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# Synthesis, QSRT studies and antibacterial activity of 4-aryl-3-chloro-1-(3,5-dimethyl-isoxazol-4-yl)-azetidin-2-ones

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A new series of 4-aryl-3-chloro-1-(3,5-dimethyl-isoxazol-4-yl)-azetidin-2-ones **4** have been prepared from 4-amino-3,5-dimethylisoxazole **1**. Compound **1** on treatment with aromatic aldehydes **2a-i** furnishes the Schiff bases **3a-i**, which are then reacted with chloroacetyl chloride in presence of triethyl amine to afford the title compounds *viz*., isoxazolyl azetidin-2-ones **4a-i**. The structures of β-lactams **4a-i** have been confirmed by IR, $^1$H and $^{13}$C NMR and mass spectral data. QSRT studies have been performed, and the compounds **4a-i**have been evaluated for their *in vitro* antibacterial activity. Compounds **4b**, **4c** and **4d** exhibited promising antibacterial activity.

**Keywords**: Isoxazolyl azetidin-2-ones, Schiff base, cycloaddition, QSRT studies, antibacterial activity

The β-lactams (azetidin-2-ones) are one of the best known and extensively investigated heterocyclic ring system as a result of both their biological activity as antibiotics[1], and their utilities as synthetic intermediates[2]. Hence, the synthesis of β-lactam antibiotics has occupied an important place in the field of medicinal and pharmaceutical research. Azetidin-2-ones and its derivatives possess various pharmacological properties such as antihypertensive, anti-inflammatory, antihyperlipidemic, antimicrobial, antitubercular and anticonvulsant[3-6]. In addition to their use as medicines, β-lactams are increasingly being used as synthons for other biologically important molecules[7-12]. Similarly, isoxazole derivatives represent an interesting class of compounds possessing a wide spectrum of biological activities. A large number of isoxazole derivatives exhibit antibacterial[13], anticonvulsant[14], analgesic[15], and anticancer activities[16]. Attracted by these scaffolds *viz*., isoxazoles and β-lactams, and their pharmacological properties, it was decided to develop new targets by molecular hybridization for antibacterial evaluation. As a sequel to our work on the synthesis of pharmaceutically active isoxazole derivatives[17-19], we, herein, report the synthesis, QSRT (Qualitative Structure Relationship Technique) studies and antibacterial activity of isoxazolyl azetidin-2-ones.

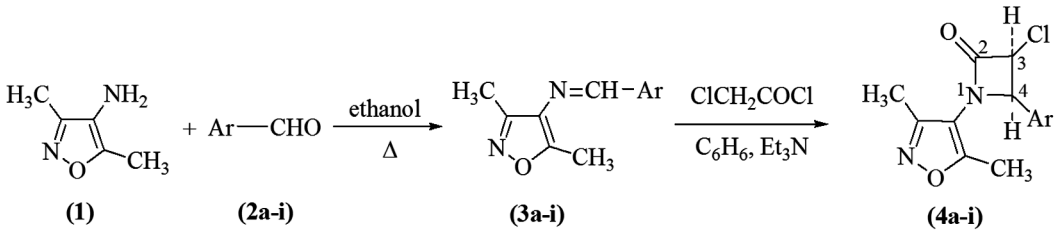
## Results and Discussion

### Chemistry

The reaction of 4-amino-3,5-dimethylisoxazole **1**with aromatic aldehydes **2a-i** in boiling ethanol solution furnished the condensation products *viz*., 4-benzalamino-3,5-dimethylisoxazoles **3a-i**[19]. Compounds **3a-i**on treatment with chloroacetyl chloride in presence of triethyl amine underwent cycloaddition to give 4-aryl-3-chloro-1-(3,5-dimethyl-isoxazol-4-yl)-azetidin-2-ones **4a-i** (Scheme I).

The IR spectra of **4a** exhibited a strong absorption band at 1700 cm$^{-1}$ due to C=O functional group. $^1$H NMR spectra of **4a** manifested two characteristic doublets at δ 5.10 and 5.30 due to $C_4$-H and $C_3$-H protons respectively with coupling constant (*J*) values 5.40 Hz. The coupling constant (*J*) values of $C_4$-H and $C_3$-H protons of β-lactam ring indicates their *cis*-geometry[20]. $^{13}$C NMR spectra of **4** displayed $C_4$ and $C_3$ and carbonyl carbon signals at δ 62.0, 63.2 and 164.8 respectively confirming, β-lactam ring formation. The mass spectra of **4a** agrees very well with the proposed β-lactam ring by displaying the molecular ion $[M + H]^+$ at *m/z* 277.

