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Original article

Synthesis, biological evaluation of new oxazolidino-sulfonamides as potential antimicrobial agents

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ABSTRACT

A number of linezolid-like oxazolidino-sulfonamides (**7a**–**y** and **8a**–**b**) were designed and synthesized with a view to develop antimicrobial agents with improved properties. Most of the synthesized compounds showed good to moderate activity against a panel of standard Gram-positive and Gram-negative bacteria and fungal strains. The compounds **7i** and **7v** exhibited significant activity, with a MIC value of 2.0–6.0 μg/mL against a panel of Gram-positive and Gram-negative bacteria. These compounds also showed activity against *Candida albicans*, with a MIC value of 4.0 μg/mL. A correlation of the antimicrobial activity with calculated lipophilicity values (*C* log *P*) is also presented.

1. Introduction

The emergence of antibiotic resistance has posed a serious threat to the well-being of mankind [1,2]. Infections caused by drug resistant Gram-positive bacteria cause serious health problems and can be fatal at times. Methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-resistant coagulase negative *Staphylococci* (MR-CNS), penicillin-resistant *Streptococcus pneumoniae* (PRSP) and vancomycin-resistant *Enterococcus* (VRE) are a few organisms that have developed multidrug resistance [3–5]. Linezolid [6,7] **1** is the first and only oxazolidinone drug which was approved by FDA in the year 2000 for the treatment of multidrug resistant Gram-positive bacterial infections. Within a short span of its launch, linezolid-resistant strains of *S. aureus* and *Enterococcus faecium* [9,10] began to emerge. There is an urgent necessity for newer and improved antibiotics with broad antimicrobial spectrum that are also active against linezolid-resistant strains. Numerous efforts have been carried out to improve the potency and the antimicrobial spectrum of this drug [11–15]. Some research groups have modified or replaced the C-ring of the oxazolidinone that resulted in considerable improvement in the potency of oxazolidinones [16–20]. So many interesting reviews have been published by different groups on oxazolidinone antibacterial research [16,21–27].

The oxazolidino-sulfonamide derivative **2** [28] was designed and synthesized (Fig. 1) as a part of our previous studies directed at the development of new class of antibiotics to counter drug-resistant microbes [28–30]. In continuation of these efforts we report the design, synthesis and antimicrobial evaluation of a number of oxazolidino-sulfonamides (**7a**–**y** and **8a**–**b**). In addition, attempts have also been made to correlate antimicrobial activity to physicochemical properties, such as, lipophilicity (calculated as the *C* log *P* values) of the compounds.

2. Chemistry

The synthesis of the target compounds (**7a**–**y** and **8a**–**b**) was carried out as outlined in Scheme 1 from the chiral azide derivatives **5a**–**c**, which in turn was prepared in good yield as described previously [7,8]. The structures of target compounds are listed in Table 1. Further chemical transformation of **5a**–**c** to **6a**–**c** involved the reduction of azide group to afford the corresponding chiral amines [7,8]. Subsequently, the amines **6a**–**c** were treated with commercially available aryl/heteroaryl sulfonyl chlorides in the presence of triethylamine to furnish the corresponding oxazolidinone-sulfonamide derivatives **7a**–**y**. Deprotection of the *tert*-butoxycarbonyl group on the piperazine N-4-position of the compounds **7x**–**y**, carried out by using trifluoroacetic acid in CH_2Cl_2, generated the piperazine derivative **8a**–**b**.

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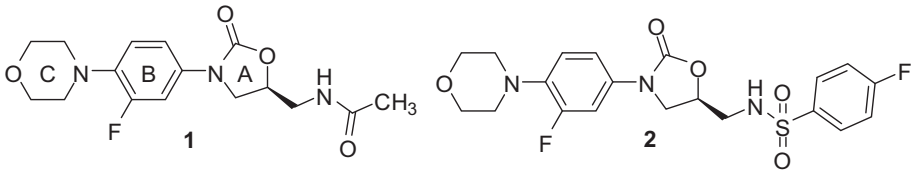


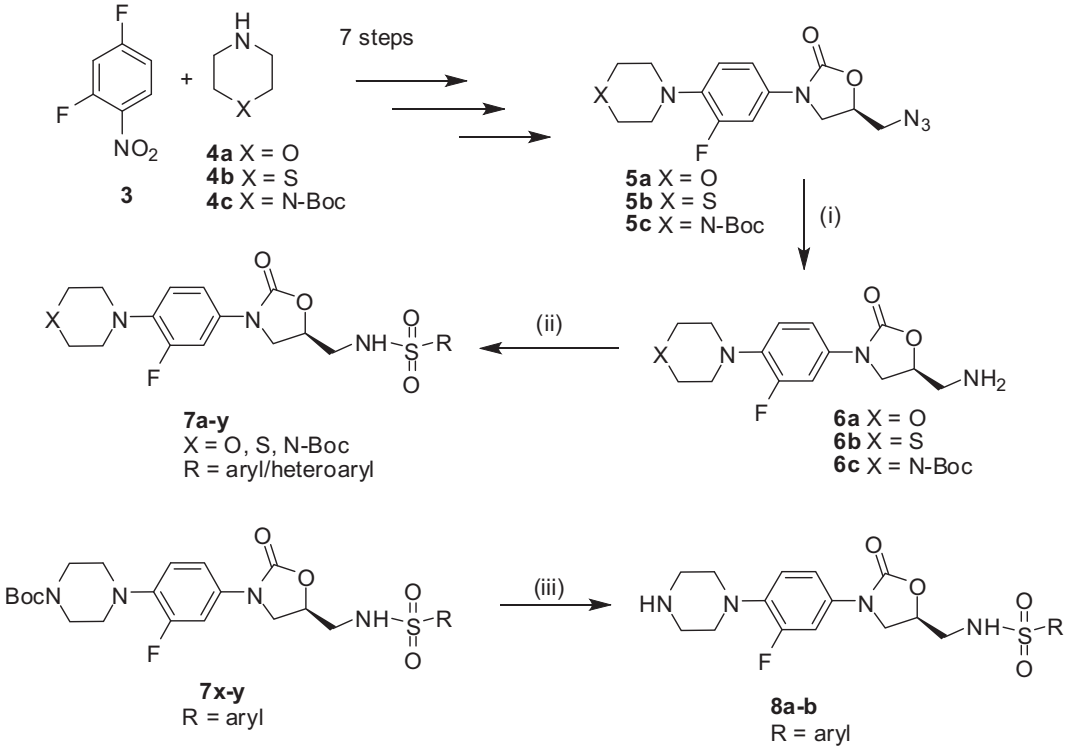
Fig. 1. Chemical structures of linezolid **1** and lead molecule **2**.

3. Results and discussion

The newly synthesized oxazolidino-sulfonamides (**7a**–**y** and **8a**–**b**) were evaluated for their antimicrobial activity against a panel of standard Gram-positive bacteria like *Bacillus subtilis* (MTCC 121), *Staphylococcus MLS-16* MTCC 2940, *Micrococus luteus* MTCC 2470 and *S. aureus* MTCC 96, as well as Gram-negative bacteria, *Escherichia coli* (MTCC 739), *Pseudomonas aeruginosa* MTCC 2453 and *Klebsiella planticola* MTCC 530. Additionally, the antifungal activity was also evaluated against *Candida albicans* MTCC 3017. The minimum inhibitory concentrations (MICs, μg/mL) determined by the agar dilution method on Mueller-Hinton (HM) agar for these compounds are summarized in Table 2.

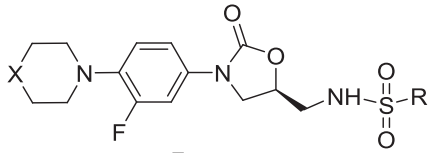
The results illustrate that most of these compounds show significant antimicrobial activity against the tested strains (MIC values ranging from 2.0 to 8.0 μg/mL) except *E. coli* MTCC 739 and *K. planticola* MTCC 530 (Table 2). Interestingly, compound **2**, which had shown good activity against *Mycobacterium tuberculosis* $H_{37}Rv$ [28], was not active against the above mentioned strains. Compound **7v** showed excellent activity against *B. subtilis* MTCC 121 (2.0 μg/mL), *Staphylococcus MLS-16* MTCC 2940 (4.0 μg/mL), *S. aureus* MTCC 96 (4.0 μg/mL), *P. aeruginosa* MTCC 2453 (4.0 μg/mL) and *C. albicans* MTCC 3017 (4.0 μg/mL). **7l** showed very good activity against all the tested organisms *B. subtilis* MTCC 121 (4.0 μg/mL), *Staphylococcus MLS-16* MTCC 2940 (4.0 μg/mL), *P. aeruginosa* MTCC 2453 (4.0 μg/mL), *S. aureus* MTCC 96 (4.0 μg/mL) and *C. albicans* MTCC 3017 (4.0 μg/mL). The active compounds **7i**, **7v**, **8a** and **8b** showed very good inhibitory zone at 20 μg/mL concentration when compared to standard compounds such as, linezolid and fluconazole (Table 3). However, when the new compounds (**7a**–**y** and **8a**–**b**) were evaluated for their potency against *M. tuberculosis* $H_{37}Rv$, no significant activity was observed.

The structure activity relationship (SAR) analysis reveals that the compounds having electron-withdrawing groups like F,–$COCH_3$ and CF_3 (**7b**, **7c**, **7l**, **8a** and **8b**) on aryl ring of sulfonamides can confer significant antimicrobial activity. This effect is more pronounced when the electron withdrawing substituent is at the 4-position of the aryl sulfonamide unit. Compounds possessing chlorinated aryl rings (**7a** and **7k**) showed only moderate levels of activity against all the tested strains. The oxazolidinone-sulfonamides with unprotected nitrogen on the piperazine ring (**8a**–**b**) exhibited better antibacterial activity than the corresponding *N*-Boc protected compounds (**7x**–**y**). The phenyl ring of compound **2** was replaced with a variety of heterocyclic rings (**7e**–**g**, **7i**, **7r**–**t** and **7v**). Among these compounds, the derivatives **7i** and **7v** where the benzene ring of sulphonamide was replaced by a thiophene unit, displayed significant increase in activity.

