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REPORT

Synthesis of new antibacterial agents encompassing tosyl, piperidine, propanamide and 1,3,4-oxadiazole functionalities

Almas Sattar[1], Aziz-ur-Rehman[1,*], Muhammad Athar Abbasi[1], Sabahat Zahra Siddiqui[1], Shahid Rasool[1] and Syed Adnan Ali Shah[2,3]

[1]Department of Chemistry, Government College University, Lahore, Pakistan
[2]Faculty of Pharmacy, Universiti Teknology MARA, Puncak Alam Campus, Bandar Puncak Alam, Selangor Darul Ehsan, Malaysia.
[3]Atta-ur-Rahman Institute for Natural Products Discovery (AuRIns), Level 9, FF3, Universiti Teknology MARA, Puncak Alam Campus, Bandar Puncak Alam, Selangor Darul Ehsan, Malaysia.

Abstract: A series of propanamide compounds 6a-l was derived by *N*-substitution reactions, encompassing tosyl, piperidine and 1,3,4-oxadiazole moieties. The intended array of compounds 6a-l was afforded by a series of five steps reaction scheme. 1-Tosylpiperidin-4-carboxylate (1) was synthesized by the reaction of tosyl chloride (a) with ethyl isonipecotate (b) under mild basic conditions. Compound 1 was subjected to nucleophillic substitution by hydrazine to synthesize 1-tosylpiperidin-4-carbohydrazide (2). The compound, 5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazole-2-thiol (3) was synthesized by intermolecular cyclization of compound 2 by CS_2 under strong basic conditions. The target compounds, 6a-l, were finally synthesized from 3 by reacting with different electrophiles, 5a-l, in an aprotic polar solvent with sodium hydride as an activator. The different propanamoyl electrophiles, 5a-l, were synthesized by the reaction of different aromatic and aliphatic amines, 4a-l, with 3-bromopropionyl chloride under mild basic conditions. The structural elucidation was carried out using modern spectroscopic techniques including IR, ^{1}H-NMR and EI-MS. The antibacterial potential of synthesized compounds was assessed against five bacterial strains. Compounds 6a, 6c, 6d, 6e and 6f were found to be potent antibacterial agents.

Keywords: 1,3,4-Oxadiazole, tosyl chloride, piperidine, ethyl isonipecotate, antibacterial activity.

INTRODUCTION

During last four years our research group have synthesized a large number of 2,5-disubstituted derivatives of 1,3,4-oxadiazole and established that these compounds are biologically potent (Koparır *et al*., 2005; Hemavathi *et al*., 2011; Siddiqui *et al.*, 2013; Aziz-ur-Rehman *et al.*, 2014; Aziz-ur-Rehman *et al.*, 2012b; Rasool *et al.*, 2015). In the present work we have extended our synthetic work to synthesize a new array of derivatives of 3-[5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-ylthio]propanamide (6a-l), bearing three different conspicuous moieties including tosyl, piperidine and 1,3,4-oxadiazole. All these moieties have their own significant importance regarding their applications in medicinal field.

The antibacterial evaluation was performed against Gram-negative (*Salmonella typhi*, *Pseudomonas aeruginosa* and *Escherichia coli)* and Gram-positive *(Staphylococcus aureus* and *Bacillus subtilis*) bacterial strains employing dilution method (Kaspady *et al.*, 2009). The undertaken research work was a successful endeavour to fabricate multifunctional compounds. The biological evaluation concluded some compounds to be potent antibacterial agents.

The previous studies on 1,3,4-oxadizole derivatives have demonstrated the potency of these compounds as bioactive ones. The various prominent bioactivity results of 1,3,4-oxadiazole derivatives include anti-carcinogenic (Hussain *et al.*, 2009), anti-inflammatory (Bhandari *et al.*, 2008), anticoagulant (Idrees *et al.*, 2009), antibiotic (Padmavathi *et al.*, 2009), skin pigmenting (Kumar *et al.*, 2008), analgesic (Bankar *et al.*, 2010), antifungal (Shaharmohammad *et al.*, 2007), antioxidant (Vittal *et al.*, 2011) and antibacterial (Burbuliene *et al.*, 2004) activities. The other prominent functionality in the field of drugs is sulfonamide. Drugs containing sulfonamides functionality are used as preventive and chemotherapeutic agents for combating against many infectious diseases (Hansch *et al.*, 1990).

Beside other biological activities, sulfonamides are very potent antibacterial agents (Stokes *et al.*, 2012). Thousands of organic compounds containing piperidine nucleus have also been reported in clinical and preclinical studies because of their prominent biological activities (Khalid *et al.*, 2012), these compounds are potent antioxidants and have conspicuous antibacterial activity (Prashanth *et al.*, 2012 and Elavarasan *et al.*, 2014).

**Corresponding author:* e-mail: azizryk@yahoo.com

MATERIALS AND METHODS

Melting points of synthesized compounds were determined employing Griffin and George meting point apparatus using open capillary tube. Melting points were uncorrected. Pre-coated silica gel, G-25-UV_{254} aluminum plates were employed to confirm the purity of the synthesized compounds *via* thin layer chromatography (TLC) technique. The single spot of pure compounds was observed on TLC using various ratios of ethyl acetate and *n*-hexane as mobile phase. IR spectra (wave number in cm^{-1}) were recorded by employing Jasco-320-A spectrometer, using KBr pellet method. Bruker spectrometer operating at 400MHz was used to record proton nuclear magnetic resonance (^{1}H-NMR) spectra. JMS-HX-110 spectrometer, with a data system was used to record mass spectra (EI-MS).

Preparation of ethyl 1-tosylpiperidin-4-carboxylate (1)

Ethyl isonipecotate (b; 5mL, 32.472mmol) was dispersed in distilled water (35mL) in a 100mL round bottom (RB) flask. Tosyl chloride (a; 3.912g, 32.472mmol) was added slowly in 30min on continuous stirring at room temperature (28^{o}C). The reaction mixture was kept on continues stirring for 3 hours and monitored through TLC. The pH of reaction mixture was maintained at 9 to10 by 5 % aqueous solution of Na_2CO_3 till completion of reaction. The pH was adjusted to 6 by HCl (2mL, 11M) to quench the precipitates. The reaction mixture was aged for 15min. The precipitates of compound 1 were filtered, washed with distilled water and dried. The title compound was re-crystallized from chloroform.

Preparation of 1-tosylpiperidin-4-carbohydrazide (2)

Ethyl 1-tosylpiperidin-4-carboxylate (1; 2.5g, 8.375 mmol) was dispersed in methanol (20mL) in a 100mL RB flask. Hydrazine monohydrate (80%, 8mL) was added on stirring and refluxed for 4 hours. The progress of reaction was supervised by TLC. The white needle shaped crystals of desired compound 2 were afforded after distillation of two third solvent and addition of excess distilled water to the reaction mass. The crystals were filtered, rinsed with distilled water and desiccated. The title compound was re-crystallized from chloroform.