All the newly synthesized compounds **4a-i** were confirmed by their IR, $^1$H and $^{13}$C NMR, and mass spectral data. C, H, N analyses are satisfactory and confirmed elemental composition and purity of the newly synthesized compounds **4a-i**.




| 4 Ar | 4 Ar | 4 Ar |
|---|---|---|
| a: $C_6H_5$ | d: 2,4-$(Cl)_2C_6H_3$ | g: 3-Br $C_6H_4$ |
| b: 4-Cl $C_6H_4$ | e: 3,4-$(OCH_3)_2$ $C_6H_3$ | h: 2-thienyl |
| c: 4-$NO_2$ $C_6H_4$ | f: 3-$OCH_3C_6H_4$ | i: 2-furyl |

Scheme I

Table I — Lipinski and Physico-chemical parameters of compounds **4a-i**

| Compd | Lipinski's properties | | | | | | Log D (at *p*H) | | | | | BCF BIO | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | MW | HBD | HBA | TPSA | RB | Log P | 1.6 | 4.6 | 6.5 | 7.4 | 8.2 | BCF | $K_{OC}$ |
| **4a** | 276.72 | 0 | 4 | 46.34 | 2 | 3.33 | 3.33 | 3.33 | 3.33 | 3.33 | 3.33 | 13.2 | 220 |
| **4b** | 311.16 | 0 | 4 | 46.34 | 2 | 3.67 | 3.67 | 3.67 | 3.67 | 3.67 | 3.67 | 37.3 | 464 |
| **4c** | 321.71 | 0 | 7 | 95.17 | 3 | 3.37 | 3.37 | 3.37 | 3.37 | 3.37 | 3.37 | 8.21 | 157 |
| **4d** | 345.61 | 0 | 4 | 46.34 | 2 | 4.91 | 4.91 | 4.91 | 4.91 | 4.91 | 4.91 | 108 | 994 |
| **4e** | 336.77 | 0 | 6 | 64.8 | 4 | 2.56 | 2.56 | 2.56 | 2.56 | 2.56 | 2.56 | 8.31 | 158 |
| **4f** | 306.74 | 0 | 5 | 55.57 | 3 | 2.97 | 2.97 | 2.97 | 2.97 | 2.97 | 2.97 | 11.4 | 198 |
| **4g** | 355.61 | 0 | 4 | 46.34 | 2 | 3.88 | 3.88 | 3.88 | 3.88 | 3.88 | 3.88 | 50.8 | 579 |
| **4h** | 282.75 | 0 | 4 | 74.58 | 2 | 3.05 | 3.04 | 3.05 | 3.05 | 3.05 | 3.05 | 7.50 | 147 |
| **4i** | 266.68 | 0 | 5 | 59.48 | 2 | 2.43 | 2.43 | 2.43 | 2.43 | 2.43 | 2.43 | 3.03 | 77.0 |

## QSRT studies

According to Lipinski's 'Rule of Five'[21] all the synthesized compounds **4a-i** are within drug likeness creteria. From BCF and adsorption coefficient data[22], all compounds **4a-i** are non-bioaccumulative, so there is very less chance to be incorporated in to biological food chains from environment. Among all the tested compounds **4d** and **4i** are having high values (Table I). Compounds **4b, 4c** and **4d** show 86 to 90% PPB value, hence they are strongly bound *i.e.*, the fraction of metabolised or excreted drug will be 10-14% only. Rest of the compounds **4a, 4e, 4f** and **4i** are weakly bound. Remaining compounds are moderately bound. All compounds **4a-i** bind to human serum albumin[23]. Among all the compounds, **4d** is having high value. Compounds **4a-i** are considered to be good p-gp inhibitors[24]. From AMES data compound **4c** may act as a carcinogenic agent[25,26]. All compounds **4a-i** possess β-lactam ring mustard fragment[27] (Figure 1). Haloethyl mustards form adducts with guanine nucleobases, hence may be considered to exhibit genotoxic nature. From hERG data, all compounds **4a-i** are found to possess non-cardio toxicity[28]. Relative binding affinity (RBA)