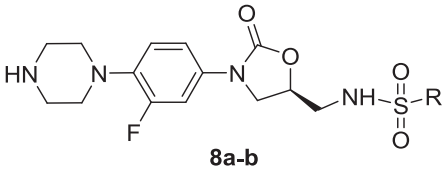


Scheme 1. Synthetic route of oxazolidino-sulfonamides (**7a**–**y** and **8a**–**b**): Reagents & conditions: (i) Pd/C, ethanol, H_2, 4 h; (ii) aryl/heteroaryl sulfonyl chlorides, TEA, THF, rt, 1 h; (iii) TFA, dry CH_2Cl_2, 0 °C-rt, 1 h.

Table 1
Structures of compounds (**7a**–**y** and **8a**–**b**).



7a-y



8a-b

Compd	X	R	M. formula	M. wt	*C* log *P*
2	O	4-F–C_6H_4	$C_{20}H_{21}F_2N_3O_5S$	453.4	2.39
7a	O	3-Cl–C_6H_4	$C_{20}H_{21}ClFN_3O_5S$	469.9	2.96
7b	O	4-$COCH_3$–C_6H_4	$C_{22}H_{24}FN_3O_6S$	477.5	2.03
7c	O	3-Cl,4-F–C_6H_3	$C_{20}H_{20}ClF_2N_3O_5S$	487.9	3.21
7d	O	4-OC_6H_5–C_6H_4	$C_{26}H_{26}FN_3O_6S$	527.5	4.04
7e	O	2-Acetamido-4-methyl-5-thiazolyl-	$C_{20}H_{24}FN_5O_6S_2$	513.5	1.81
7f	O	8-Quinolinyl-	$C_{23}H_{23}FN_4O_5S$	486.5	2.64
7g	O	4-(Phenylsulfonyl)-2-thiophenyl-	$C_{24}H_{24}FN_3O_7S_3$	581.6	2.93
7h	O	4-CF_3–C_6H_4	$C_{21}H_{21}F_4N_3O_5S$	503.4	3.35
7i	O	2-Thiophenyl-	$C_{18}H_{20}FN_3O_5S_2$	441.5	1.86
7j	O	2-Cl,4-F–C_6H_3	$C_{20}H_{20}ClF_2N_3O_5S$	487.9	2.91
7k	O	3,5-Cl_2–C_6H_3	$C_{20}H_{20}Cl_2FN_3O_5S$	504.3	3.78
7l	O	2,3,4-$F_3C_6H_2$	$C_{20}H_{19}F_4N_3O_5S$	489.4	2.68
7m	O	3,4-F_2–C_6H_3	$C_{20}H_{20}F_3N_3O_5S$	471.4	2.57
7n	S	3-Cl–C_6H_4	$C_{20}H_{21}ClFN_3O_4S_2$	485.9	3.79
7o	S	4-$COCH_3$–C_6H_4	$C_{22}H_{24}FN_3O_5S_2$	493.5	2.86
7p	S	3-Cl,4-F–C_6H_3	$C_{20}H_{20}ClF_2N_3O_4S_2$	503.9	4.04
7q	S	4-OC_6H_5–C_6H_4	$C_{26}H_{26}FN_3O_5S_2$	543.6	4.87
7r	S	2-Acetamido-4-methyl-5-thiazolyl-	$C_{20}H_{24}FN_5O_5S_3$	529.6	2.64
7s	S	8-Quinolinyl-	$C_{23}H_{23}FN_4O_4S_2$	502.5	3.47
7t	S	4-(Phenylsulfonyl)-2-thiophenyl-	$C_{24}H_{24}FN_3O_6S_4$	597.7	3.77
7u	S	4-CF_3–C_6H_4	$C_{21}H_{21}F_4N_3O_4S_2$	519.5	4.19
7v	S	2-Thiophenyl-	$C_{18}H_{20}FN_3O_4S_3$	457.5	2.69
7w	S	4-F–C_6H_4	$C_{20}H_{21}F_2N_3O_4S_2$	469.5	3.22
7x	N-Boc	4-CF_3–C_6H_4	$C_{26}H_{30}F_4N_4O_6S$	602.6	5.45
7y	N-Boc	4-F–C_6H_4	$C_{25}H_{30}F_2N_4O_6S$	552.5	4.48
8a	NH	4-CF_3–C_6H_4	$C_{21}H_{22}F_4N_4O_4S$	502.4	3.34
8b	NH	4-F–C_6H_4	$C_{20}H_{22}F_2N_4O_4S$	452.4	2.37

In an attempt to correlate the biological activity with calculated physical properties of the synthesized compounds, a lipophilicity estimation using the software Chem Draw version 10.0 was carried out. Lipophilicity values are represented by *C* log *P* values listed in Table 1, as obtained from Chem Draw 10.0 [31]. As a rule of thumb for a drug like molecule, the *C* log *P* value must be lower than 5 to by-pass the cell barrier. Interestingly, the MIC values of the active compounds seems to correlate to some extent with the hydrophobicity (*C* log *P*), **7d** (X = O, R = –C_6H_4(4-OC_6H_5), *C* log *P*: 4.04; MIC: 4.0 μg/mL against *Staphylococcus MLS-16* MTCC 2940 and *S. aureus* MTCC 96), **7i** (X = O, R = 2-thiophenyl-, *C* log *P*: 1.86; MIC: 4.0 μg/mL against *B. subtilis* MTCC 121, *Staphylococcus MLS-16* MTCC 2940, *P. aeruginosa* MTCC 2453, *S. aureus* MTCC 96 and *C. albicans* MTCC 3017) and **7v** (X = O, R = 2-thiophenyl-, *C* log *P*: 2.69; MIC: 2.0 μg/mL against *B. subtilis* MTCC 121 and 4.0 μg/mL against *Staphylococcus MLS-16* MTCC 2940, *P. aeruginosa* MTCC 2453, *S. aureus* MTCC 96 and *C. albicans* MTCC 3017).

4. Conclusion

In conclusion, a number of newly synthesized oxazolidinosulfonamide derivatives (**7a**–**y** and **8a**–**b**) demonstrated significant *in vitro* antimicrobial activity comparable to reference compounds, namely, linezolid and fluconazole. Incorporation of electron withdrawing substituents on the 4-position of the aryl ring of the sulphonamide subunit is beneficial. Replacement of the phenyl ring of the aryl sulphonamide moiety by a thiophene unit also improved the antimicrobial activity.

5. Experimental section

5.1. Characterization

All chemicals were purchased from Lancaster (Alfa Aesar, Johnson Matthey Co, Ward Hill, MA, USA), Sigma–Aldrich (St Louis, MO, USA) and Spectrochem Pvt Ltd (Mumbai, India). Reactions were monitored by TLC, performed on silica gel glass plates containing 60 F-254 and visualization on TLC was achieved by UV light or iodine indicator. Column chromatography was performed with Merck (Navi Mumbai, India) 60–120 mesh silica gel. ^{1}H NMR spectra were recorded on Avance (300 MHz); Bruker, Fallanden, Switzerland instruments. Chemical shifts (δ) were reported in ppm, downfield from internal TMS standard. Spectral patterns were designated as s, singlet; d, doublet; dd, double doublet; t, triplet; bs, broad singlet; m, multiplet. ESI spectra were recorded on Micro mass, Quattro LC using ESI+ software with capillary voltage of 3.98 kV and ESI mode positive ion trap detector. High-resolution mass spectra (HRMS) were recorded on QSTAR XL Hybrid MS/MS mass spectrometer. IR spectra were recorded on an FT-IR spectrometer and only major peaks are reported in cm^{-1}.

5.1.1. (R)-3-Chloro-N-((3-(3-fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-benz-enesulfonamide (**7a**)

The target compound **7a** was obtained by reacting **6a** (295 mg, 1 mmol) with 3-Chlorobenzenesulfonyl chloride (253 mg, 1.2 mmol), and triethylamine (50 mg, 2 mmol) in dry CH_2Cl_2 (15 mL). After stirring the reaction mixture for 3 h, the reaction

Table 2
Antibacterial and antifungal activity of the compounds (**7a**–**y** and **8a**–**b**) against several standard strains (MICs, μg/mL).