Preparation of 5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-thiol (3)

1-Tosylpiperidin-4-carbohydrazide (2; 2.0g, 6.73mmol) was suspended in methanol (25mL) in a 100mL RB flask. Potassium hydroxide (1.0g, 17.86mmol) was dissolved on reflux and then carbon disulfide (CS_2) (3.0mL, 49.38 mmol) was slowly poured at room temperature. The reaction contents were refluxed for 6 hours and reaction progress was monitored *via* TLC. Off white compound 3 was afforded by the addition of chilled distilled water (50mL) and dilute HCl to adjust pH 2-3. The solid desired compound 3 was filtered, rinsed with chilled distilled water and dried. The title compound was re-crystallized from chloroform.

Procedure for the synthesis of molecules (5a-l)

Aryl/aralkyl amines (4a-l, 5.5mmol) were suspended in distilled water (10mL) in a flat bottom flask (250mL) and 5% Na_2CO_3 solution was added to adjust the pH 8.0 to 9.0. The reaction mixture was stirred for 0.25 hours at room temperature. 3-Bromopropionyl chloride (0.55mL; 5.5mmol) was added drop wise to the reaction mixture in about 5 min on vigorous shaking. The reaction flask was further stirred for 1 hour till the formation of solid precipitates. The reaction completion was confirmed by TLC. The solid products were filtered through filter paper, washed with cold distilled water and desiccated to produce elctrophiles, 5a-l. The title compounds were re-crystallized from chloroform.

Procedure for the synthesis of molecules (6a-l)

5-(1-Tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-thiol (3; 0.0339g, 0.1mmol) was dissolved in *N,N*-dimethyl formamide (DMF, 10mL) in 50mL RB flask. Sodium hydride (0.002g, 0.0833mmol) was mixed and continuously stirred for 15min at room temperature (28^{o}C). Equimolar electrophiles (5a-l) were added and stirring was continued for 3-4 hours. The reaction completion was assessed by TLC. Solid products were afforded after addition of excess distilled water which were filtered, washed and dried at room temperature. The title compounds were re-crystallized from chloroform.

Biological activity assays

Antibacterial activity assay

Anti-bacterial activity was executed under aseptic conditions in sterile 96-well micro-plates. The principle used in this method was that as the population of microbes increases the absorbance reading also increases (Kaspady *et al.*, 2009). Two gram-positive bacteria; *Staphylococcus aureus* and *Bacillus subtilis* and three gram-negative bacteria; *Pseudomonas aeruginosa*, *Salmonella typhi* and *Escherichia coli* were screened for antibacterial activity of synthesized compounds. The samples under consideration were poured into 200µL wells having appropriate dilutions with suitable solvent. The 24 hours fresh bacterial culture was diluted using nutrient broth and 180µL of it was added into the wells. The initial reading of absorbance was maintained from 0.12 to 0.19 at 540nm. The totality of volume in each well was kept to 200µL after the addition of samples solution. The incubation temperature was 37^{o}C, it was maintained for 24 hours and during the incubation period the caps of wells were closed. Using micro plate reader absorbance was taken at 540nm. The difference in the absorbance reading was index of increase in bacterial growth. The calculation of percent inhibition was done by using formula given underneath. The results are mean triplicates. The standard used here is Ciprofloxacin.

$$\text{Inhibition (\%)} = \frac{\text{x} - \text{Test}}{\text{y}} \times 100$$

Where X represents Absorbance with bacterial culture, Test represents Absorbance in test sample and y represent the control.

STATISTICAL ANALYSIS

Minimum Inhibitory Concentration (MIC) were accounted after apposite dilutions and results were computed using EZ-Fit Perrella Scientific Inc. Amherst USA software. The thrice calculated values were statistically analyzed by ME-2010 and thus the %age inhibition and MIC values are provided as mean ± SEM.

Spectral characterization of synthesized compounds

Ethyl 1-(4-tosyl)piperidin-4-carboxylate (1)

White amorphous solid; Yield: 89%; M.P.: 70-72°C; Molecular formula: $C_{15}H_{21}NO_4S$; Molecular weight: 311; IR (KBr, cm^{-1}) υ_{max}: 3067 (C-H stretching of aromatic ring), 1732 (C=O stretching), 1531 (C=C aromatic stretching), 1335 (-SO_2- stretching), 1079 (C-O bond stretching); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 7.62 (d, *J* = 8.0 Hz, 2H, H-2" & H-6"), 7.32 (d, *J* = 8.0 Hz, 2H, H-3" & H-5"), 3.98 (q, *J* = 7.2 Hz, 2H, $CH_3\underline{CH_2}$O-), 3.71-3.68 (m, 2H, H_e-2' & H_e-6'), 2.73-2.62 (m, 1H, H-4'), 2.54-2.48 (m, 2H, H_a-2' & H_a-6'), 2.42 (s, 3H, CH_3-4"), 2.10-2.08 (m, 2H, H_e-3' & H_e-5'), 1.60-1.86 (m, 2H, H_a-3' & H_a-5'), 1.15 (t, *J* = 7.2 Hz, $\underline{CH_3}CH_2$O-); EI-MS (*m/z*): 311 $[M]^+$, 266 $[C_{13}H_{16}NO_3S]^+$, 238 $[C_{12}H_{16}NO_2S]^+$, 184 $[C_8H_{10}NO_2S]^+$, 170 $[C_7H_8NO_2S]^+$, 155 $[C_7H_7O_2S]^+$, 91 $[C_7H_7]^+$.

Tosylpiperidin-4-carbohydrazide (2)

White crystalline solid; Yield: 91%; M.P.: 128-130 °C; Molecular formula: $C_{13}H_{19}N_3O_3S$; Molecular weight: 297; IR (KBr, cm^{-1}) υ_{max}: 3348 (N-H stretching), 3063 (C-H stretching of aromatic ring), 1682 (C=O stretching), 1534 (C=C aromatic stretching), 1339 (-SO_2- stretching); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 7.61 (d, *J* = 8.0 Hz, 2H, H-2" & H-6"), 7.33 (d, *J* = 8.0 Hz, 2H, H-3" & H-5"), 3.72-3.69 (m, 2H, H_e-2' & H_e-6'), 2.73-2.62 (m, 1H, H-4'), 2.53-2.49 (m, 2H, H_a-2' & H_a-6'), 2.42 (s, 3H, CH_3-4"), 2.12-2.10 (m, 2H, H_e-3' & H_e-5'), 1.58-1.84 (m, 2H, H_a-3' & H_a-5'); EI-MS (*m/z*): 297 $[M]^+$, 266 $[C_{13}H_{16}NO_3S]^+$, 238 $[C_{12}H_{16}NO_2S]^+$, 184 $[C_8H_{10}NO_2S]^+$, 170 $[C_7H_8NO_2S]^+$, 155 $[C_7H_7O_2S]^+$, 91 $[C_7H_7]^+$.