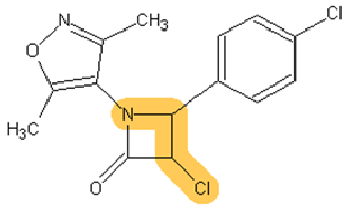


Figure 1 — Mustard fragment

values are within the range. So compounds **4a-i** may possibly bind to alpha estrogen receptor[29,30] (Table II). From all parameters compounds **4b**, **4c** and **4d** follow Lipinski rule of five, high PPB value, ready to bind human serum albumin. Compound **4c** is found to possess carcinogenic character, whereas **4b** and **4d** do not have carcinogenic character. All the compounds **4a-i** are having geno-toxicity, and they are possibly bind to alpha estrogen receptor. So, among all compounds **4b** and **4d** are found to possess drug like character.

## Antibacterial activity

The antibacterial activity results showed that compounds **4a-i** displayed a better activity and were more active than standard drug *Ciprofloxacin* (Table III) due to the presence of β-lactam ring. The

Table II — ADME parameters and toxicity parameters of compounds **4a-i**

| Compd | DBP | | p-gp inhibition | | AMES | hERg Inhibitors | Endocrine Disruptions | |
|---|---|---|---|---|---|---|---|---|
| | PPB (%) | Log $K_a^{HSA}$ | Probability | $K_i$ | | | Log RBA>-3 | Log RBA>0 |
| **4a** | 77.39 | 4.29 | 0.07 | 0.01 | 0.36 | 0.09 | 0.15 | 0 |
| **4b** | 88.23 | 4.57 | 0.1 | 0 | 0.3 | 0.12 | 0.29 | 0 |
| **4c** | 86.07 | 4.05 | 0.09 | 0.01 | 0.83 | 0.07 | 0.15 | 0 |
| **4d** | 90.54 | 4.97 | 0.12 | 0 | 0.25 | 0.23 | 0.4 | 0.01 |
| **4e** | 74.51 | 4.25 | 0.11 | 0.01 | 0.33 | 0.1 | 0.15 | 0 |
| **4f** | 74.82 | 4.24 | 0.08 | 0.01 | 0.33 | 0.09 | 0.18 | 0 |
| **4g** | 83.22 | 4.45 | 0.1 | 0 | 0.32 | 0.1 | 0.34 | 0 |
| **4h** | 80 | 4.15 | 0.04 | 0 | 0.36 | 0.03 | 0.09 | 0 |
| **4i** | 73.55 | 4.15 | 0.05 | 0 | 0.41 | 0.07 | 0.04 | 0 |

Table III — Antibacterial screening of 4-aryl-3-chloro-1-(3,5-dimethylisoxazol-4-yl)azetidin-2-ones **4a-i**

| Compd | Ar | Conc. (μg/mL) | Minimum Inhibitory Concentration (MIC)[a,b] | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Gram-positive | | | Gram-negative | | |
| | | | *Bs* | *Bsp* | *Sa* | *Pa* | *Ka* | *Cv* |
| **4a** | $C_6H_5$ | 100 | 18 | 8 | 20 | 20 | 25 | 20 |
| **4b** | 4-$ClC_6H_4$ | 100 | 12 | 12 | 10 | 10 | 13 | 11 |
| **4c** | 4-$NO_2C_6H_4$ | 100 | 8 | 10 | 12 | 15 | 13 | 13 |
| **4d** | 2,4-$(Cl)_2C_6H_3$ | 100 | 8 | 9 | 11 | 12 | 11 | 10 |
| **4e** | 3,4-$(OCH_3)_2C_6H_3$ | 100 | 15 | 14 | 15 | 16 | 16 | 15 |
| **4f** | 3-$OCH_3C_6H_4$ | 100 | 16 | 16 | 16 | 15 | 15 | 18 |
| **4g** | 3-$BrC_6H_4$ | 100 | 15 | 15 | 15 | 10 | 11 | 11 |
| **4h** | 2-thienyl | 100 | 15 | 14 | 14 | 20 | 20 | 18 |
| **4i** | 2-furyl | 100 | 15 | 18 | 16 | 20 | 16 | 18 |
| Ciprofloxacin | | 100 | 20 | 20 | 25 | 30 | 25 | 25 |

[a]Negative control (acetone)-No activity
[b]Values are indicated in μg/mL

activity was expressed in terms of minimum inhibitory concentration (MIC). The compounds **4b, 4c** and **4d** are highly active, because the activity is considerably affected by the presence of groups like chloro and nitro as substituents on benzene ring, besides the presence of isoxazole and β-lactam rings. Compounds **4e, 4f, 4g, 4h** and **4i** carrying thienyl and furyl groups, methoxy and bromo substitutions on benzene ring exhibited good activity. Compound **4a** showed least activity, because it has no substituent on the benzene ring. However, the degree of inhibition varied both with the test compound as well as with the bacteria used in the present investigation.