Compd	*B. s*[a]	*S. M*[b]	*M. l*[c]	*S. a*[d]	*M. t*[e]	*E. c*[f]	*P. a*[g]	*K. p*[h]	*C. a*[i]
2	10.0	10.0	—[j]	NT	1.0	NT	10.0	NT	10.0
7a	6.0	6.0	8.0	6.0	—[k]	—[j]	—[j]	—[j]	8.0
7b	6.0	6.0	6.0	6.0	—[k]	—[j]	—[j]	—[j]	6.0
7c	6.0	6.0	6.0	6.0	—[k]	—[j]	—[j]	—[j]	6.0
7d	8.0	**4.0**	8.0	**4.0**	—[k]	—[j]	—[j]	—[j]	6.0
7e	8.0	20.0	—[j]	20.0	—[k]	—[j]	8.0	—[j]	20.0
7f	8.0	10.0	8.0	10.0	—[k]	—[j]	6.0	—[j]	20.0
7g	—[j]	—[j]	—[j]	—[j]	—[k]	—[j]	—[j]	—[j]	—[j]
7h	8.0	10.0	8.0	10.0	—[k]	—[j]	8.0	—[j]	20.0
7i	**4.0**	**4.0**	6.0	**4.0**	—[k]	—[j]	**4.0**	—[j]	**4.0**
7j	8.0	20.0	—[j]	20.0	—[k]	—[j]	—[j]	—[j]	—[j]
7k	8.0	8.0	—[j]	8.0	—[k]	—[j]	40.0	—[j]	8.0
7l	6.0	6.0	—[j]	6.0	—[k]	—[j]	8.0	—[j]	6.0
7m	10.0	10.0	—[j]	NT	—[k]	NT	10.0	NT	10.0
7n	20.0	—[j]	—[j]	—[j]	—[k]	—[j]	10.0	—[j]	—[j]
7o	10.0	8.0	—[j]	8.0	—[k]	—[j]	—[j]	—[j]	20.0
7p	10.0	8.0	—[j]	8.0	—[k]	—[j]	—[j]	—[j]	20.0
7q	—[j]	8.0	—[j]	8.0	—[k]	—[j]	20.0	—[j]	20.0
7r	10.0	8.0	—[j]	8.0	—[k]	—[j]	8.0	—[j]	8.0
7s	8.0	6.0	—[j]	6.0	—[k]	—[j]	8.0	—[j]	8.0
7t	8.0	6.0	—[j]	6.0	—[k]	—[j]	8.0	—[j]	8.0
7u	10.0	8.0	—[j]	8.0	—[k]	—[j]	8.0	—[j]	8.0
7v	**2.0**	**4.0**	6.0	**4.0**	—[k]	—[j]	**4.0**	—[j]	**4.0**
7w	8.0	10.0	10.0	10.0	—[k]	—[j]	10.0	—[j]	10.0
7x	8.0	10.0	20.0	10.0	—[k]	—[j]	10.0	—[j]	20.0
7y	20.0	10.0	10.0	10.0	—[k]	—[j]	20.0	—[j]	10.0
8a	8.0	6.0	8.0	6.0	NT	—[j]	8.0	—[j]	10.0
8b	10.0	8.0	**4.0**	8.0	NT	—[j]	**4.0**	—[j]	8.0
LZ	1.5	1.5	1.0	1.5		–	–	–	–
FLZ	–	–	–	–		–	–	–	1.0

The tests were performed in duplicate and repeated thrice. NT (not tested); LZ (linezolid); FLZ (fluconazole).
[a] *Bacillus subtilis* MTCC 121.
[b] *Staphylococcus* MLS-16 MTCC 2940.
[c] *Micrococcus luteus* MTCC 2470.
[d] *Staphylococcus aureus* MTCC 96.
[e] *Mycobacterium tuberculosis* $H_{37}Rv$.
[f] *Escherichia coli* MTCC 739.
[g] *Pseudomonas aeruginosa* MTCC 2453.
[h] *Klebsiella planticola* MTCC 530.
[i] *Candida albicans* MTCC 3017.
[j] Not active at 80 μg/mL.
[k] Not active at 32 μg/mL.
The bold signifies low MIC values.

mixture was poured on to crushed ice (5 g) and the reaction mixture extracted with CH_2Cl_2 (2 × 10 mL) and purified by column chromatography with chloroform/methanol (50/1) as eluent to afford final product as white solid (Yield 281 mg, 60%), m.p: 180–182 °C. IR (KBr pellet, cm^{-1}): 3320, 2978, 2834, 1746, 1616, 1574, 1414, 1325, 1159, 814. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.85 (s, 1H, Ar–*H*), 7.75 (d, 1H, *J* = 7.7 Hz Ar–*H*), 7.53 (t, 1H, *J* = 7.9 Hz, Ar–*H*), 7.47 (t, 1H, *J* = 7.7 Hz, Ar–*H*), 7.07 (dd, 1H, *J* = 15.0, 2.4 Hz, oxa-Ar–*H*), 7.07 (dd, 1H, *J* = 9.0 Hz, oxa-Ar–*H*), 6.86 (t, 1H, *J* = 9.0 Hz, oxa-Ar–*H*), 5.85 (bs, 1H, –N*H*), 4.81 (m, 1H, oxa-C*H*–), 4.05–3.90 (m, 2H, oxa-CH_2–), 3.87 (t, 4H, *J* = 4.5 Hz, morpholin–OCH_2–), 3.42–3.20 (m, 2H, oxa-CH_2–), 3.05 (t, 4H, *J* = 4.5 Hz, morpholin–CH_2–); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.7, 153.5, 141.5, 135.6, 134.4, 131.9, 129.9, 126.3, 124.4, 118.2, 113.3, 106.9, 106.7, 70.5, 66.2, 50.4, 46.6, 44.6; ESIMS: *m*/*z* 470 $(M + H)^+$; HRMS (ESI) *m*/*z* calcd. for $C_{20}H_{22}ClFN_3O_5S$ $(M + H)^+$, 470.0953; found, 470.0941.

Table 3
Preliminary antibacterial and antifungal activity of oxazolidinone-sulfonamides (zone of inhibition in mm) at 20 μg/mL.

Compd	*B. s*[a]	*S. M*[b]	*M. l*[c]	*S. a*[d]	*E. c*[e]	*P. a*[f]	*K. p*[g]	*C. a*[h]
7i	20	18	15	20	NT	19	NT	18
7w	23	17	14	18	NT	17	NT	16
8a	16	15	13	17	NT	16	NT	15
8b	20	17	14	17	NT	18	NT	16
LZ	10	18	20	28	NT	12	NT	–
FLZ	–	–	–	–	–	–	–	20

The tests were performed in duplicate and repeated thrice; NT (not tested); LZ (linezolid); FLZ (fluconazole).
[a] *Bacillus subtilis* MTCC 121.
[b] *Staphylococcus* MLS-16 MTCC 2940.
[c] *Micrococcus luteus* MTCC 2470.
[d] *Staphylococcus aureus* MTCC 96.
[e] *Escherichia coli* MTCC 739.
[f] *Pseudomonas aeruginosa* MTCC 2453.
[g] *Klebsiella planticola* MTCC 530.
[h] *Candida albicans* MTCC 3017.

5.1.2. (R)-4-Acetyl-N-((3-(3-fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-benzenesulfonamide (**7b**)

The compound **7b** was prepared according to the above described method using **6a** (295 mg, 1 mmol) and 4-Acetylbenzenesulfonyl chloride (262 mg, 1.2 mmol) with yield 262 mg (55%), m.p: 193–195 °C; IR (KBr pellet, cm^{-1}): 3290, 2918, 2849, 1749, 1687, 1518, 1380, 1327, 1158, 831; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.41–8.36 (m, 2H, Ar–*H*), 7.51–7.46 (dd, 1H, *J* = 15.0, 2.6 Hz, oxa-Ar–*H*), 7.34–7.31 (d, 2H, *J* = 8.3 Hz, Ar–*H*), 7.07 (dd, 1H, *J* = 9.0 Hz, oxa-Ar–*H*), 6.91 (t, 1H, *J* = 9.0 Hz, oxa-Ar–*H*), 6.52 (bs, 1H, –N*H*), 4.76 (m, 1H, oxa-C*H*–), 4.02 (t, 1H, *J* = 9.0 Hz oxa-CH*H*–), 3.87 (t, 1H, *J* = 9.0 Hz oxa-C*H*H–), 3.82 (t, 4H, *J* = 4.5 Hz, morpholin–OCH_2–), 3.59 (m, 2H, oxa-CH_2–), 3.13 (t, 4H, *J* = 4.5 Hz, morpholin–CH_2–), 3.01 (s, 3H, –COCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 196.0, 156.9, 153.8, 144.0, 139.6, 133.1, 128.7, 126.9, 120.7, 113.7, 107.3, 107.0, 70.8, 66.2, 53.0, 47.0, 44.9, 27.5; ESIMS: *m*/*z* 478 $(M + H)^+$; HRMS (ESI) *m*/*z* calcd. for $C_{22}H_{25}FN_3O_6S$ $(M + H)^+$, 478.1448; found, 478.1453.

5.1.3. (R)-3-Chloro-4-fluoro-N-((3-(3-fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)benzenesulfonamide (**7c**)

The compound **7c** was prepared according to the above described method using **6a** (295 mg, 1 mmol) and 3-Chloro-4-fluorobenzenesulfonyl chloride (275 mg, 1.2 mmol) with yield 317 mg (65%) m.p: 150–151 °C; IR (KBr pellet, cm^{-1}): 3292, 2914, 2839, 1741, 1519, 1332, 1149, 826; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.78 (t, 1H, *J* = 6.5 Hz, Ar–*H*), 7.63 (t, 1H, *J* = 6.5 Hz, Ar–*H*), 7.42–7.37 (dd, 1H, *J* = 15.0, 2.6 Hz, oxa-Ar–*H*), 7.22 (t, 1H, *J* = 7.3 Hz, Ar–*H*), 7.07 (dd, 1H, *J* = 9.0, 1.8 Hz, oxa-Ar–*H*), 6.91 (t, 1H, *J* = 9.0 Hz, oxa-Ar–*H*), 5.70 (bs, 1H, –N*H*), 4.82–4.72 (m, 1H, oxa-C*H*–), 4.04 (t, 1H, *J* = 9.0 Hz, oxa-CH*H*–), 3.93 (t, 1H, *J* = 9.0 Hz, oxa-CH*H*–), 3.88–3.85 (t, 4H, *J* = 4.5 Hz, morpholin–OCH_2–), 3.56–3.35 (m, 2H, oxa-CH_2–), 3.05 (t, 4H, *J* = 4.5 Hz, morpholin–CH_2–); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.0, 153.9, 152.1, 135.1, 133.2, 132.0, 128.6, 126.5, 123.4, 120.2, 118.6, 112.1, 105.3, 104.9, 70.5, 66.2, 50.4, 46.6, 44.6; ESIMS: *m*/*z* 488 $(M + H)^+$; HRMS (ESI) *m*/*z* calcd. for $C_{20}H_{21}ClF_2N_3O_5S$ $(M + H)^+$, 488.0859; found, 488.0840.