5-(1-Tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-thiol (3)

White amorphous solid; Yield: 87%; M.P.: 230-233°C; Molecular formula: $C_{14}H_{17}N_3O_3S_2$; Molecular weight: 339; IR (KBr, cm^{-1}) υ_{max}: 3067 (C-H stretching of aromatic ring), 2522 (S-H bond stretching), 1641 (C=N stretching of oxadiazole ring), 1541 (C=C aromatic stretching), 1345 (-SO_2- stretching), 1249 & 1079 (C-O-C bond stretching); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 7.63 (d, *J* = 8.0 Hz, 2H, H-2" & H-6"), 7.32 (d, *J* = 8.0 Hz, 2H, H-3" & H-5"), 3.71-3.68 (m, 2H, H_e-2' & H_e-6'), 2.74-2.63 (m, 1H, H-4'), 2.54-2.48 (m, 2H, H_a-2' & H_a-6'), 2.42 (s, 3H, CH_3-4"), 2.10-2.08 (m, 2H, H_e-3' & H_e-5'), 1.59-1.85 (m, 2H, H_a-3' & H_a-5'); EI-MS (*m/z*): 339 $[M]^+$, 266 $[C_{13}H_{16}NO_3S]^+$, 238 $[C_{12}H_{16}NO_2S]^+$, 184 $[C_8H_{10}NO_2S]^+$, 170 $[C_7H_8NO_2S]^+$, 155 $[C_7H_7O_2S]^+$, 91 $[C_7H_7]^+$.

N-Phenyl-3-[5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-ylthio]propanamide (6a)

White amorphous solid; Yield: 85%; M.P.: 119-121°C; Molecular formula: $C_{23}H_{26}N_4O_4S_2$; Molecular weight: 486; IR (KBr, cm^{-1}) υ_{max}: 3435 (N-H stretching), 3067 (C-H stretching of aromatic ring), 2885 (CH_2 stretching), 1731 (C=O stretching), 1625 (C=N stretching), 1532 (C=C aromatic stretching), 1334 (-SO_2- stretching);^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 7.63 (d, *J* = 8.0 Hz, 2H, H-2" & H-6"), 7.49 (d, *J* = 8.0 Hz, 2H, H-2"' & H-6"'), 7.32-7-27 (m, 4H, H-3" & H-5", H-3"' & H-5"'), 7.09 (br. t, *J* = 7.6 Hz, 1H, H-4"'), 3.72-3.69 (m, 2H, H_e-2' & H_e-6'), 3.52 (t, *J* = 6.4 Hz, 2H, H-2""), 2.93 (t, *J* = 6.4 Hz, 2H, H-3""), 2.82-2.80 (m, 1H, H-4'), 2.56-2.51 (m, 2H, H_a-2' & H_a-6'), 2.42 (s, 3H, CH_3-4"), 2.12-2.09 (m, 2H, H_e-3' & H_e-5'), 2.00-1.94 (m, 2H, H_a-3' & H_a-5'); EI-MS (*m/z*): 486 $[M]^+$, 339 $[C_{14}H_{17}N_3O_3S_2]^+$, 266 $[C_{13}H_{16}NO_3S]^+$, 264 $[C_{13}H_{16}O_2N_2S]^+$, 238 $[C_{12}H_{16}NO_2S]^+$, 210 $[C_{10}H_{12}NO_3S]^+$, 155 $[C_7H_7O_2S]^+$, 148 $[C_9H_{10}NO]^+$, 120 $[C_7H_6NO]^+$, 93 $[C_6H_7N]^+$, 92 $[C_6H_6N]^+$, 91 $[C_7H_7]^+$, 65 $[C_5H_5]^+$, 51 $[C_4H_3]^+$.

N-(4-Tolyl)-3-[5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-ylthio]propanamide (6b)

Dirty white amorphous solid; Yield: 83%; M.P.: 126-128°C; Molecular formula: $C_{24}H_{28}N_4O_4S_2$; Molecular weight: 500; IR (KBr, cm^{-1}) υ_{max}: 3437 (N-H stretching), 3062 (C-H stretching of aromatic ring), 2887 (CH_2 stretching), 1731 (C=O stretching), 1623 (C=N stretching), 1532 (C=C aromatic stretching), 1331 (-SO_2- stretching), 1079; ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 7.63 (d, *J* = 8.0 Hz, 2H, H-2" & H-6"), 7.36 (br. d, *J* = 7.2 Hz, 2H, H-2"' & H-6"'), 7.31 (d, *J* = 8.0 Hz, 2H, H-3" & H-5"), 7.09 (br. d, *J* = 7.2 Hz, 2H, H-3"' & H-5"'), 3.71-3.69 (m, 2H, H_e-2' & H_e-6'), 3.53 (br. s, 2H, H-2""), 2.92 (br. s, 2H, H-3""), 2.81-2.79 (m, 1H, H-4'), 2.54-2.52 (m, 2H, H_a-2' & H_a-6'), 2.42 (s, 3H, CH_3-4"), 2.29 (s, 3H, CH_3-4"'), 2.13-2.09 (m, 2H, H_e-3' & H_e-5'), 2.07-1.94 (m, 2H, H_a-3' & H_a-5'); EI-MS (*m/z*): 500 $[M]^+$, 339 $[C_{14}H_{17}N_3O_3S_2]^+$, 266 $[C_{13}H_{16}NO_3S]^+$, 264 $[C_{13}H_{16}O_2N_2S]^+$, 238 $[C_{12}H_{16}NO_2S]^+$, 210 $[C_{10}H_{12}NO_3S]^+$, 162 $[C_{10}H_{12}NO]^+$, 155 $[C_7H_7O_2S]^+$, 134 $[C_8H_8NO]^+$, 107 $[C_7H_9N]^+$, 106 $[C_7H_8N]^+$, 91 $[C_7H_7]^+$.

N-(2,3-Dimethylphenyl)-3-[5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-ylthio]propanamide (6c)

Light pink amorphous solid; Yield: 87%; M.P.: 120-122°C; Molecular formula: $C_{25}H_{30}N_4O_4S_2$; Molecular

weight: 514; IR (KBr, cm^{-1}) υ_{max}: 3438 (N-H stretching), 3064 (C-H stretching of aromatic ring), 2888 (CH_2 stretching), 1728 (C=O stretching), 1628 (C=N stretching), 1529 (C=C aromatic stretching), 1332 (-SO_2- stretching); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 7.63 (d, *J* = 8.0 Hz, 2H, H-2" & H-6"), 7.58-7.55 (m, 1H, H-6'"), 7.31 (d, *J* = 8.0 Hz, 2H, H-3" & H-5"), 7.20-6.93 (m, 2H, H-4'" & H-5'"), 3.71-3.68 (m, 2H, H_e-2' & H_e-6'), 3.53 (t, *J* = 6.4 Hz, 2H, H-2""), 2.95 (t, *J* = 6.4 Hz, 2H, H-3""), 2.83-2.81 (m, 1H, H-4'), 2.57-2.52 (m, 2H, H_a-2' & H_a-6'), 2.42 (s, 3H, CH_3-4"), 2.26 (s, 3H, CH_3-2'"), 2.18 (s, 3H, CH_3-3'"), 2.12-2.09 (m, 2H, H_e-3' & H_e-5'), 1.97-1.94 (m, 2H, H_a-3' & H_a-5'); EI-MS (*m/z*): 514 $[M]^+$, 339 $[C_{14}H_{17}N_3O_3S_2]^+$, 266 $[C_{13}H_{16}NO_3S]^+$, 264 $[C_{13}H_{16}O_2N_2S]^+$, 238 $[C_{12}H_{16}NO_2S]^+$, 210 $[C_{10}H_{12}NO_3S]^+$, 176 $[C_{11}H_{14}NO]^+$, 155 $[C_7H_7O_2S]^+$, 148 $[C_9H_{10}NO]^+$, 121 $[C_8H_{11}N]^+$, 120 $[C_8H_{10}N]^+$, 91 $[C_7H_7]^+$.