## Experimental Section

All the melting points were determined on a Cintex melting point apparatus and are uncorrected. Analytical TLC was performed on Merck precoated 60 $F_{254}$ silica gel plates. Visualization was done by exposing to UV light. IR spectra (KBr pellet) were recorded on a Perkin-Elmer BX series FT-IR spectrometer. $^1$H NMR (300 MHz) and $^{13}$C NMR (75 MHz) spectra were recorded on a Bruker spectrometer in $CDCl_3$ with TMS as internal standard. ESI mass spectra were recorded on an Agilent LC-MSD mass spectrometer. Elemental analyses were performed on a Carlo Erba 106 and Perkin-Elmer model 240 analysers. All the chemicals were procured from Sigma-Aldrich and used as such without further purification.

### General procedure for synthesis of 4-aryl-3-chloro-1-(3,5-dimethylisoxazol-4-yl-azetidin-2-ones, 4a-i

To a well stirred solution of *N*-arylidene-3,5-dimethyl-isoxazol-4-amines **3a**(0.01 mol) and triethyl amine (0.02mol) in dry benzene (10mL), was added chloroacetyl chloride (0.02 mol) drop-wise at RT for 15 min. After complete addition, the reaction mixture was refluxed for 4 h, and separated triethyl amine hydrochloride was removed by filtration. The solvent was distilled under vaccum, and the crude product was purified by column chromatography by elution with *n*-hexane and ethyl acetate (8:2).

**3-Chloro-1-(3,5-dimethylisoxazol-4-yl)-4-phenyl-azetidin-2-one, 4a**: m.p. 118-19°C. Yield 68%. IR (KBr): 1700 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ

2.11 (s, 3H, isoxazole-$CH_3$), 2.25 (s, 3H, isoxazole-$CH_3$), 5.10 (d, 1H, $J$ = 5.4 Hz, $C_4$-H), 5.30 (d, 1H, $J$ = 5.4 Hz, $C_3$-H), 7.30 (m, 5H, Ar-H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 10.1, 10.9, 62.0, 63.2, 114.7, 126.7, 127.1, 127.6, 128.8, 129.4, 138.0, 158.0, 164.8, 166.0; ESI-MS: *m/z* 277 $[M + H]^+$. Anal. Calcd for $C_{14}H_{13}ClN_2O_2$: C, 60.77; H, 4.74; N, 10.12. Found: C, 60.74; H, 4.72; N, 10.11%.

**3-Chloro-4-(4-chlorophenyl)-1-(3,5-dimethylisoxazol-4-yl)azetidin-2-one, 4b**: m.p. 138-40°C. Yield 70%. IR (KBr): 1695 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.00 (s, 3H, isoxazole-$CH_3$), 2.08 (s, 3H, isoxazole-$CH_3$), 5.00 (d, 1H, $J$ = 5.4 Hz, $C_4$-H), 5.20 (d, 1H, $J$ = 5.4 Hz, $C_3$-H), 7.20 (d, 2H, $J$ = 7.8 Hz, Ar-H), 7.31 (d, 2H, $J$ = 7.8 Hz, Ar-H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 9.9, 10.9, 62.0, 63.1, 113.8, 128.0, 128.9, 134.9, 135.5, 158.0, 164.9, 166.0; ESI-MS: *m/z* 311 $[M + H]^+$. Anal. Calcd for $C_{14}H_{12}Cl_2N_2O_2$: C, 54.04; H, 3.89; N, 9.00. Found: C, 54.02; H, 3.87; N, 8.99%.