5.1.4. (R)-N-((3-(3-Fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-4-phenoxy-benzenesulfonamide (**7d**)

The compound **7d** was prepared according to the above described method using **6a** (295 mg, 1 mmol) and 4-Phenoxybenzenesulfonyl chloride (322 mg, 1.2 mmol) with yield 358 mg (68%), m.p: 193–194 °C; IR (KBr pellet, cm^{-1}): 3338, 2910, 2838, 2360, 1736, 1584, 1518, 1487, 1154, 835; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.77 (d, 2H, *J* = 8.1 Hz, Ar–*H*), 7.44 (m, 2H, Ar–*H*), 7.40 (dd, 1H, *J* = 15.0, 2.6 Hz, oxa-Ar–*H*), 7.21 (m, 1H, Ar–*H*), 7.08–7.01 (m, 3H, Ar–*H* and oxa-Ar–*H*), 6.91 (t, 1H, *J* = 9.0 Hz, oxa-Ar–*H*), 5.35 (bs, 1H, –N*H*), 4.79–4.71 (m, 1H, oxa-C*H*–), 4.02 (t, 1H, *J* = 9.0 Hz, oxa-CH*H*–), 3.92 (t, 1H, *J* = 9.0 Hz, oxa-CH*H*–), 3.86 (t, 4H, *J* = 4.5 Hz, morpholin–OCH_2–), 3.39–3.20 (m, 2H, oxa-CH_2–), 3.05 (t, 4H, *J* = 4.5 Hz, morpholin–CH_2–); ^{13}C NMR ($CDCl_3$, 75 MHz):

δ 161.7, 156.5, 154.9, 154.6, 154.1, 137.6, 134.5, 132.8, 130.1, 129.1, 125.0, 120.2, 117.7, 113.9, 107.6, 107.4, 71.1, 66.2, 53.2, 47.2, 45.0; ESIMS: *m/z* 528 $(M + H)^+$; HRMS (ESI) *m/z* calcd. for $C_{26}H_{27}FN_3O_6S$ $(M + H)^+$, 528.1605; found, 528.1586.

5.1.5. (R)-N-(5-(N-((3-(3-Fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)sulfamoyl)-4-methylthiazol-2-yl) acetamide (**7e**)

The compound **7e** was prepared according to the above described method using **6a** (295 mg, 1 mmol) and 2-acetamido-4-methyl-1,3-thiazole-5-sulfonyl chloride (305 mg, 1.2 mmol) with yield 231 mg (45%), m.p: 200–201 °C; IR (KBr pellet, cm^{-1}): 3302, 3276, 2961, 2834, 2360, 1736, 1693, 1514, 1336, 1152, 859; ^1H NMR (DMSO-d_6, 300 MHz): δ 12.27 (s, 1H, −N*H*CO−), 8.21 (t, 1H, *J* = 6.5 Hz, Ar−*H*), 7.68 (s, 1H, thiophene−*H*), 7.47 (dd, 1H, *J* = 14.5, 2.4 Hz, oxa-Ar−*H*), 7.07 (dd, 1H, *J* = 9.0, 1.8 Hz, oxa-Ar−*H*), 6.95 (t, 1H, *J* = 9.0 Hz, oxa-Ar−*H*), 5.70 (bs, 1H, −NH), 4.77–4.69 (m, 1H, oxa-C*H*−), 4.02 (t, 1H, *J* = 9.0 Hz, oxa-CH*H*−), 3.94 (t, 1H, *J* = 9.0 Hz, oxa-CH*H*−), 3.82 (t, 4H, *J* = 4.5 Hz, morpholin−OCH_2−), 3.27–3.23 (m, 2H, oxa-CH_2−), 3.07 (t, 4H, *J* = 4.5 Hz, morpholin−CH_2−), 2.20 (s, 3H, −COCH_3), 2.05 (s, 3H, −CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.3, 155.3, 153.4, 142.3, 134.5, 132.8, 125.3, 124.4, 118.7, 112.9, 107.4, 71.9, 66.8, 50.8, 47.5, 41.8, 23.4, 12.5; ESIMS: *m/z* 514 $(M + H)^+$; HRMS (ESI) *m/z* calcd. for $C_{20}H_{25}FN_5O_6S_2$ $(M + H)^+$, 514.1230; found, 514.1253.

5.1.6. (R)-N-((3-(3-Fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)quinoline-8-sulfonamide (**7f**)

The compound **7f** was prepared according to the above described method using **6a** (295 mg, 1 mmol) and 8-quinolinesulfonyl chloride (273 mg, 1.2 mmol) with yield 243 mg (50%), m.p: 183–184 °C; IR (KBr pellet, cm^{-1}): 3306, 2854, 2360, 1733, 1516, 1320, 1116, 834; ^1H NMR (DMSO-d_6, 300 MHz): δ 9.06 (d, 1H, *J* = 3.7 Hz, quino-*H*), 8.38 (d, 1H, *J* = 6.0 Hz, quino-*H*), 8.23 (d, 1H, *J* = 8.3 Hz, quino-*H*), 8.01 (d, 1H, *J* = 8.3 Hz, quino-*H*), 7.59–7.55 (m, 1H, quino-*H*), 7.29 (dd, 1H, *J* = 14.6, 2.6 Hz, oxa-Ar−*H*), 6.89 (dd, 1H, *J* = 9.0, 1.8 Hz, oxa-Ar−*H*), 6.83 (t, 1H, *J* = 9.0 Hz, oxa-Ar−*H*), 4.74–4.66 (m, 1H, oxa-C*H*−), 3.97–3.95 (m, 2H, oxa-C*HH*−), 3.82 (t, 4H, *J* = 4.5 Hz, morpholin−OCH_2−), 3.27–3.24 (m, 2H, oxa-CH_2−), 3.02 (t, 4H, *J* = 4.5 Hz, morpholin−CH_2−); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 175.2, 151.6, 142.8, 137.0, 135.4, 133.6, 132.8, 132.4, 130.7, 130.4, 128.7, 125.6, 122.5, 121.1, 118.7, 113.8, 107.2, 70.9, 66.9, 50.9, 47.2, 45.3; ESIMS: *m/z* 487 $(M + H)^+$; HRMS (ESI) *m/z* calcd. for $C_{23}H_{24}FN_4O_5S$ $(M + H)^+$, 487.1446; found, 487.1448.

5.1.7. (R)-N-((3-(3-Fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-4-(phenylsulfonyl)thiophene-2-sulfonamide (**7g**)

The compound **7g** was prepared according to the above described method using **6a** (295 mg, 1 mmol) and 4-(phenylsulfonyl)thiophene-2-sulfonylchloride (387 mg, 1.2 mmol) with yield 232 mg (40%) m.p: 153–155 °C; IR (KBr pellet, cm^{-1}): 3306, 2901, 2360, 1760, 1733, 1516, 1336, 1143, 829; ^1H NMR (DMSO-d_6, 300 MHz): δ 8.57 (t, 1H, *J* = 5.3 Hz, Ar−*H*), 8.41 (d, 1H, *J* = 5.3 Hz, Ar−*H*), 7.97 (d, 2H, *J* = 7.3 Hz, Ar−*H*), 7.80 (s, 1H, Ar−*H*), 7.67 (t, 2H, *J* = 7.3 Hz, Ar−*H*), 7.59 (t, 2H, *J* = 7.3 Hz, Ar−*H*), 7.49 (d, 1H, *J* = 14.6, 2.4 Hz, oxa-Ar−*H*), 7.06 (d, 1H, *J* = 9.0 Hz, oxa-Ar−*H*), 6.94 (t, 1H, *J* = 9.0 Hz, oxa-Ar−*H*), 4.78–4.72 (m, 1H, oxa-C*H*−), 4.04 (t, 1H, *J* = 8.9 Hz, oxa-CH*H*−), 3.88 (t, 1H, *J* = 8.9 Hz, oxa-C*H*H−), 3.83 (t, 4H, *J* = 4.5 Hz, morpholin−OCH_2−), 3.34–3.32 (m, 2H, oxa-CH_2−), 3.08 (t, 4H, *J* = 4.5 Hz, morpholin−CH_2−); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 152.2, 151.7, 143.3, 140.2, 139.0, 135.3, 134.2, 132.3, 131.7, 128.0, 127.1, 125.8, 117.3, 112.3, 105.6, 105.2, 69.3, 64.9, 49.2, 45.4, 43.9; ESIMS: *m/z* 582 $(M + H)^+$; HRMS (ESI) *m/z* calcd. for $C_{24}H_{25}FN_3O_7S_3$ $(M + H)^+$, 582.0839; found, 582.0825.

5.1.8. (R)-N-((3-(3-Fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-4-(trifluoromethyl)benzenesulfonamide (**7h**)

The compound **7h** was prepared according to the above described method using **6a** (295 mg, 1 mmol) and 4-(trifluoromethyl)benzene-1-sulfonyl chloride (294 mg, 1.2 mmol) with yield 302 mg (60%), m.p: 143–144 °C; IR (KBr pellet, cm^{-1}): 3297, 2921, 2360, 1746, 1519, 1326, 1160, 834; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.99 (d, 2H, *J* = 8.7 Hz, Ar−*H*), 7.78 (d, 2H, *J* = 8.7 Hz, Ar−*H*), 7.39 (dd, 1H, *J* = 14.6, 2.4 Hz, oxa-Ar−*H*), 7.06 (d, 1H, *J* = 8.9 Hz, oxa-Ar−*H*), 6.90 (t, 1H, *J* = 8.9 Hz, oxa-Ar−*H*), 5.66 (bs, 1H, −N*H*), 4.77–4.72 (m, 1H, oxa-C*H*−), 4.02 (t, 1H, *J* = 8.9 Hz, oxa-CH*H*−), 3.90 (t, 1H, *J* = 8.9 Hz, oxa-C*H*H−), 3.86 (t, 4H, *J* = 4.5 Hz, morpholin−OCH_2−), 3.42–3.31 (m, 2H, oxa-CH_2−), 3.05 (t, 4H, *J* = 4.5 Hz, morpholin−CH_2−); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.7, 153.5, 135.6, 134.4, 131.9, 129.9, 126.3, 124.4, 119.6, 118.2, 113.3, 106.9, 106.7, 70.5, 66.2, 50.4, 46.6, 44.6; ESIMS: *m/z* 504 $(M + H)^+$; HRMS (ESI) *m/z* calcd. for $C_{21}H_{22}F_4N_3O_5S$ $(M + H)^+$, 504.1216; found, 504.1223.