N-(2,4-Dimethylphenyl)-3-[5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-ylthio]propanamide (6d)

Light pink amorphous solid; Yield: 79%; M.P.: 168-170 ^{o}C; Molecular formula: $C_{25}H_{30}N_4O_4S_2$; Molecular weight: 514; IR (KBr, cm^{-1}) υ_{max}: 3437 (N-H stretching), 3066 (C-H stretching of aromatic ring), 2878 (CH_2 stretching), 1724 (C=O stretching), 1638 (C=N stretching), 1532 (C=C aromatic stretching), 1341 (-SO_2- stretching); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 7.63 (d, *J* = 8.0 Hz, 2H, H-2" & H-6"), 7.58-7.55 (m, 1H, H-6'"), 7.31 (d, *J* = 8.0 Hz, 2H, H-3" & H-5"), 7.18-6.92 (m, 2H, H-3'" & H-5'",), 3.71-3.68 (m, 2H, H_e-2' & H_e-6'), 3.53 (t, *J* = 6.4 Hz, 2H, H-2""), 2.95 (t, *J* = 6.4 Hz, 2H, H-3""), 2.83-2.81 (m, 1H, H-4'), 2.57-2.52 (m, 2H, H_a-2' & H_a-6'), 2.42 (s, 3H, CH_3-4"), 2.27 (s, 3H, CH_3-2'"), 2.21 (s, 3H, CH_3-4'"), 2.12-2.09 (m, 2H, H_e-3' & H_e-5'), 1.97-1.94 (m, 2H, H_a-3' & H_a-5'); EI-MS (*m/z*): 514 $[M]^+$, 339 $[C_{14}H_{17}N_3O_3S_2]^+$, 266 $[C_{13}H_{16}NO_3S]^+$, 264 $[C_{13}H_{16}O_2N_2S]^+$, 238 $[C_{12}H_{16}NO_2S]^+$, 210 $[C_{10}H_{12}NO_3S]^+$, 176 $[C_{11}H_{14}NO]^+$, 155 $[C_7H_7O_2S]^+$, 148 $[C_9H_{10}NO]^+$, 121 $[C_8H_{11}N]^+$, 120 $[C_8H_{10}N]^+$, 91 $[C_7H_7]^+$.

N-(2,5-Dimethylphenyl)-3-[5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-ylthio]propanamide (6e)

White amorphous solid; Yield: 84%; M.P.: 134-136^{o}C; Molecular formula: $C_{25}H_{30}N_4O_4S_2$; Molecular weight: 514; IR (KBr, cm^{-1}) υ_{max}: 3434 (N-H stretching), 3066 (C-H stretching of aromatic ring), 2886 (CH_2 stretching), 1732 (C=O stretching), 1625 (C=N stretching), 1534 (C=C aromatic stretching), 1334 (-SO_2- stretching); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 7.64-7.60 (m,3H, H-2", H-6" & H-6'"), 7.31 (d, *J* = 8.0 Hz, 2H, H-3" & H-5"), 7.04 (br. d, *J* = 7.6 Hz, 1H, H-3'"), 6.87 (br. d, *J* = 7.2 Hz, 1H, H-4'"), 3.71-3.68 (m, 2H, H_e-2' & H_e-6'), 3.54 (br. s, 2H, H-2""), 2.96 (br. s, 2H, H-3""), 2.84-2.79 (m, 1H, H-4'), 2.57-2.52 (m, 2H, H_a-2' & H_a-6'), 2.42 (s, 3H, CH_3-4"), 2.29 (s, 3H, CH_3-5'"), 2.18 (s, 3H, CH_3-2'"), 2.15-2.08 (m, 2H, H_e-3' & H_e-5'), 2.05-1.94 (m, 2H, H_a-3' & H_a-5'); EI-MS (*m/z*): 514 $[M]^+$, 339 $[C_{14}H_{17}N_3O_3S_2]^+$, 266 $[C_{13}H_{16}NO_3S]^+$, 264 $[C_{13}H_{16}O_2N_2S]^+$, 238 $[C_{12}H_{16}NO_2S]^+$, 210 $[C_{10}H_{12}NO_3S]^+$, 176 $[C_{11}H_{14}NO]^+$, 155 $[C_7H_7O_2S]^+$, 148 $[C_9H_{10}NO]^+$, 121 $[C_8H_{11}N]^+$, 120 $[C_8H_{10}N]^+$, 91 $[C_7H_7]^+$.

N-(2,6-Dimethylphenyl)-3-[5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-ylthio]propanamide (6f)

Light green amorphous solid; Yield: 82%; M.P.: 137-139^{o}C; Molecular formula: $C_{25}H_{30}N_4O_4S_2$; Molecular weight: 514; IR (KBr, cm^{-1}) υ_{max}: 3450 (N-H stretching), 3062 (C-H stretching of aromatic ring), 2889 (CH_2 stretching), 1727 (C=O stretching), 1630 (C=N stretching), 1529 (C=C aromatic stretching), 1339 (-SO_2- stretching); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 7.63 (d, *J* = 8.0 Hz, 2H, H-2" & H-6"), 7.31 (d, *J* = 8.0 Hz, 2H, H-3" & H-5"), 7.10-7.05 (m, 3H, H-3'", H-4'" & H-5'"), 3.72-3.69 (m, 2H, H_e-2' & H_e-6'), 3.57 (t, *J* = 6.4 Hz, 2H, H-2""), 3.01-2.98 (m, 2H, H-3""), 2.92-2.83 (m, 1H, H-4'), 2.58-2.53 (m, 2H, H_a-2' & H_a-6'), 2.42 (s, 3H, CH_3-4"), 2.28-2.23 (m, 2H, H_e-3' & H_e-5'), 2.20 (s, 6H, CH_3-2'" & CH_3-6'"), 2.08-1.95 (m, 2H, H_a-3' & H_a-5'); EI-MS (*m/z*): 514 $[M]^+$, 339 $[C_{14}H_{17}N_3O_3S_2]^+$, 266 $[C_{13}H_{16}NO_3S]^+$, 264 $[C_{13}H_{16}O_2N_2S]^+$, 238 $[C_{12}H_{16}NO_2S]^+$, 210 $[C_{10}H_{12}NO_3S]^+$, 176 $[C_{11}H_{14}NO]^+$, 155 $[C_7H_7O_2S]^+$, 148 $[C_9H_{10}NO]^+$, 121 $[C_8H_{11}N]^+$, 120 $[C_8H_{10}N]^+$, 91 $[C_7H_7]^+$.