**3-Chloro-1-(3,5-dimethylisoxazol-4-yl)-4-(4-nitrophenyl)azetidin-2-one, 4c**: m.p. 182-83°C. Yield 71%. IR (KBr): 1708 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.01 (s, 3H, isoxazole-$CH_3$), 2.10 (s, 3H, isoxazole-$CH_3$), 5.12 (d, 1H, $J$ = 5.4 Hz, $C_4$-H), 5.30 (d, 1H, $J$ = 5.4 Hz, $C_3$-H), 7.39 (d, 2H, $J$ = 8.1 Hz, Ar-H), 8.22 (d, 2H, $J$ = 8.1 Hz, Ar-H); $^{13}$C NMR, (75 MHz, $CDCl_3$): δ 9.9, 10.9, 62.9, 63.9, 113.9, 123.9, 126.8, 144.0, 147.5, 158.2, 164.8, 166.0; ESI-MS: *m/z* 322 $[M + H]^+$. Anal. Calcd for $C_{14}H_{12}ClN_3O_4$: C, 52.27; H, 3.76; N, 13.06. Found: C, 52.24; H, 3.74; N, 13.05%.

**3-Chloro-4-(2,4-dichlorophenyl)-1-(3,5-dimethylisoxazol-4-yl)azetidin-2-one, 4d**: m.p. 127-29°C. Yield 72%. IR (KBr): 1701 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.05 (s, 3H, isoxazole-$CH_3$), 2.09 (s, 3H, isoxazole-$CH_3$), 5.18 (d, 1H, $J$ = 5.4 Hz, $C_4$-H), 5.38 (d, 1H, $J$ = 5.4 Hz, $C_3$-H), 7.20-7.48 (m, 3H, Ar-H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 10.0, 10.9, 61.8, 62.9, 114.0, 127.9, 128.9, 133.2, 134.5, 135.0, 140.0, 157.9, 165.5, 166.7; ESI-MS: *m/z* 345 $[M + H]^+$. Anal. Calcd for $C_{14}H_{11}Cl_3N_2O_2$: C, 48.65; H, 3.21; N, 8.11. Found: C, 48.66; H, 3.19; N, 8.09%.

**3-Chloro-4-(3,4-dimethoxyphenyl)-1-(3,5-dimethylisoxazol-4-yl)azetidin-2-one, 4e**: m.p. 122-23°C. Yield 70%. IR (KBr): 1711 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.02 (s, 3H, isoxazole-$CH_3$), 2.09 (s, 3H, isoxazole-$CH_3$), 3.81(s, 6H, $(OCH_3)_2$) , 5.13 (d, 1H, $J$ = 5.4 Hz, $C_4$-H), 5.31 (d, 1H, $J$ = 5.4 Hz, $C_3$-H), 6.78-6.92 (m, 3H, Ar-H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 10.2, 10.8, 58.6, 59.2, 62.0, 62.9, 113.0, 114.1, 116.0, 122.7, 139.8, 150.2, 150.9, 158.2, 165.0, 166.8; ESI-MS: *m/z* 337 $[M + H]^+$. Anal. Calcd for $C_{16}H_{17}ClN_2O_4$: C, 57.06; H, 5.09; N, 8.32. Found: C, 57.05; H, 5.07; N, 8.31%.

**3-Chloro-4-(3-methoxyphenyl)-1-(3,5-dimethylisoxazol-4-yl)azetidin-2-one, 4f**: m.p. 104-105°C. Yield 70%. IR (KBr): 1712 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.05 (s, 3H, isoxazole-$CH_3$), 2.19 (s, 3H, isoxazole-$CH_3$), 3.78 (s, 3H, $OCH_3$), 5.21 (d, 1H, $J$ = 5.4 Hz, $C_4$-H), 5.39 (d, 1H, $J$ = 5.4 Hz, $C_3$-H), 6.68 (s, 1H, Ar-H), 6.82-7.21 (m, 3H, Ar-H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 10.0, 10.9, 55.9, 61.0, 62.9, 112.8, 113.0, 114.2, 121.0, 129.2, 138.0, 156.0, 158.9, 165.2, 166.2; ESI-MS: *m/z* 307 $[M + H]^+$. Anal. Calcd for $C_{15}H_{15}ClN_2O_3$: C, 58.73; H, 4.93; N, 9.13. Found: C, 58.76; H, 4.94; N, 9.14%.