5.1.9. (R)-N-((3-(3-Fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)thiophene-2-sulfonamide (**7i**)

The compound **7i** was prepared according to the above described method using **6a** (299 mg, 1 mmol) and 2-thiophenesulfonyl chloride (219 mg, 1.2 mmol) with yield 264 mg (60%) m.p: 140–142 °C; IR (KBr pellet, cm^{-1}): 3290, 2921, 2360, 1732, 1510, 1326, 1160, 831; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.62 (m, 2H, thiophene−*H*), 7.40 (dd, 1H, *J* = 14.6, 2.4 Hz, oxa-Ar−*H*), 7.11 (m, 1H, thiophene−*H*), 7.06 (d, 1H, *J* = 9.0 Hz, oxa-Ar−*H*), 6.91 (t, 1H, *J* = 9.0 Hz, oxa-Ar−*H*), 5.55 (bs, 1H, −N*H*), 4.79–4.74 (m, 1H, oxa-C*H*−), 4.02 (t, 1H, *J* = 8.9 Hz, oxa-CH*H*−), 3.93 (t, 1H, *J* = 8.9 Hz, oxa-C*H*H−), 3.86 (t, 4H, *J* = 4.5 Hz, morpholin−OCH_2−), 3.43–3.30 (m, 2H, oxa-CH_2−), 3.05 (t, 4H, *J* = 4.5 Hz, morpholin−CH_2−); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 156.5, 153.5, 135.6, 126.3, 126.2, 124.4, 118.2, 118.2, 113.3, 106.9, 106.7, 70.5, 66.2, 50.4, 46.6, 44.6; ESIMS: *m/z* 442 $(M + H)^+$; HRMS (ESI) *m/z* calcd. for $C_{18}H_{21}FN_3O_5S_2$ $(M + H)^+$, 442.0907; found, 442.0913.

5.1.10. (R)-2-Chloro-4-fluoro-N-((3-(3-fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)-methyl) benzenesulfonamide (**7j**)

The compound **7j** was prepared according to the above described method using **6a** (299 mg, 1 mmol) and 2-chloro-4-fluorobenzenesulfonyl chloride (275 mg, 1.2 mmol) with yield 297 mg (61%), m.p: 153–154 °C; IR (KBr pellet, cm^{-1}): 3328, 2901, 2360, 1736, 1519, 1239, 1164, 839; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.06 (d, 1H, *J* = 8.6, 5.6 Hz, Ar−*H*), 7.35 (dd, 1H, *J* = 14.6, 2.5 Hz, oxa-Ar−*H*), 7.21 (dd, 1H, *J* = 8.0, 2.5 Hz, Ar−*H*), 7.10 (td, 1H, *J* = 7.3, 2.4 Hz, Ar−*H*), 7.03 (t, 1H, *J* = 8.9 Hz, oxa-Ar−*H*), 6.86 (t, 1H, *J* = 8.9 Hz, oxa-Ar−*H*), 5.76 (bs, 1H, −N*H*), 4.73–4.65 (m, 1H, oxa-C*H*−), 3.98 (t, 1H, *J* = 8.9 Hz, oxa-CH*H*−), 3.86 (t, 1H, *J* = 8.9 Hz, oxa-C*H*H−), 3.83 (t, 4H, *J* = 4.5 Hz, morpholin−OCH_2−), 3.42–3.23 (m, 2H, oxa-CH_2−), 3.02 (t, 4H, *J* = 4.5 Hz, morpholin−CH_2−); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.9, 157.0, 153.8, 136.6, 133.3, 132.9, 132.5, 119.6, 119.2, 118.7, 114.7, 114.4, 113.9, 107.6, 107.2, 70.8, 66.9, 50.9, 47.1, 45.3; ESIMS: *m/z* 470 $(M + H)^+$; HRMS (ESI) *m/z* calcd. for $C_{20}H_{21}ClF_2N_3O_5S$ $(M + H)^+$, 488.0859; found, 488.0912.

5.1.11. (R)-3,5-Dichloro-N-((3-(3-fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-benzenesulfonamide (**7k**)

The compound **7k** was prepared according to the above described method using **6a** (295 mg, 1 mmol) and 3,5-dichlorobenzenesulfonyl chloride (295 mg, 1.2 mmol) with yield 317 mg (63%), m.p: 166–167 °C; IR (KBr pellet, cm^{-1}): 3328, 2910, 2361, 1736, 1516, 1240, 1164, 849; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.38 (bs, 1H, −N*H*), 7.76 (d, 2H, *J* = 1.7 Hz, Ar−*H*), 7.55 (t, 1H, *J* = 1.7 Hz, Ar−*H*), 7.46 (dd, 1H, *J* = 14.6, 2.5 Hz, oxa-Ar−*H*), 7.07

(dd, 1H, J = 9.0, 1.8 Hz, oxa-Ar–*H*), 6.91 (t, 1H, J = 9.0 Hz, oxa-Ar–*H*), 4.76–4.68 (m, 1H, oxa-C*H*–), 4.03 (t, 1H, J = 9.0 Hz, oxa-CH*H*–), 3.88 (t, 1H, J = 9.0 Hz, oxa-CH*H*–), 3.79 (t, 4H, J = 4.5 Hz, morpholin–OCH_2–), 3.26–3.18 (m, 2H, oxa-CH_2–), 3.01 (t, 4H, J = 4.5 Hz, morpholin–CH_2–); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.2, 153.1, 141.1, 136.7, 135.6, 128.7, 127.2, 125.8, 124.6, 123.1, 121.0, 119.6, 112.9, 71.9, 66.7, 50.9, 47.5, 42.5; ESIMS: m/z 504 $(M + H)^+$; HRMS (ESI) m/z calcd. for $C_{20}H_{21}Cl_2FN_3O_5S$ $(M + H)^+$, 504.0563; found, 504.0535.

5.1.12. (R)-2,3,4-Trifluoro-N-((3-(3-fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)benzenesulfonamide (**7l**)

The compound **7l** was prepared according to the above described method using **6a** (295 mg, 1 mmol) and 2,3,4-trifluorobenzenesulfonyl chloride (0.17 mL, 1.2 mmol) with yield 327 mg (67%), m.p: 144–145 °C; IR (KBr pellet, cm^{-1}): 3328, 2901, 2360, 1736, 1519, 1330, 1239, 1164, 839; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.74 (d, 1H, J = 8.0 Hz, Ar–*H*), 7.56 (d, 1H, J = 7.9 Hz, Ar–*H*), 7.36 (dd, 1H, J = 14.6, 2.5 Hz, oxa-Ar–*H*), 7.06 (dd, 1H, J = 9.0, 1.8 Hz, oxa-Ar–*H*), 6.94 (t, 1H, J = 9.0 Hz, oxa-Ar–H), 5.42 (bs, 1H, –N*H*), 4.80–4.70 (m, 1H, oxa-C*H*–), 4.03 (t, 1H, J = 9.0 Hz, oxa-CH*H*–), 3.91 (t, 1H, J = 9.0 Hz, oxa-CH*H*–), 3.37–3.24 (m, 6H, oxa-CH_2–, morpholin–OCH_2–), 2.80 (t, 4H, J = 4.5 Hz, morpholin–CH_2–); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 156.4, 155.5, 154.5, 154.1, 153.4, 135.6, 132.8, 129.7, 128.2, 124.9, 118.8, 114.1, 107.6, 71.3, 67.0, 51.0, 47.3, 45.5; ESIMS: m/z 490 $(M + H)^+$; HRMS (ESI) m/z calcd. for $C_{20}H_{20}F_4N_3O_5S$ $(M + H)^+$, 490.1060; found, 490.1071.

5.1.13. (R)-3,4-Difluoro-N-((3-(3-fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-benzenesulfonamide (**7m**)

The compound **7m** was prepared according to the above described method using **6a** (295 mg, 1 mmol) and 3,4-difluorobenzenesulfonyl chloride (0.16 mL, 1.2 mmol) with yield 310 mg (65%), m.p: 153–154 °C; IR (KBr pellet, cm^{-1}): 3328, 2910, 2360, 1736, 1521, 1330, 1239, 1164, 839; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.78 (t, 1H, J = 8.0 Hz, Ar–*H*), 7.61 (t, 1H, J = 7.9 Hz, Ar–*H*), 7.35 (dd, 1H, J = 14.6, 2.5 Hz, oxa-Ar–*H*), 7.22 (s, 1H, Ar–*H*), 7.06 (dd, 1H, J = 9.0, 1.8 Hz, oxa-Ar–*H*), 6.87 (t, 1H, J = 9.0 Hz, oxa-Ar–*H*), 5.70 (bs, 1H, –N*H*), 4.80–4.72 (m, 1H, oxa-C*H*–), 4.02 (t, 1H, J = 9.0 Hz, oxa-CH*H*–), 3.93 (t, 1H, J = 9.0 Hz, oxa-CH*H*–), 3.83 (t, 4H, J = 4.5 Hz, morpholin–OCH_2–), 3.54–3.36 (m, 2H, oxa-CH_2–), 3.03 (t, 4H, J = 4.5 Hz, morpholin–CH_2–); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 156.3, 155.4, 154.0, 153.3, 135.5, 132.6, 129.6, 128.1, 124.8, 118.7, 114.1, 107.9, 107.7, 71.9, 66.8, 50.8, 47.5, 41.8; ESIMS: m/z 472 $(M + H)^+$; HRMS (ESI) m/z calcd. for $C_{20}H_{21}F_3N_3O_5S$ $(M + H)^+$, 472.1154; found, 490.1162.