N-(3,4-Dimethylphenyl)-3-[5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-ylthio]propanamide (6g)

Light pink amorphous solid; Yield: 85%; M.P.: 124-126 ^{o}C; Molecular formula: $C_{25}H_{30}N_4O_4S_2$; Molecular weight: 514; IR (KBr, cm^{-1}) υ_{max}: 3438 (N-H stretching), 3065 (C-H stretching of aromatic ring), 2883 (CH_2 stretching), 1728 (C=O stretching), 1631 (C=N stretching), 1532 (C=C aromatic stretching), 1327 (-SO_2- stretching); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 7.63 (d, *J* = 8.0 Hz, 2H, H-2" & H-6"), 7.39 (br. s, 1H, H-2'"), 7.31 (d, *J* = 8.0 Hz, 2H, H-3" & H-5"), 7.18 (br. d, *J* = 7.2 Hz, 2H, H-5'"), 7.04 (br. d, *J* = 8.0 Hz, 2H, H-6'"), 3.71-3.68 (m, 2H, H_e-2' & H_e-6'), 3.51 (t, *J* = 6.4 Hz, 2H, H-2""), 2.90 (t, *J* = 6.4 Hz, 2H, H-3""), 2.79-2.86 (m, 1H, H-4'), 2.57-2.51 (m, 2H, H_a-2' & H_a-6'), 2.42 (s, 3H, CH_3-4"), 2.21 (s, 3H, CH_3-3'"), 2.19 (s, 3H, CH_3-4'"), 2.11-2.09 (m, 2H, H_e-3' & H_e-5'), 1.99-1.93 (m, 2H, H_a-3' & H_a-5'); EI-MS (*m/z*): 514 $[M]^+$, 339 $[C_{14}H_{17}N_3O_3S_2]^+$, 266 $[C_{13}H_{16}NO_3S]^+$, 264 $[C_{13}H_{16}O_2N_2S]^+$, 238 $[C_{12}H_{16}NO_2S]^+$, 210 $[C_{10}H_{12}NO_3S]^+$, 176 $[C_{11}H_{14}NO]^+$, 155 $[C_7H_7O_2S]^+$, 148 $[C_9H_{10}NO]^+$, 121 $[C_8H_{11}N]^+$, 120 $[C_8H_{10}N]^+$, 91 $[C_7H_7]^+$.

N-(3,5-Dimethylphenyl)-3-[5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-ylthio]propanamide (6h)

Light green amorphous solid; Yield: 88%; M.P.: 147-149 ^{o}C; Molecular formula: $C_{25}H_{30}N_4O_4S_2$; Molecular weight: 514; IR (KBr, cm^{-1}) υ_{max}: 3439 (N-H stretching), 3063 (C-H stretching of aromatic ring), 2889 (CH_2 stretching), 1731 (C=O stretching), 1621 (C=N stretching), 1536 (C=C aromatic stretching), 1330 (-SO_2- stretching); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 7.63 (d, *J* = 8.0 Hz, 2H, H-2" & H-6"), 7.31 (d, *J* = 8.0 Hz, 2H, H-3" & H-5"), 7.11 (s, 2H, H-2'" & H-6'"), 6.74 (s, 1H, H-4'"), 3.72-3.69

(m, 2H, H_e-2' & H_e-6'), 3.49 (t, *J* = 6.4 Hz, 2H, H-2''''), 2.91 (t, *J* = 6.4 Hz, 2H, H-3''''), 2.85-2.79 (m, 1H, H-4'), 2.57-2.51 (m, 2H, H_a-2' & H_a-6'), 2.42 (s, 3H, CH_3-4''), 2.26 (s, 6H, CH_3-3''' & CH_3-5'''), 2.12-2.09 (m, 2H, H_e-3' & H_e-5'), 1.99-1.94 (m, 2H, H_a-3' & H_a-5'); EI-MS (*m/z*): 514 $[M]^+$, 339 $[C_{14}H_{17}N_3O_3S_2]^+$, 266 $[C_{13}H_{16}NO_3S]^+$, 264 $[C_{13}H_{16}O_2N_2S]^+$, 238 $[C_{12}H_{16}NO_2S]^+$, 210 $[C_{10}H_{12}NO_3S]^+$, 176 $[C_{11}H_{14}NO]^+$, 155 $[C_7H_7O_2S]^+$, 148 $[C_9H_{10}NO]^+$, 121 $[C_8H_{11}N]^+$, 120 $[C_8H_{10}N]^+$, 91 $[C_7H_7]^+$.

N-(4-Ethylphenyl)-3-[5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-ylthio]propanamide (6i)

Pink amorphous solid; Yield: 84%; M.P.: 173-175°C; Molecular formula: $C_{25}H_{30}N_4O_4S_2$; Molecular weight: 514; IR (KBr, cm^{-1}) υ_{max}: 3437 (N-H stretching), 3063 (C-H stretching of aromatic ring), 2881 (CH_2 stretching), 1734 (C=O stretching), 1627 (C=N stretching), 1536 (C=C aromatic stretching), 1332 (-SO_2- stretching); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 7.63 (d, *J* = 8.0 Hz, 2H, H-2'' & H-6''), 7.38 (d, *J* = 8.0 Hz, 2H, H-2''' & H-6'''), 7.31 (d, *J* = 8.0 Hz, 2H, H-3'' & H-5''), 7.12 (d, *J* = 8.0 Hz, 2H, H-3''' & H-5'''), 3.71-3.68 (m, 2H, H_e-2' & H_e-6'), 3.49 (t, *J* = 6.4 Hz, 2H, H-2''''), 2.92 (t, *J* = 6.4 Hz, 2H, H-3''''), 2.85-2.79 (m, 1H, H-4'), 2.61-2.52 (m, 4H, H_a-2', H_a-6' & $CH_3\underline{CH_2}$-4''), 2.42 (s, 3H, CH_3-4''), 2.12-2.09 (m, 2H, H_e-3' & H_e-5'), 1.99-1.94 (m, 2H, H_a-3' & H_a-5'), 1.90 (t, *J* = 7.2 Hz, 3H, $\underline{CH_3}CH_2$-4'''); EI-MS (*m/z*): 514 $[M]^+$, 339 $[C_{14}H_{17}N_3O_3S_2]^+$, 266 $[C_{13}H_{16}NO_3S]^+$, 264 $[C_{13}H_{16}O_2N_2S]^+$, 238 $[C_{12}H_{16}NO_2S]^+$, 210 $[C_{10}H_{12}NO_3S]^+$, 176 $[C_{11}H_{14}NO]^+$, 155 $[C_7H_7O_2S]^+$, 148 $[C_9H_{10}NO]^+$, 121 $[C_8H_{11}N]^+$, 120 $[C_8H_{10}N]^+$, 91 $[C_7H_7]^+$.