**4-(3-Bromophenyl)-3-chloro-1-(3,5-dimethylisoxazol-4-yl)azetidin-2-one, 4g**: m.p. 99-100°C. Yield 70%. IR (KBr): 1710 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.00 (s, 3H, isoxazole-$CH_3$), 2.11 (s, 3H, isoxazole-$CH_3$), 5.20 (d, 1H, $J$ = 5.4 Hz, $C_4$-H), 5.38 (d, 1H, $J$ = 5.4 Hz, $C_3$-H); 7.22-7.68 (m, 4H, Ar-H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 9.9, 11.0, 61.9, 62.1, 114.5, 121.8, 125.6, 129.3, 130.5, 131.9, 147.1, 157.9, 165.5, 167.1; ESI-MS: *m/z* 355 $[M + H]^+$. Anal. Calcd for $C_{14}H_{12}BrClN_2O_2$: C, 47.28; H, 3.40; N, 7.88. Found: C, 47.30; H, 3.41; N, 7.89%.

**3-Chloro-1-(3,5-dimethylisoxazol-4-yl)-4-(thiophen-2-yl)azetidin-2-one, 4h**: m.p. 152-53°C. Yield 69%. IR (KBr): 1712 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.05 (s, 3H, isoxazole-$CH_3$), 2.19 (s, 3H, isoxazole-$CH_3$), 5.21 (d, 1H, $J$ = 5.4 Hz, $C_4$-H), 5.39 (d, 1H, $J$ = 5.4 Hz, $C_3$-H), 6.82-7.21 (m, 3H, Ar-H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 10.1, 10.8, 61.2, 62.5, 113.9, 122.9, 126.8, 127.4, 128.5, 158.0, 164.5, 166.7; ESI-MS: *m/z* 283 $[M + H]^+$. Anal. Calcd for $C_{12}H_{11}ClN_2O_2S$: C, 50.97; H, 3.92; N, 9.91. Found: C, 50.95; H, 3.90; N, 9.90%.

**3-Chloro-4-(furan-2-yl)-1-(3,5-dimethylisoxazol-4-yl)azetidin-2-one, 4i**: m.p. 142-43°C. Yield 68%. IR (KBr): 1704 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.08 (s, 3H, isoxazole-$CH_3$), 2.18 (s, 3H, isoxazole-$CH_3$), 5.21 (d, 1H, $J$ = 5.4 Hz, $C_4$-H), 5.38 (d, 1H, $J$ = 5.4 Hz, $C_3$-H), 7.42-7.65 (m, 3H, Ar-H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 10.0, 10.8, 61.0, 62.2, 110.0, 112.2, 114.3, 140.6, 148.9, 157.6, 164.2, 166.0;ESI-MS: *m/z* 267 $[M + H]^+$. Anal. Calcd for

$C_{12}H_{11}ClN_2O_3$: C, 54.05; H, 4.16; N, 10.50. Found: C, 54.07; H, 4.17; N, 10.51%.

## QSRT studies

For all the synthesized compounds **4a-i** QSRT parameters *viz*., physico chemical properties, ADME, and toxicity parameters are calculated by using Chemsketch ACD-Lab online software[31].

## Antibacterial activity

The antibacterial activity was done by broth dilution method[32] and expressed as minimum inhibitory concentration. The ready made nutrient broth medium (Himedia, 24 g) was suspended in distilled water (100 mL) and heated to boiling until it dissolved completely. The medium and test tubes were autoclaved at pressure of 15 lb/in$^2$ for 20 min. A set of sterilized test tubes with nutrient broth medium was capped with cotton plugs. The test compounds **4a-i**were dissolved in suitable solvent (acetone) and concentration of 100 µg/mL of test compound was added in the first test tube, which was serially diluted. A fixed volume of 0.5 mL overnight culture was added in all test tubes and were incubated at 37°C for 24 h. After 24 h, these tubes were measured for turbidity. Bacterial strains used for the present investigation are *Bacillus subtilis* (*Bs*), *Bacillus sphaericus* (*Bsp*), *Staphylococcus aureus* (*Sa*), *Pseudomonas aeruginosa* (*Pa*), *Klebsiella aerogenes* (*Ka*), and *Chromobacterium violaceum* (*Cv*). *Ciprofloxacin* was used as standard drug for comparison.

## Conclusion

In conclusion, we report the synthesis of new isoxazolyl azetidin-2-ones using inexpensive and commercially available materials with potent antibacterial properties. The newly synthesized compounds **4a-i** have been studied for their QSRT, and evaluated for their antibacterial activity. QSAR studies revealed that compounds **4b, 4c** and **4d** may be bioactive. Antibacterial studies also indicated that, among all the tested compounds **4a-i**, compounds **4b, 4c** and **4d** exhibit potential antibacterial activity which are in accordance with QSRT studies.

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