5.1.14. (R)-3-Chloro-N-((3-(3-fluoro-4-thiomorpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-benzenesulfonamide (**7n**)

The compound **7n** was prepared according to the above described method using **6b** (311 mg, 1 mmol) and 3-chlorobenzenesulfonyl chloride (253 mg, 1.2 mmol) with yield 281 mg (58%), m.p: 155–156 °C; IR (KBr pellet, cm^{-1}): 3292, 2902, 2839, 1735, 1519, 1332, 1162, 806; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.85 (s, 1H, Ar–*H*), 7.75 (d, 1H, J = 7.7 Hz Ar–*H*), 7.53 (t, 1H, J = 7.9 Hz, Ar–*H*), 7.47 (t, 1H, J = 7.7 Hz, Ar–*H*), 7.07 (dd, 1H, J = 15.0, 2.4 Hz, oxa-Ar–*H*), 7.07 (dd, 1H, J = 9.0 Hz, oxa-Ar–*H*), 6.86 (t, 1H, J = 9.0 Hz, oxa-Ar–*H*), 5.85 (bs, 1H, –N*H*), 4.81 (m, 1H, oxa-C*H*–), 4.05–3.90 (m, 2H, oxa-CH_2–), 3.41–3.34 (m, 2H, oxa-CH_2–), 3.29 (t, 4H, J = 4.5 Hz, thiomorpholin–SCH_2–), 2.80 (t, 4H, J = 4.5 Hz, thiomorpholin–CH_2–); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.8, 152.9, 141.0, 135.9, 133.6, 131.3, 129.5, 125.6, 123.8, 119.1, 112.7, 106.1105.8, 70.0, 52.1, 46.0, 44.1, 26.7; ESIMS: m/z 470 $(M + H)^+$; HRMS (ESI) m/z calcd. for $C_{20}H_{22}ClFN_3O_4S_2$ $(M + H)^+$, 486.0724; found, 486.0751.

5.1.15. (R)-4-Acetyl-N-((3-(3-fluoro-4-thiomorpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-benzenesulfonamide (**7o**)

The compound **7o** was prepared according to the above described method using **6b** (311 mg, 1 mmol) and 4-acetylbenzenesulfonyl chloride (262 mg, 1.2 mmol) with yield 271 mg (55%), m.p: 193–194 °C; IR (KBr pellet, cm^{-1}): 3294, 2918, 2849, 1749, 1687, 1518, 1380, 1327, 1158, 844; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.06 (d, 2H, J = 7.7 Hz, Ar–*H*), 7.94 (d, 2H, J = 7.7 Hz, Ar–*H*), 7.38 (dd, 1H, J = 14.8, 2.6 Hz, oxa-Ar–*H*), 7.05 (dd, 1H, J = 8.6 Hz, oxa-Ar–*H*), 6.92 (t, 1H, J = 8.6 Hz, oxa-Ar–*H*), 5.75 (bs, 1H, –N*H*), 4.79–4.69 (m, 1H, oxa-C*H*–), 4.00 (t, 1H, J = 9.0 Hz oxa-CH*H*–), 3.90 (t, 1H, J = 9.0 Hz, oxa-CH*H*–), 3.39–3.35 (m, 2H, oxa-CH_2–), 3.29 (t, 4H, J = 4.5 Hz, thiomorpholin–SCH_2–), 2.85 (t, 4H, J = 4.5 Hz, thiomorpholin–CH_2–), 2.64 (s, 3H, –$COCH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 196.0, 156.9, 153.8, 144.0, 139.6, 133.1, 128.7, 126.9, 120.7, 113.7, 107.3, 107.0, 70.8, 53.0, 47.0, 44.9, 27.7, 26.6; ESIMS: m/z 494 $(M + H)^+$; HRMS (ESI) m/z calcd. for $C_{22}H_{25}FN_3O_5S_2$ $(M + H)^+$, 494.1220; found, 494.1241.

5.1.16. (R)-3-Chloro-4-fluoro-N-((3-(3-fluoro-4-thiomorpholinophenyl)-2-oxooxazolidin-5-yl)methyl) benzenesulfonamide (**7p**)

The compound **7p** was prepared according to the above described method using **6b** (311 mg, 1 mmol) and 3-chloro-4-fluorobenzenesulfonyl chloride (275 mg, 1.2 mmol) with yield 262 mg (52%), m.p: 155–156 °C; IR (KBr pellet, cm^{-1}): 3310, 2902, 2839, 1735, 1519, 1332, 1162, 826; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.39 (bs, 1H, –N*H*), 7.77 (t, 1H, J = 8.1 Hz, Ar–*H*), 7.63 (t, 1H, J = 8.1 Hz, Ar–*H*), 7.44 (dd, 1H, J = 15.0, 2.6 Hz, oxa-Ar–*H*), 7.25 (t, 1H, J = 7.3 Hz, Ar–*H*), 7.07 (dd, 1H, J = 9.0, 1.8 Hz, oxa-Ar–*H*), 6.95 (t, 1H, J = 9.0 Hz, oxa-Ar–*H*), 4.76 (m, 1H, oxa-C*H*–), 4.05–3.93 (m, 2H, oxa-CH_2–), 3.41–3.33 (m, 2H, oxa-CH_2–), 3.28 (t, 4H, J = 4.5 Hz, thiomorpholin–SCH_2–), 2.79 (t, 4H, J = 4.5 Hz, thiomorpholin–CH_2–); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.0, 153.9, 152.1, 135.1, 133.2, 132.0, 128.6, 126.5, 123.4, 120.2, 118.6, 112.1, 105.3, 104.9, 69.3, 51.5, 45.3, 43.5, 25.9; ESIMS: m/z 504 (M^+ + H); HRMS (ESI) m/z calcd. for $C_{20}H_{21}ClF_2N_3O_4S_2$ $(M + H)^+$, 504.0630; found, 504.0638.

5.1.17. (R)-N-((3-(3-Fluoro-4-thiomorpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-4-phenoxybenzenesulfonamide (**7q**)

The compound **7q** was prepared according to the above described method using **6b** (311 mg, 1 mmol) and 4-phenoxybenzenesulfonyl chloride (322 mg, 1.2 mmol) with yield 271 mg (50%), m.p: 144–145 °C; IR (KBr pellet, cm^{-1}): 3328, 2901, 2838, 2360, 1760, 1518, 1487, 1154, 834; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.77 (d, 2H, J = 8.1 Hz, Ar–*H*), 7.44 (m, 2H, Ar–*H*), 7.40 (dd, 1H, J = 15.0, 2.6 Hz, oxa-Ar–*H*), 7.34 (d, 2H, J = 8.1 Hz, Ar–*H*), 7.19 (m, 1H, Ar–*H*), 7.14 (t, 2H, J = 6.7 Hz, Ar–*H*), 7.07 (dd, 1H, J = 9.0, 1.8 Hz, oxa-Ar–*H*), 6.95 (t, 1H, J = 9.0 Hz, oxa-Ar–*H*), 5.57 (bs, 1H, –N*H*), 4.76 (m, 1H, oxa-C*H*–), 4.05–3.93 (m, 2H, oxa-CH_2–), 3.41–3.33 (m, 2H, oxa-CH_2–), 3.28 (t, 4H, J = 4.5 Hz, thiomorpholin–SCH_2–), 2.79 (t, 4H, J = 4.5 Hz, thiomorpholin–CH_2–); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.7, 156.5, 154.9, 154.6, 154.1, 137.6, 134.5, 132.8, 130.1, 129.1, 125.0, 120.2, 117.7, 113.9, 107.6, 107.4, 71.1, 53.2, 47.2, 45.3, 27.9; ESIMS: m/z 544 $(M + H)^+$; HRMS (ESI) m/z calcd. for $C_{26}H_{27}FN_3O_5S_2$ $(M + H)^+$, 544.1376; found, 544.1382.

5.1.18. (R)-N-(5-(N-((3-(3-Fluoro-4-thiomorpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-sulfamoyl)-4-methylthiazol-2-yl) acetamide (**7r**)

The compound **7r** was prepared according to the above described method using **6b** (311 mg, 1 mmol) and 2-acetamido-4-methyl-1,3-thiazole-5-sulfonyl chloride (305 mg, 1.2 mmol) with yield 211 mg (40%), m.p: 184–185 °C; IR (KBr pellet, cm^{-1}): 3276, 3178, 2961, 2834, 2360, 1733, 1681, 1514, 1149, 1336, 861; ^{1}H NMR (DMSO-d_6,

300 MHz): δ 12.26 (s, 1H, −NHCO−), 8.22 (t, 1H, J = 6.5 Hz, Ar−H), 7.67 (s, 1H, thiophene−H), 7.47 (dd, 1H, J = 14.5, 2.4 Hz, oxa-Ar−H), 7.07 (dd, 1H, J = 9.0, 1.8 Hz, oxa-Ar−H), 6.96 (t, 1H, J = 9.0 Hz, oxa-Ar−H), 5.70 (bs, 1H, −NH), 4.77–4.69 (m, 1H, oxa-CH−), 4.02 (t, 1H, J = 9.0 Hz, oxa-CHH−), 3.94 (t, 1H, J = 9.0 Hz, oxa-CHH−), 3.41–3.33 (m, 2H, oxa-CH_2−), 3.28 (t, 4H, J = 4.5 Hz, thiomorpholin−SCH_2−), 2.88 (t, 4H, J = 4.5 Hz, thiomorpholin−CH_2−), 2.20 (s, 3H, −COCH_3), 2.06 (s, 3H, −CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.3, 155.3, 153.4, 142.3, 134.5, 132.8, 125.3, 124.4, 118.7, 112.9, 107.4, 70.2, 52.5, 46.2, 44.2, 27.2, 23.4, 12.5; ESIMS: m/z 530 (M^+ + H); HRMS (ESI) m/z calcd. for $C_{20}H_{25}FN_5O_5S_3$ (M + H)$^+$, 530.1002; found, 530.1030.