N-(2-Ethyl-6-methylphenyl)-3-[5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-ylthio]propanamide (6j)

Brown crystalline solid; Yield: 79%; M.P.: 155-157°C; Molecular formula: $C_{26}H_{32}N_4O_4S_2$; Molecular weight: 528; IR (KBr, cm^{-1}) υ_{max}: 3435 (N-H stretching), 3068 (C-H stretching of aromatic ring), 2885 (CH_2 stretching), 1733 (C=O stretching), 1625 (C=N stretching), 1538 (C=C aromatic stretching), 1334 (-SO_2- stretching); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 7.63 (d, *J*=8.4 Hz, 2H, H-2'' & H-6''), 7.31 (d, *J* = 8.0 Hz, 2H, H-3'' & H-5''), 7.15-7.05 (m, 3H, H-3''', H-4''' & H-5'''), 3.71-3.68 (m, 2H, H_e-2' & H_e-6'), 3.56 (t, *J* = 6.4 Hz, 2H, H-2''''), 2.98 (t, *J* = 6.4 Hz, 2H, H-3''''), 2.86-2.78 (m, 1H, H-4'), 2.57-2.51 (m, 4H, H_a-2', H_a-6' & $CH_3\underline{CH_2}$-2'''), 2.42 (s, 3H, CH_3-4''), 2.19 (s, 3H, CH_3-6'''), 2.12-2.09 (m, 2H, H_e-3' & H_e-5'), 1.97-1.90 (m, 2H, H_a-3' & H_a-5'), 1.90 (t, *J* = 7.2 Hz, 3H, $\underline{CH_3}CH_2$-2'''); EI-MS (*m/z*): 528 $[M]^+$, 339 $[C_{14}H_{17}N_3O_3S_2]^+$, 266 $[C_{13}H_{16}NO_3S]^+$, 264 $[C_{13}H_{16}O_2N_2S]^+$, 238 $[C_{12}H_{16}NO_2S]^+$, 210 $[C_{10}H_{12}NO_3S]^+$, 190 $[C_{12}H_{16}NO]^+$, 162 $[C_{10}H_{12}NO]^+$, 155 $[C_7H_7O_2S]^+$, 135 $[C_9H_{13}N]^+$, 134 $[C_9H_{12}N]^+$, 91 $[C_7H_7]^+$.

N-(4-Ethoxyphenyl)-3-[5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-ylthio]propanamide (6k)

Dark brown amorphous solid; Yield: 89%; M.P.: 144-146 °C; Molecular formula: $C_{25}H_{30}N_5O_4S_2$; Molecular weight: 530; IR (KBr, cm^{-1}) υ_{max}: 3430 (N-H stretching), 3068 (C-H stretching of aromatic ring), 2890 (CH_2 stretching), 1738 (C=O stretching), 1631 (C=N stretching), 1535 (C=C aromatic stretching), 1331 (-SO_2- stretching), 1081 (C-O bond stretching); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 7.63 (d, *J* = 8.0 Hz, 2H, H-2'' & H-6''), 7.37 (d, *J* = 8.0 Hz, 2H, H-2''' & H-6'''), 7.31 (d, *J* = 8.0 Hz, 2H, H-3'' & H-5''), 6.82 (d, *J* = 8.0 Hz, 2H, H-3''' & H-5'''), 3.98 (q, *J* = 6.8 Hz, 2H, $CH_3\underline{CH_2}$O-4'''), 3.71-3.69 (m, 2H, H_e-2' & H_e-6'), 3.51 (t, *J* = 6.4 Hz, 2H, H-2''''), 2.90 (t, *J* = 6.4 Hz, 2H, H-3''''), 2.84-2.78 (m, 1H, H-4'), 2.42 (s, 3H, CH_3-4''), 2.12-2.09 (m, 2H, H_e-3' & H_e-5'), 1.99-1.91 (m, 2H, H_a-3' & H_a-5'), 1.37 (t, *J* = 6.8 Hz, 3H, $\underline{CH_3}CH_2O$-4'''); EI-MS (*m/z*): 530 $[M]^+$, 339 $[C_{14}H_{17}N_3O_3S_2]^+$, 266 $[C_{13}H_{16}NO_3S]^+$, 264 $[C_{13}H_{16}O_2N_2S]^+$, 238 $[C_{12}H_{16}NO_2S]^+$, 210 $[C_{10}H_{12}NO_3S]^+$, 155 $[C_7H_7O_2S]^+$, 192 $[C_{11}H_{14}NO_2]^+$, 164 $[C_9H_{10}NO_2]^+$, 141 $[C_8H_{11}NO]^+$, 140 $[C_8H_{10}NO]^+$.

N-Cyclohexyl-3-[5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-ylthio]propanamide (6l)

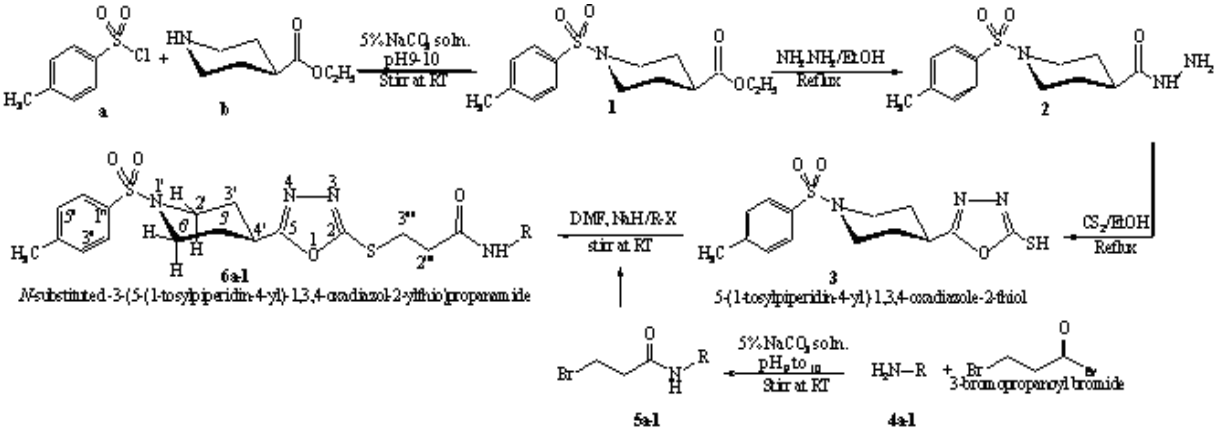
Creamy white amorphous solid; Yield: 78%; M.P.: 132-134°C; Molecular formula: $C_{23}H_{32}N_4O_4S_2$; Molecular weight: 492; IR (KBr, cm^{-1}) υ_{max}: 3439 (N-H stretching), 3062 (C-H stretching of aromatic ring), 2889 (CH_2 stretching), 1731 (C=O stretching), 1630 (C=N stretching), 1537 (C=C aromatic stretching), 1333 (-SO_2- stretching); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 7.63 (d, *J* = 8.0 Hz, 2H, H-2'' & H-6''), 7.31 (d, *J* = 8.0 Hz, 2H, H-3'' & H-5''), 3.75-3.68 (m, 3H, H-1''', H_e-2' & H_e-6'), 3.45 (t, *J* = 6.4 Hz, 2H, H-2''''), 2.88-2.74 (m, 3H, H-3'''' & H-4'), 2.57-2.52 (m, 2H, H_a-2' & H_a-6'), 2.42 (s, 3H, CH_3-4''), 2.12-2.09 (m, 2H, H_e-3' & H_e-5'), 1.97-1.87 (m, 6H, H_a-3', H_a-5', H-2'''' & H-6''''), 1.70-1.57 (m, 2H, H_e-3'''' & H_e-5''''), 1.35-1.29 (m, 2H, H_a-3'''' & H_a-5''''), 1.20-1.00 (m, 2H, H-4''''); EI-MS (*m/z*): 492 $[M]^+$, 339 $[C_{14}H_{17}N_3O_3S_2]^+$, 266 $[C_{13}H_{16}NO_3S]^+$, 264 $[C_{13}H_{16}O_2N_2S]^+$, 238 $[C_{12}H_{16}NO_2S]^+$, 210 $[C_{10}H_{12}NO_3S]^+$, 155 $[C_7H_7O_2S]^+$, 153 $[C_9H_{15}NO]^+$, 125 $[C_7H_{11}NO]^+$, 95 $[C_6H_5N]^+$, 97 $[C_6H_{11}N]^+$, 91 $[C_7H_7]^+$.

