-1}$; **$^1$H NMR (300 MHz, $CDCl_3$):** δ 8.20-7.30 (m, 7H, Ar), 5.79 (dd, 1Hx, Jcis = 10.8 Hz, Jtrans = 8.4 Hz), 3.85 (dd, 1Ha, Jgem = 16.8 Hz, Jcis = 10.8 Hz), 3.42 (dd, 1H, Jgem = 16.5 Hz, Jtrans = 8.4 Hz), 2.33 (s, 3H, $CH_3$); **LCMS:** 283 [M +1]; **Elemental analysis** (CHN) Calculated for **$C_{16}H_{14}N_2O_3$**: C, 68.08; H, 5.00; N, 9.92; found C, 68.10; H, 4.95; N, 9.86.

### 4. Antibacterial activity:

The target molecules were tested for antibacterial activity against S. aureus (MTCC-96), B. subtilis (MTCC-441) [Gram-positive bacteria], and E. coli (MTCC-443), S. paratyphi-B (MTCC-733) [Gram-negative bacteria] by using agar diffusion method.[13] The antibiotic Ciprofloxacin was used as standard drug. The screening results indicate that compounds (2b), (2c) and (2d) were found to be active against S. aureus (MTCC-96). Compounds (2a), was found to moderately active be active against S. aureus (MTCC-96), where as compounds (2b) and (2c) were found to be inactive be active against S. aureus (MTCC-96).

The compounds (2a), (2d) were found to be active against B. subtilis (MTCC-441). Compounds (2a) and (2c) were found to be moderately active against B. subtilis (MTCC-441).Compounds (2b) was found to less active against B. subtilis (MTCC-441), where as compound (2d) was found to be inactive against B. subtilis (MTCC-441).

Compound (2a) was found to active against E. coli (MTCC-443). Compounds (2a), (2b) were found to be moderately active against E. coli (MTCC-443), whereas (2c) and (2d) were found to be less active against E. coli (MTCC-443). Compounds (2b), (2d) were found to be active against S. paratyphi-B (MTCC-733). Compounds (2a), (2c) were found to be moderately active against S. paratyphi-B (MTCC-733).

**5.Acknowledgement:** Author is grateful to UGC, New Delhi for financial support of MRP entitled as,"Study of Green Perspectives of Ionic Liquids for Synthesis of Heterocycles"

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