5.1.19. (R)-N-((3-(3-Fluoro-4-thiomorpholinophenyl)-2-oxooxazolidin-5-yl)methyl)quinoline-8-sulfonamide (7s)

The compound **7s** was prepared according to the above described method using **6b** (311 mg, 1 mmol) and 8-quinolinesulfonyl chloride (273 mg, 1.2 mmol) with yield 251 mg (45%), m.p: 177–178 °C; IR (KBr pellet, cm^{-1}): 3291, 2854, 2360, 1733, 1516, 1320, 1120, 836; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 9.06 (d, 1H, J = 3.7 Hz, quino-H), 8.38 (d, 1H, J = 6.0 Hz, quino-H), 8.23 (d, 1H, J = 8.3 Hz, quino-H), 8.01 (d, 1H, J = 8.3 Hz, quino-H), 7.59–7.55 (m, 1H, quino-H), 7.29 (dd, 1H, J = 14.6, 2.6 Hz, oxa-Ar−H), 6.89 (dd, 1H, J = 9.0, 1.8 Hz, oxa-Ar−H), 6.83 (t, 1H, J = 9.0 Hz, oxa-Ar−H), 4.74–4.66 (m, 1H, oxa-CH−), 3.97–3.95 (m, 2H, oxa-CHH−), 3.41–3.33 (m, 2H, oxa-CH_2−), 3.28 (t, 4H, J = 4.5 Hz, thiomorpholin−SCH_2−), 2.79 (t, 4H, J = 4.5 Hz, thiomorpholin−CH_2−); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 155.3, 153.4, 149.7, 143.2, 142.3, 136.1, 134.1, 132.8, 128.5, 127.8, 125.3, 124.4, 122.3, 121.1, 118.7, 112.9, 70.1, 52.5, 46.3, 44.2, 27.4; ESIMS: m/z 503 (M^+ + H); HRMS (ESI) m/z calcd. for $C_{23}H_{24}FN_4O_4S_2$ (M + H)$^+$, 503.1223; found, 503.1237.

5.1.20. (R)-N-((3-(3-Fluoro-4-thiomorpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-4-(phenylsulfonyl)thiophene-2-sulfonamide (7t)

The compound **7t** was prepared according to the above described method using **6b** (311 mg, 1 mmol) and 4-(phenylsulfonyl) thiophene-2-sulfonylchloride (387 mg, 1.2 mmol) with yield 251 mg (42%), m.p: 163–164 °C; IR (KBr pellet, cm^{-1}): 3299, 2901, 2360, 1760, 1733, 1516, 1336, 1131, 825; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 8.57 (t, 1H, J = 5.3 Hz, Ar−H), 8.41 (d, 1H, J = 5.3 Hz, Ar−H), 7.97 (d, 2H, J = 7.3 Hz, Ar−H), 7.80 (s, 1H, Ar−H), 7.67 (t, 2H, J = 7.3 Hz, Ar−H), 7.59 (t, 2H, J = 7.3 Hz, Ar−H), 7.49 (d, 1H, J = 14.6, 2.4 Hz, oxa-Ar−H), 7.06 (d, 1H, J = 9.0 Hz, oxa-Ar−H), 6.94 (t, 1H, J = 9.0 Hz, oxa-Ar−H), 4.78–4.72 (m, 1H, oxa-CH−), 4.04 (t, 1H, J = 8.9 Hz, oxa-CHH−), 3.88 (t, 1H, J = 8.9 Hz, oxa-CHH−), 3.39–3.34 (m, 2H, oxa-CH_2−), 3.28 (t, 4H, J = 4.5 Hz, morpholin−OCH_2−), 2.84 (t, 4H, J = 4.5 Hz, morpholin−CH_2−); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 157.2, 153.0, 144.0, 141.1, 139.6, 136.1, 132.9, 128.7, 127.9, 127.1, 126.5, 119.0, 112.9, 106.5, 106.1, 69.9, 52.3, 46.2, 44.5, 26.9; ESIMS: m/z 598 (M + H)$^+$; HRMS (ESI) m/z calcd. for $C_{24}H_{25}FN_3O_6S_4$ (M + H)$^+$, 598.0610; found, 598.0635.

5.1.21. (R)-N-((3-(3-Fluoro-4-thiomorpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-4-(trifluoromethyl)benzenesulfonamide (7u)

The compound **7u** was prepared according to the above described method using **6b** (311 mg, 1 mmol) and 4-(trifluoromethyl)benzene-1-sulfonyl chloride (294 mg, 1.2 mmol) with yield 301 mg (58%), m.p: 155–156 °C; IR (KBr pellet, cm^{-1}): 3295, 2921, 2360, 1746, 1516, 1326, 1160, 829; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.99 (d, 2H, J = 8.3 Hz, Ar−H), 7.78 (d, 2H, J = 8.3 Hz, Ar−H), 7.39 (dd, 1H, J = 14.6, 2.4 Hz, oxa-Ar−H), 7.06 (d, 1H, J = 8.9 Hz, oxa-Ar−H), 6.91 (t, 1H, J = 8.9 Hz, oxa-Ar−H), 5.66 (bs, 1H, −NH), 4.77–4.70 (m, 1H, oxa-CH−), 4.02 (t, 1H, J = 8.9 Hz, oxa-CHH−), 3.92 (t, 1H, J = 8.9 Hz, oxa-CHH−), 3.41–3.33 (m, 2H, oxa-CH_2−), 3.28 (t, 4H, J = 4.5 Hz, thiomorpholin−SCH_2−), 2.79 (t, 4H, J = 4.5 Hz, thiomorpholin−CH_2−); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 156.2, 153.1, 135.6, 128.7, 128.6, 119.6, 115.4, 115.1, 112.9, 112.5, 106.5, 106.1, 70.2, 52.5, 46.2, 44.2, 26.8; ESIMS: m/z 520 (M + H)$^+$; HRMS (ESI) m/z calcd. for $C_{21}H_{22}F_4N_3O_4S_2$ (M + H)$^+$, 520.0988; found, 520.0995.

5.1.22. (R)-N-((3-(3-Fluoro-4-thiomorpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-thiophene-2-sulfonamide (7v)

The compound **7v** was prepared according to the above described method using **6b** (311 mg, 1 mmol) and 2-thiophenesulfonyl chloride (219 mg, 1.2 mmol) with yield 256 mg (56%), m.p: 133–135 °C; IR (KBr pellet, cm^{-1}): 3289, 2919, 2360, 1735, 1510, 1326, 1160, 829; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.61 (m, 2H, thiophene−H), 7.42 (dd, 1H, J = 14.6, 2.4 Hz, oxa-Ar−H), 7.11 (m, 1H, thiophene−H), 7.06 (d, 1H, J = 9.0 Hz, oxa-Ar−H), 6.91 (t, 1H, J = 9.0 Hz, oxa-Ar−H), 5.55 (bs, 1H, −NH), 4.79–4.74 (m, 1H, oxa-CH−), 4.02 (t, 1H, J = 8.9 Hz, oxa-CHH−), 3.93 (t, 1H, J = 8.9 Hz, oxa-CHH−), 3.41–3.33 (m, 2H, oxa-CH_2−), 3.28 (t, 4H, J = 4.5 Hz, thiomorpholin−SCH_2−), 2.80 (t, 4H, J = 4.5 Hz, thiomorpholin−CH_2−); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.3, 152.4, 152.0, 139.7, 135.3, 135.2, 132.1, 132.0, 130.3, 129.9, 125.9, 118.8, 112.2, 105.5, 105.2, 69.4, 51.6, 45.5, 43.8, 26.1; ESIMS: m/z 458 (M + H)$^+$; HRMS (ESI) m/z calcd. for $C_{18}H_{21}FN_3O_4S_3$ (M + H)$^+$, 458.0678; found, 458.0688.

5.1.23. (R)-4-Fluoro-N-((3-(3-fluoro-4-thiomorpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-benzenesulfonamide (7w)

The compound **7w** was prepared according to the above described method using **6b** (311 mg, 1 mmol) and 4-flurobenzenesulfonyl chloride (234 mg, 1.2 mmol) with yield 286 mg (61%) m.p: 153–154 °C; IR (KBr pellet, cm^{-1}): 3328, 2901, 2360, 1736, 1519, 1239, 1164, 839; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.85–7.80 (m, 2H, Ar−H), 7.72–7.71 (m, 2H, Ar−H), 7.42 (dd, 1H, J = 15.0, 2.4 Hz, oxa-Ar−H), 7.07 (dd, 1H, J = 8.7 Hz, oxa-Ar−H), 6.86 (t, 1H, J = 9.3 Hz, oxa-Ar−H), 6.02 (bs, 1H, −NH), 5.11 (m, 1H, oxa-CH−), 4.34–3.97 (m, 2H, J = 9.3 Hz, oxa-CH_2−), 3.44–3.35 (m, 2H, oxa-CH_2−), 3.28 (t, 4H, J = 4.5 Hz, thiomorpholin−SCH_2−), 2.79 (t, 4H, J = 4.5 Hz, thiomorpholin−CH_2−); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.5, 156.2, 153.1, 135.6, 128.7, 119.6, 115.4, 115.1, 112.9, 106.5, 106.1, 70.2, 52.5, 46.2, 44.2, 26.8; ESIMS: m/z 470 (M + H)$^+$; HRMS (ESI) m/z calcd. for $C_{20}H_{22}F_2N_3O_4S_2$ (M + H)$^+$, 470.1020; found, 470.1039.