RESULTS

The goal of our research was to synthesize compounds derived from 3-[5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-ylthio]propanamide and to evaluate their antibacterial potency. A series of twelve compounds, 6a-l was synthesized according to Scheme-1. The different substituents are given in table 1.

Antibacterial activity against Gram-bacteria is presented in table-2 and table-3. Ciprofloxacin was used as standard in this study. Five bacterial strains were included in the study. Two bacterial strains were Gram-positive and three were Gram-negative. The compounds, 6b, 6g, 6h, 6i, 6j, 6k and 6l could not show strong antibacterial activity against all bacterial strains. From the tabulated data in table 2 and 3, it can also be inferred that these compounds

are not broad spectrum antibacterial agents. Compounds 6a, 6c, 6d, 6e and 6f showed excellent to moderate MIC values for all the strains under study which showed that these compounds could prove broad spectrum antibacterial agents.



Scheme 1: Synthesis of *N*-substituted-3-[5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-ylthio]propanamide (6a-l)

Table 1: Different aryl/aralky groups

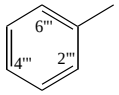
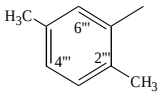
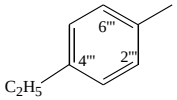
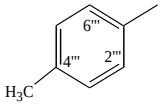
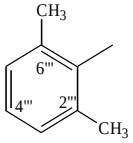
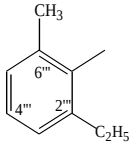
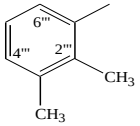
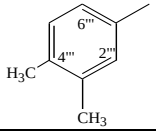
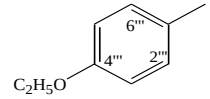
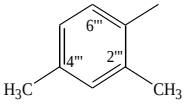
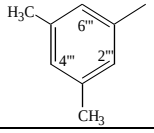
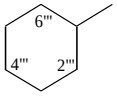
Compd.	R	Compd.	R	Compd.	R
6a		6e		6i	
6b		6f		6j	
6c		6g		6k	
6d		6h		6l	

Table 2: The % inhibition of antibacterial activity for synthesized compounds

Compounds	% Inhibition				
	S. typhi (-)	*E. coli (-)*	*B. subtilis (+)*	*S. aureus (+)*	*P. aeruginosa (-)*
6a	83.50±1.00	60.00±0.25	80.46±0.17	84.50±0.93	69.60±0.69
6b	59.57±0.76	64.20±0.49	71.38±0.68	75.50±0.35	43.00±0.67
6c	74.70±0.66	66.30±0.23	85.23±0.25	79.40±0.71	71.80±0.18
6d	71.10±0.74	69.50±0.77	88.23±0.10	82.70±0.38	80.10±0.46
6e	66.80±0.76	64.10±0.53	75.23±0.01	66.80±0.95	59.40±0.81
6f	74.00±0.59	80.60±0.17	78.08±0.15	76.10±0.63	74.60±0.07
6g	63.30±0.53	45.90±0.40	72.00±0.73	70.90±0.29	64.70±0.57
6h	60.90±0.72	49.00±0.52	80.15±0.90	79.80±0.33	75.40±0.95
6i	58.90±0.60	46.00±0.10	10.00±0.38	78.90±0.14	68.70±0.33
6j	74.00±0.97	49.00±0.35	64.62±0.15	51.30±0.45	70.50±0.78
6k	58.90±1.20	54.20±0.41	84.00±0.96	76.50±0.81	70.60±0.43
6l	49.50±0.59	59.60±0.23	68.69±0.29	72.30±0.29	64.70±0.80
Ciprofloxacin	92.86±0.70	92.67±0.52	91.63±0.15	91.47±0.10	92.34±0.35

Table 3: The MIC of antibacterial activity for synthesized compounds

Compounds	MIC				
	S. typhi (-)	*E. coli (-)*	*B. subtilis (+)*	*S. aureus (+)*	*P. aeruginosa (-)*
6a	8.76±0.45	15.87±0.90	8.43±0.36	8.49±0.25	10.38±0.50
6b	14.78±0.36	12.87±0.62	10.27±0.84	8.95±0.12	-
6c	9.54±0.95	11.96±0.52	8.17±0.72	8.38±0.31	9.78±0.30
6d	10.43±0.52	10.75±0.19	8.10±0.28	8.84±0.50	8.72±0.19
6e	12.87±0.29	12.83±0.96	8.79±0.78	11.69±0.92	15.87±0.78
6f	9.65±0.59	8.64±0.52	8.37±0.53	8.80±0.25	9.78±0.59
6g	12.65±0.70	-	9.84±0.22	10.42±0.50	12.83±0.90
6h	14.80±0.25	-	8.36±0.85	8.35±0.41	9.35±0.67
6i	17.47±0.50	-	-	8.78±0.90	10.14±0.18
6j	9.83±0.17	-	12.53±0.44	19.37±0.38	10.74±0.90
6k	16.89±0.47	17.98±0.90	8.10±0.48	9.12±0.46	10.37±0.50
6l	_	15.87±0.47	10.37±0.97	10.74±0.65	12.38±0.57
Ciprofloxacin	7.41±0.16	7.64±0.25	7.53±0.98	7.82±0.50	7.59±0.15

Note: MIC = Minimum Inhibitory Concentration

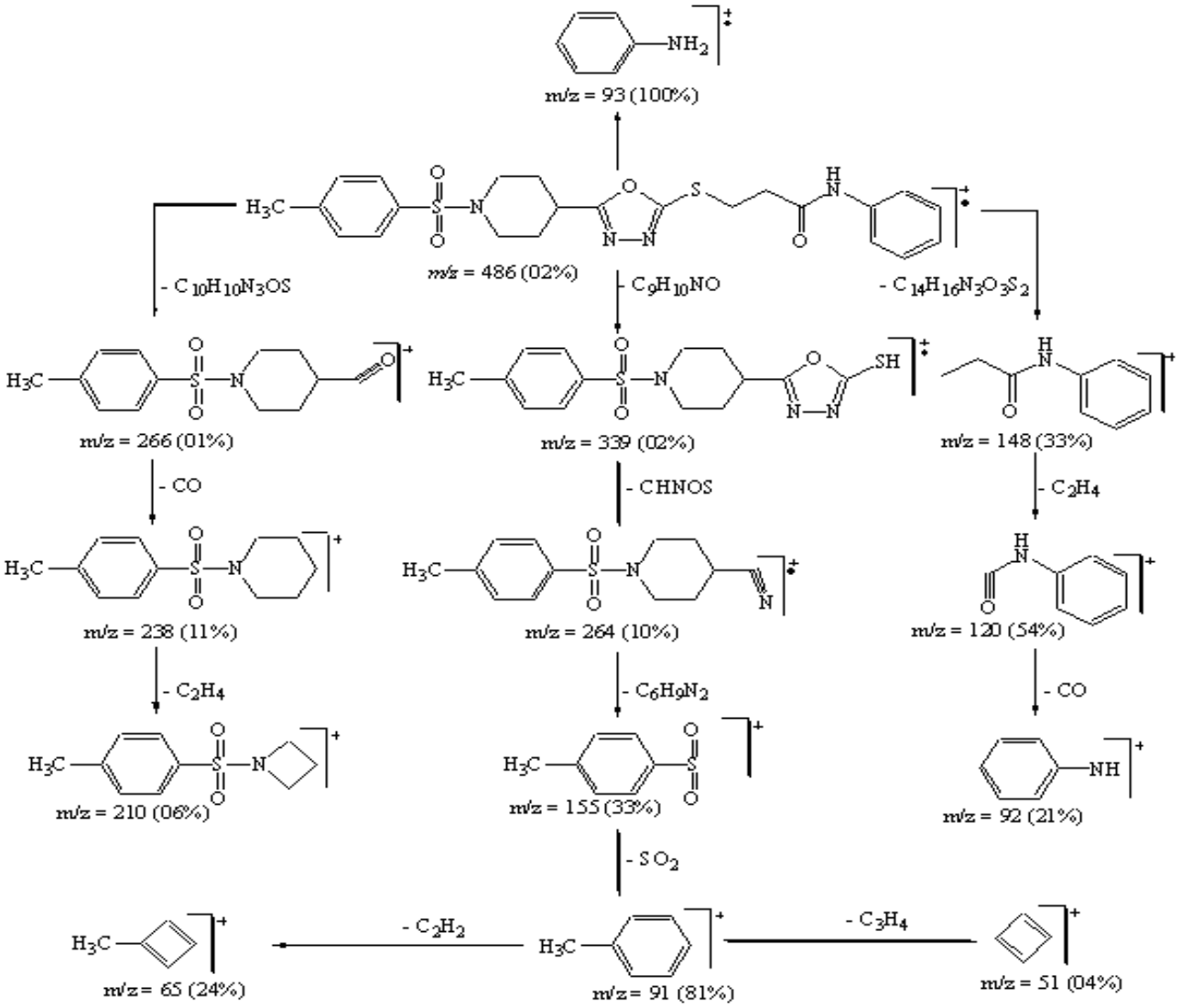


Fig. 1: Mass fragmentation pattern of 6a

DISCUSSION

The molecule 6a was synthesized as white powdered solid. The molecular formula $C_{23}H_{26}N_4O_4S_2$ was determined by molecular ion peak at *m/z* at 486 in EI-MS and by counting the number of protons in the ^{1}H-NMR spectrum. The IR spectrum demonstrated absorption peaks at 3435, 3067, 2885, 1731, 1625, 1532, 1334 cm^{-1} which were consigned to N-H stretching, C-H absorption band of aromatic ring, CH_2 absorption band, C=O absorption band, C=N absorption band, C=C aromatic absorption band and -SO_2- absorption band respectively. In EI-MS spectrum, the peak at *m/z* 339 showed the removal of *N*-phenylpropionamide group from 6a. Peak at *m*/*z* 266 showed the elimination of *N*-phenylpropionamide and partial cleavage of oxadiazole ring from 6a. Peak at *m*/*z* 155 represented the presence of tosyl group and that at *m/z* 148 showed the removal of 5-(1-tosylpiperidin-4-yl)-1,3,4-oxadiazol-2-thiol from 6a. Peaks at *m*/*z* 93 and 92 represented the presence of phenyl amine moiety and that at *m/z* 91 represented the presence of tolyl group. The other significant fragments are given in Fig. 1. In the aromatic absorption region of ^{1}H-NMR signal appeared at δ 7.63 (d, *J* = 8.0 Hz, 2H, H-2" & H-6") and 7.32-7-27 (m, 4H, H-3" & H-5", H-3"' & H-5"') indicating the para disubstituted benzene ring linked to tosyl moiety. This multiplet and the signals at 7.49 (d, *J* = 8.0 Hz, 2H, H-2"' & H-6"') and 7.09 (br. t, *J* = 7.6 Hz, 1H, H-4"') indicated the presence of phenyl moiety. The signals resonating at δ 3.72-3.69 (m, 2H, H_e-2' & H_e-6'), 2.56-2.51 (m, 2H, H_a-2' & H_a-6'), 2.12-2.09 (m, 2H, H_e-3' & H_e-5') and 2.00-1.94 (m, 2H, H_a-3' & H_a-5') were assigned to piperidine moiety. The two triplets appearing at 3.52 (t, *J* = 6.4 Hz, 2H, H-2"") and 2.93 (t, *J* = 6.4 Hz, 2H, H-3"") were assigned to two methylene groups of propionamide moiety. The singlet at δ 2.42 (s, 3H, CH_3-4") indicated the presence of methyl substituent of tosyl group. The structures of other compounds were determined similarly using EI-MS, IR and ^{1}H-NMR techniques.

Antibacterial activity

The similar compounds bearing 1,3,4-oxadiazole moiety were found to be less potent antibacterial agents (Aziz-ur-Rehman *et al.,* 2012b). The 1,3,4-oxadiazole acetamide derivatives of morpholine were found to be more potent antibacterial agents (Gul *et al.,* 2017) and that of coumarin were found to be moderately active antibacterial agents (Rasool *et al.,* 2016). The series of compounds bearing similar heterocyclic cores resulted into least antibacterial activity (Khalid *et al.,* 2012) and so phenylsulfonyl and acetamoyl moieties have been replaced in current study in the similar heterocyclic cores. The results showed that compound 6a having no substituent on phenyl group attached to nitrogen of propanamoyl moiety is potent antibacterial agents against all the bacterial strains under study except *E. coli*. The phenyl group having two methyl substituents, one of which is on position-2 could also prove to be prominent antibacterial agents. The decreased potency of 6l can be attributed to the absence of aromatic benzene ring. The results of tabulated data for the compounds 6a, 6b and 6i bearing *para* substituents infers that the increase in substituent size has negative effect on antibacterial potency. Also the increase in chain due to hetero atom has positive effect as demonstrated by more potency of 6k as compared to 6i. The most potent antibacterial agents among all studied compounds in the present work were 6c, 6d, and 6f. The elevated potency of these compounds could be attributed to phenyl group having two methyl groups at 2,3-, 2,4- or 2,6- positions, respectively.

CONCLUSION

The excellent % yield ranging from 78 to 88 indicated the ease of synthesis of derived compounds of 3-[5-(1-tosylpiperidin- 4 - y l) -1, 3, 4- oxadiazol - 2 - ylthio] propanamide. The aim of this study was to introduce new molecules with better potential and low toxicity. Bioactivity potential of these molecules has been compared with ciprofloxacin. The significant bioactive molecules 6a, 6c, 6d, 6e and 6f could be considered for drug discovery program as new drug candidates owing to their low MIC values. Therefore, these molecules can be further processed to evaluate their toxicity and reliability for use as new drug candidate. Thus new *N*-substituted derivatives of this nucleus can be synthesized to attain further low MIC values for their antibacterial potency along with other prospective biological activities.

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