5.1.24. (R)-4-(2-Fluoro-4-(2-oxo-5-((4-(trifluoromethyl) phenylsulfonamido)methyl)-oxazolidin-3-yl)phenyl)piperazin-1-yl pivalate (7x)

The compound **7x** was prepared according to the above described method using **6c** (394 mg, 1 mmol) and 4-(trifluoromethyl)benzene-1-sulfonyl chloride (294 mg, 1.2 mmol) with yield 367 mg (61%) m.p: 166–167 °C; IR (KBr pellet, cm^{-1}): 3150, 2930, 2858, 2360, 1759, 1698, 1513, 1409, 1160, 846; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.99 (d, 2H, J = 8.3 Hz, Ar−H), 7.78 (d, 2H, J = 8.3 Hz, Ar−H), 7.38 (dd, 1H, J = 14.6, 2.4 Hz, oxa-Ar−H), 7.04 (d, 1H, J = 9.0 Hz, oxa-Ar−H), 6.89 (t, 1H, J = 8.9 Hz, oxa-Ar−H), 5.95 (bs, 1H, −NH), 4.78–4.70 (m, 1H, oxa-CH−), 4.02 (t, 1H, J = 8.9 Hz, oxa-CHH−), 3.92 (t, 1H, J = 8.9 Hz, oxa-CHH−), 3.58 (t, 4H, J = 4.7 Hz, piperzine−NCH_2−), 3.41–3.22 (m, 2H, oxa-CH_2−), 2.98 (t, 4H, J = 4.7 Hz, piperzine−CH_2−), 1.45 (s, 9H, −C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.0, 154.4, 154.0, 152.2, 143.3, 137.3, 127.5, 127.4, 126.4, 119.3, 114.1, 107.8, 107.4, 104.8, 79.9, 71.0, 50.6, 50.5, 47.2, 45.4, 28.4; ESIMS: m/z 603 (M + H)$^+$; HRMS (ESI) m/z calcd. for $C_{26}H_{31}F_4N_4O_6S$ (M + H)$^+$, 603.1894; found, 603.1889.

5.1.25. (R)-4-(2-Fluoro-4-(5-((4-fluorophenylsulfonamido)methyl)-2-oxooxazolidin-3-yl)phenyl)piperazin-1-yl pivalate (7y)

The compound **7y** was prepared according to the above described method using **6c** (394 mg, 1 mmol) and 4-

flurobenzenesulfonyl chloride (234 mg, 1.2 mmol) with yield 348 mg (63%) m.p: 152–153 °C; IR (KBr pellet, cm^{-1}): 3112, 2937, 2858, 2360, 1760, 1696, 1513, 1409, 1160, 846; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.90–7.85 (m, 2H, Ar–*H*), 7.43 (dd, 1H, *J* = 15.0, 2.4 Hz, oxa-Ar–*H*), 7.21–7.15 (m, 2H, Ar–*H*), 7.07–7.00 (m, 2H, oxa-Ar–*H*), 5.74 (bs, 1H, –N*H*), 4.74 (m, 1H, oxa-C*H*–), 4.04–3.90 (m, 2H, *J* = 9.3 Hz, oxa-CH_2–), 3.63 (t, 4H, *J* = 4.7 Hz, piperzine–NCH_2–), 3.37–3.19 (m, 2H, oxa-CH_2–), 3.04 (t, 4H, *J* = 4.7 Hz, piperzine–CH_2–), 1.48 (s, 9H, –C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.4, 154.6, 154.1, 136.6, 135.7, 129.7, 129.5, 119.3, 119.2, 116.6, 116.3, 114.0, 107.7, 107.4, 79.9, 71.1, 50.6, 50.5, 47.2, 45.3, 28.4; ESIMS: *m*/*z* 470 $(M + H)^+$; HRMS (ESI) *m*/*z* calcd. for $C_{25}H_{31}F_2N_4O_6S$ $(M + H)^+$, 553.1932; found, 553.1955.

5.1.26. (R)-N-((3-(3-Fluoro-4-(piperazin-1-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)-4-(trifluoromethyl)benzenesulfonamide (**8a**)

The target compound **8a** was obtained by slow addition of trifluoroacetic acid (4 mmol) to the solution of **7x** (241 mg, 0.4 mmol) in dry dichloromethane (25 mL) at 0 °C to room temperature for 1 h, after completion of reaction as indicate by TLC the reaction mixture was neutralized by aq $NaHCO_3$ solution, the isolated product was triturated in ether and then recrystallized from methanol. (Yield 160 mg, 80%) m.p: 173–174 °C; IR (KBr pellet, cm^{-1}): 3150, 2930, 2858, 2360, 1759, 1512, 1160, 846; ^1H NMR (DMSO-d_6, 300 MHz): δ 7.99 (d, 2H, *J* = 8.3 Hz, Ar–*H*), 7.78 (d, 2H, *J* = 8.3 Hz, Ar–*H*), 7.38 (dd, 1H, *J* = 14.6, 2.4 Hz, oxa-Ar–*H*), 7.04 (d, 1H, *J* = 9.0 Hz, oxa-Ar–*H*), 6.89 (t, 1H, *J* = 8.9 Hz, oxa-Ar–*H*), 5.95 (bs, 1H, –N*H*), 4.78–4.70 (m, 1H, oxa-C*H*–), 4.05–3.89 (m, 2H, oxa-C*H*H–), 3.58 (t, 4H, *J* = 4.7 Hz, piperzine–NCH_2–), 3.41–3.23 (m, 2H, oxa-CH_2–), 2.98 (t, 4H, *J* = 4.7 Hz, piperzine–CH_2–); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 155.0, 154.4, 154.0, 143.3, 137.3, 127.5, 127.4, 126.4, 119.3, 114.1, 107.8, 107.4, 104.8, 71.0, 50.6, 50.5, 47.2, 45.4; ESIMS: *m*/*z* 470 $(M + H)^+$; HRMS (ESI) *m*/*z* calcd. for $C_{21}H_{23}F_4N_4O_4S$ $(M + H)^+$, 503.1376; found, 503.1385.

5.1.27. (R)-4-Fluoro-N-((3-(3-fluoro-4-(piperazin-1-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)-benzenesulfonamide (**8b**)

The compound **8b** was prepared according to the above described method using **7y** (221 mg, 0.4 mmol). (Yield 148 mg, 82%), m.p: 166–167 °C; IR (KBr pellet, cm^{-1}): 3112, 2937, 2858, 2360, 1760, 1513, 1160, 846; ^1H NMR (DMSO-d_6, 300 MHz): δ 7.89–7.84 (m, 2H, Ar–*H*), 7.42 (dd, 1H, *J* = 15.0, 2.4 Hz, oxa-Ar–*H*), 7.20–7.14 (m, 2H, oxa-Ar–*H*), 7.04–6.86 (m, 2H, oxa-Ar–*H*), 5.73 (bs, 1H, –N*H*), 4.76–4.69 (m, 1H, oxa-C*H*–), 4.03–3.89 (m, 2H, oxa-CH_2–), 3.62 (t, 4H, *J* = 4.7 Hz, piperzine–NCH_2–), 3.36–3.18 (m, 2H, oxa-CH_2–), 3.03 (t, 4H, *J* = 4.7 Hz, piperzine–CH_2–); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 163.4, 154.6, 136.6, 135.7, 129.7, 129.5, 119.3, 119.2, 116.6, 116.3, 114.0, 107.7, 107.4, 71.1, 50.6, 50.5, 47.2, 45.3; ESIMS: *m*/*z* 453 $(M + H)^+$; HRMS (ESI) *m*/*z* calcd. for $C_{20}H_{23}F_2N_4O_4S$ $(M + H)^+$, 453.1402; found, 453.1396.

5.2. Antibacterial assay

All the test compounds were dissolved in DMSO of 2 mg/mL. Empty sterilized disks of 6 mm were impregnated with compounds in the range from 1 to 80 μg/disk and placed in triplicate in the medium inoculated with fresh bacteria ($1–2 \times 104$ cfu mL^{-1}) on the freshly prepared sterile Mueller Hilton agar plates [32]. The plates were incubated at 35 °C for 24 h for zone of inhibition, if any, around the disks. The lowest concentration (higher dilution) of the test compound required to arrest the growth of tested strains was regarded as minimum inhibitory concentrations (MICs). 20 μL of DMSO was loaded on sterile disc and placed on the culture. After incubation for 24 h, observed no zone of inhibition around the disc, indicated that DMSO has no inhibitory effect on the tested strains and which was taken as a negative control. Linezolid was used as the reference compound.

5.3. Antifungal assay

The method followed for antifungal bioassay was similar to that followed for antibacterial assay where the medium was potato dextrose agar 39 g/L. The equivalent amount of solvent (DMSO) did not exhibit any activity in the assay. The treated compounds and the controls were kept in an incubator at 28 ± 2 °C for 48 h. All the compounds were tested for minimum inhibitory concentration (MIC). Fluconazole was used as positive control.

5.4. Antimycobacterial assay

The antimycobacterial activities of new oxazolidinosulfonamides (**7a**–**y** and **8a**–**b**) were evaluated against *M. tuberculosis* $H_{37}Rv$ using microplate dilution assay [33,34]. All the compounds were initially screened against *M. tuberculosis* $H_{37}Rv$ at the single concentration of 32 μg/mL in triplicate in a microtiter plate. The active compounds from this screening were further tested for Minimum Inhibitory Concentration (MIC) determination using the broth microdilution assay. The microtiter plates were incubated for 2–3 weeks at 37 °C in CO_2 incubator and read visually for the absence of growth turbidity.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ejmech.2013.01.034.

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